The effects of age and menopause on word finding abilities in midlife and late-life women

A thesis submitted for the

PhD Degree in Human Communication Sciences

Ramya Maitreyee

Department of Human Communication Sciences

The University of Sheffield

February 2016

Abstract

Word finding difficulties are a primary concern in older adults. Particularly in women, this decline has been associated with age and lowered sex hormone levels following menopause. However, a clear understanding of menopause effects on word finding abilities remains limited in the context of age effects, which are also inconsistent. The current study investigated the effects of age and menopause on word-finding abilities in women aged 46-79 years. Seventy-eight healthy women were recruited in three age groups, 46-55, 56-65 and 70-79 years. Women in the first group were classified by menopause status (Pre-, Peri-, Post-menopause). A questionnaire was used to gather demographic information and reproductive history. A battery of tasks, consisting of verbal fluency, continuous series and verbal naming, was designed to assess specific aspects of word finding abilities. A significant effect of age was observed for picture naming latency; women aged 70-79 years had longer latencies than the younger groups. There were no significant effects of age on verbal fluency, continuous series measures and naming accuracy, although an age-related declining trend was observed. Women across menopause stages (aged 46-55 years) did not differ in their word finding abilities. Correlational results indicated that word production on letter fluency was strongly associated with switching but only in premenopausal women. Vocabulary and education were consistently correlated with word finding performance across age and menopause groups. This study replicates previous reports of age effects on picture naming and partially replicates those on verbal fluency. Lack of menopause effects fits with the lack of consistency in the literature. Absence of significant effects of age and menopause on word finding abilities is discussed in relation with neuroprotective effects of high levels of education on word finding and the cognitive reserve hypotheses (Stern, 2002).

Abstract publications

Maitreyee, R., Whiteside, S., Varley, R., & Cowell, P. (2015). Effects of age and menopause on verbal fluency, *Maturitas (The European Menopause Journal), 81*(1), 216-217. http://dx.doi.org/10.1016/j.maturitas.2015.02.337

Open Conference presentations

Maitreyee, R., Whiteside, S., Varley, R., & Cowell, P. (2015, May). Effects of age and menopause on verbal fluency. Poster presented at the 10th European Congress of Menopause and Andropause, Spain.

Maitreyee, R., Whiteside, S., Varley, R., & Cowell, P. (2013, April). Temporal production of words across the menstrual cycle. Poster presented at the Annual British Psychological Society Conference, UK.

Postgraduate conference presentations

Maitreyee, R., Whiteside, S., Varley, R., & Cowell, P. (2014, July). Effects of age and menopause on word-finding abilities. Oral presentation at Post Graduate Research Conference, Department of Human Communication Sciences, University of Sheffield, UK.

Maitreyee, R., Whiteside, S., Varley, R., & Cowell, P. (2013, July). Temporal production of words across the menstrual cycle. Oral presentation at Post Graduate Research Conference, Department of Human Communication Sciences, University of Sheffield, UK.

Maitreyee, R., Whiteside, S., Varley, R., & Cowell, P. (2012, July). Do ovarian hormones influence verbal fluency? Poster presentation at Post Graduate Research Conference, Department of Human Communication Sciences, University of Sheffield, UK.

Acknowledgements

The PhD process has been a great learning experience for me, but this would not have been possible without the support of many people. I would like to express gratitude to my supervisors, Prof Patricia Cowell (Patty), Dr Sandra Whiteside and Prof Rosemary Varley, whose expertise, understanding, and patience, added considerably to my experience and growth as a researcher. I sincerely thank Patty who steered me in the right direction, strengthened my critical and analytical skills and helped me develop as an academic researcher. Sandra, thank you for your expert opinions at all stages of my work and for being available whenever I needed you. Rosemary, many thanks for being kind enough to continue giving your feedback after having left the university.

I sincerely thank the participants of the study without whom this research would not have been possible. I would also like to thank the organizations that helped me recruit participants for my research. My heartfelt thanks to all the staff of the Department of Human Communication Sciences for their interest in my work and The University of Sheffield for providing me with a rich academic environment to study. I would also like to extend my thanks to my friends and fellow PhD students, for their constant support, help and guidance. Thank you Rafizah, Noaf, Dea, Chloe, Anna, Andrew, Tom, Baharak, Katharina, Tanja, Kim, Azrita, Elizabeth, Celia, Anne and Abebayehu. Thanks to Fiona Skilling for guiding me in using PRAAT; and Carla Rhode and Helen Cameron for proofreading sections of my work. Rachel and Jake, thank you for being so supportive at every step and throughout my stay in Sheffield.

My heartfelt thanks to my immediate family, Ma, Bapa, Soumya, Bhaina and Aniruddha. The constant support that I had from them helped me overcome all hurdles and I appreciate them from the bottom of my heart. Thank you Ramesh for all the good times. Finally, I thank Almighty God for giving me strength and courage to pursue all my endeavours.

Dedication

This thesis is dedicated to Professor Christine Temple whose renowned research in developmental neuropsychology, particularly in children with genetic disorders, has inspired many professionals.

Table of Contents

List of Tables

List of Figures

Chapter 1

Introduction

1.1. Background

Global life expectancy at birth increased between 1990 and 2015 by 6.8 years (World Health Organization, WHO, 2015). A similar trend was observed for England, with life expectancies increasing from 73.7 to 79.5 years for males and from 79.1 to 83.2 years for females born between 1991-93 and 2012-14 (Office for National Statistics, ONS, 2015 November 4). Life expectancy at older ages also increased during this period in England (ONS, 2015 November 4). Decline in fertility and mortality rates (children and older adults) possibly contributed to these drastic improvements in life expectancies around the globe (National Institute on Aging, NIA, 2011). Low fertility rates provided opportunities for improved care of children; and medical advancements in immunization, improved living standards, nutritious diets and clean drinking water reduced the occurrence of infectious and parasitic diseases, thereby, increasing the age of survival in children (NIA, 2011). Effective management of cardiovascular diseases decreased mortality rates in older adults, thus contributing to an increase in life expectancies at older ages. However, the increase in life expectancies at birth and older ages differed across sexes (ONS, 2015 November 4). As seen above, average life expectancy at birth for females in England was approximately four years higher compared to men. Similarly, a woman aged 65 years in 2012 was expected to live for a further 21.2 years, whereas for men it was 18.8 years. This trend continued even at the age of 85 years with women living a year longer than men.

Along with an increase in life expectancies, there has been a rapid growth of the ageing population in the UK (ONS, 2015 June 25). The key factors that have contributed to this growth are increased birth rate, baby boom after the world wars and in the 1960s (these cohorts are now progressing towards old age), and decreasing mortality at older ages. The median age of the population has risen from 33.9 years to 40 years over a period of 40 years (1974-2014) (ONS, 2015 June 25). Future projections also suggest that by 2035, 23% of the population will be aged 65 years and above, and 5% aged 85 years and over. Based on this epidemiologic evidence, it seems reasonable to assume that in the coming years, a considerable percentage of the population will consist of older people with higher life expectancies, and that the majority of these will be women.

Increase in life expectancy reflects societal progress and development, but a primary concern is that it is also associated with an increase in age-related disorders such as dementia of the Alzheimer's type (Bayles & Tomoeda, 2007; Brayne et al., 1995). Dementia and Alzheimer's disease (AD) was the second leading factor of death in England and Wales in 2014, and twice the number of women were affected by this disease compared to men (ONS, 2015 November 9). Evidence from the Medical Research Council Cognitive Function and Ageing Study (MRC CFAS) in the UK (Brayne et al., 1995) and from studies conducted in other countries (De Deyn, Goeman, Vervaet, Dourcy-Belle-Rose, Van Dam, & Geerts, 2011) also suggests a greater prevalence and incidence of AD in women. This increased prevalence and incidence is possibly because of longer life expectancies in women, but some researchers have also related it to estrogen deficiency following menopause (Paganini-Hill & Henderson, 1994).

At present, the percentage of people receiving a timely diagnosis for dementia in the UK varies from 40 to 70% depending on the area where the individual resides (Dowrick & Southern, 2014). A major shortcoming in the field of AD research is the unavailability of sensitive measures to diagnose the disease in its early stages. One of the primary symptoms seen in people with AD is dementia which is associated with cognitive-linguistic impairments such as deficits in episodic memory, working memory and attention, word-finding difficulties, impaired understanding of instructions, difficulty maintaining conversations and repeating ideas, inappropriate topic shifts and production of meaningless utterances (Bayles & Tomoeda, 2007; Lezak, Howeison, & Loring, 2004). Healthy older adults also often show a decline in cognitive-linguistic abilities (Salthouse, 2010; Singh-Manoux et al., 2012), but the effects of healthy ageing on cognitive decline are unclear. This in turn affects the diagnosis of dementia in the early stages. Therefore, it is essential to study the effects of age on cognitive functions in healthy adults in order to develop normative data and sensitive measures to diagnose dementia. Age-related decrements in cognitive abilities have a major impact on the life of the individual, family, society and the economy (Comas-Herrera, Wittenberg, Pickard, & Knapp, 2007; Parikh, Troyer, Maione, & Murphy, 2015), thereby providing an additional rationale to carry out investigations in this field.

Of the several cognitive difficulties experienced with advancing age, word-finding difficulties are a primary concern in healthy older adults. A vast body of literature has shown that word-finding abilities deteriorate with increasing age (Brickman et al., 2005; Connor, Spiro, Obler, & Albert, 2004; Goral, Spiro, Albert, Obler, & Connor, 2007; Gordon & Kindred, 2011; Gordon & Kurczek, 2014; Kave, Knafo, & Gilboa, 2010; Lanting, Haugard, & Crossley, 2009; MacKay, Connor, & Storandt, 2005; Rodriguez-Aranda & Martinussen, 2006; Singh-Manoux et al., 2012; Troyer, Moscovitch, & Winocur, 1997). However, this has not always been replicated and some researchers have found no significant decline in this cognitive ability with progressing age (Cruice et al., 2000; Parkin & Java, 1999; Sauzeon et al., 2011; Troyer et al., 1997).

Another aspect that remains unclear is whether word-finding abilities in older adults are affected by sex. Some researchers report that women perform better compared to men on word-finding tasks (Bolla, Lindgren, Bonaccorsy, & Bleecker, 1990; Capitani, Laiacona, & Barbarotto, 1999; Capitani, Laiacona, & Basso, 1998; Pena-Casanova et al., 2009b), whereas others suggest a better performance in men (Singh-Manoux et al., 2012; Van der Elst, Van Boxtel, Van Breukelen, & Jolles, 2006; Welch, Doineau, Johnson, & King, 1996); a number have also shown no differences between the two sexes (Brickman et al., 2005; Tombaugh & Hubley, 1997; Troyer et al., 1997). The reasons underlying these inconsistencies are poorly understood. In young adults, discrepancies in findings for sex differences in cognition have been related to the hormonal status of the women sampled (Wadnerkar, Whiteside, & Cowell, 2008 June). Drawing on the dementia literature and the above-mentioned study (Wadnerkar et al., 2008 June), it is plausible that menopause status might be a factor contributing to inconsistent sex differences in older adults. A number of psychoendocrinologists have found an association between sex hormone levels and word-finding abilities in midlife women, with performance declining postmenopause (Berent-Spillson et al., 2012; Fuh, Wang, Lee, Lu, & Juang, 2006). However, this has not been consistently reported (Fuh, Wang, Lee, Lu, & Juang, 2003; Herlitz, Thilers, & Habib, 2007; Lokken & Ferraro, 2006; Ryan et al., 2012; Thilers, MacDonald, Nilsson, & Herlitz, 2010; Weber, Rubin, & Maki, 2013). It is therefore not confirmed whether an interactive effect of age and hormonal status influences word-finding abilities in older women and could thus account for the unclear effects of sex on word-finding abilities in older adults.

Thus, keeping in view the existing gaps and inconsistencies in the literature, the current study was undertaken to examine the effects of age and menopause on word-finding abilities in midlife and late-life women aged 46-79 years. The present study investigates word-finding abilities using two frequently employed tasks in the literature, verbal fluency and verbal naming.

1.2. Organization of the thesis

The overall structure of the thesis is organized into seven chapters (Chapters 2 to 8). Chapter 2 reviews available literature and lays out the theoretical background for the research. Chapter 3 discusses the first phase of the research project, which was a data mining study examining the effects of menstrual cycle phase on verbal fluency in young healthy women. This was undertaken to determine the best procedure to analyse verbal fluency responses, which is one of the core tasks for the primary study that examines the effects of age and menopause on word-finding abilities. Chapter 4 outlines and discusses the methodology for the primary study. Details of the neuropsychological test battery, sample recruitment and testing procedure are presented in this chapter. Chapters 5, 6 and 7 describe the results of the study. Chapter 5 presents details about the demographic and reproductive characteristics of the primary study sample. Chapters 6 and 7 discuss the effects of age and menopause on verbal fluency and verbal naming, respectively. Each of these chapters provides an introduction, detailed research hypotheses and a brief account of the methodology employed, before the results are presented and discussed in relation to existing literature. The final discussion and conclusions are presented in Chapter 8, which is divided into two main sections. The first section summarises the overall findings in relation to the aims and hypotheses of the primary study. The second section focusses on examining the relationship between word-finding abilities and demographic and reproductive characteristics in a subset of women chosen from the complete data set. This chapter also discusses the limitations and future implications of the study.

Chapter 2

Literature review

2.1. Introduction

Despite preserved vocabulary knowledge (Bowles & Salthouse, 2008; Kave & Halamish, 2015; Kave & Yafe, 2014; Kemper & Sumner, 2001; Verhaegen, 2003), older adults often show a decline in word-finding abilities with age (Brickman et al., 2005; Connor et al., 2004; Goral et al., 2007; Gordon & Kindred, 2011; Gordon & Kurczek, 2014; Kave et al., 2010; Singh-Manoux et al., 2012). As discussed in Chapter 1, an additional factor that has been related to decline in this particular cognitive ability in midlife and late-life women is menopause status (Berent-Spillson et al., 2012; Fuh et al., 2006; Weber et al., 2014). The current chapter reviews available studies that have investigated the effects of age and menopause on word-finding abilities. It discusses the controversies that exist among the current studies and the factors that might contribute to the conflicting findings. The chapter also highlights the gaps in the existing evidence and the need for future investigations.

The chapter is divided into two major sections: verbal fluency (section 2.2) and verbal naming (section 2.3). Each of these sections presents details about the types of tasks used to study these cognitive abilities, as well as the administration and scoring procedures. The neural regions that support performance on these tasks are also described in this section. Finally, studies that have investigated the effects of age and menopause on these cognitive abilities are reviewed.

2.2. Verbal fluency

2.2.1. Types of verbal fluency and cognitive processes involved in verbal fluency

Verbal fluency tests form a core component of neuropsychological assessments for verbal functioning. They are often included in standardized test batteries such as the Multilingual Aphasia Examination (MAE) (Benton, Hamsher, & Sivan, 1994) and the Neurosensory Center Comprehensive Examination for Aphasia (NCCEA) (Spreen & Benton, 1977) to assess language and cognitive functioning following brain damage. Verbal fluency tests have been sensitive to changes in verbal and executive functioning associated with age (Brickman et al., 2005; Lanting et al., 2009; Pena-Casanova et al., 2009b; Singh-Manoux et al., 2012; Zimmerman, Parente, Joanette, & Fonseca, 2014; Troyer et al., 1997) and hormonal fluctuations in healthy adults (Berent-Spillson et al., 2012; Fuh et al., 2003, 2006; Hampson, 1990a, 1990b; Henderson et al., 2013; Wadnerkar et al., 2008 June). These tasks have gained popularity among researchers and clinicians because they are sensitive measures of verbal functioning and are quick and easy to administer. Common forms of verbal fluency include category and letter fluency. Category fluency (also called semantic fluency) requires participants to produce as many exemplars as possible from a semantic set such as animals, fruits, vehicles or supermarket items (Newcombe, 1969). Letter fluency (also called phonemic fluency) requires the participant to produce as many exemplars as possible starting with a particular letter such as F, A, S (Benton, 1968; Borkowski, Benton, & Spreen, 1967). Participants are generally given a stipulated time of one-minute to complete each task.

Performance on verbal fluency tests requires an intact long-term verbal-semantic memory and accessing this semantic memory by a number of executive processes such as initiation, self-monitoring, inhibition, working memory, cognitive flexibility and set-switching (Abwender, Swan, Bowermann, & Connolly, 2001; Azuma, 2004; Hirshorn & Thompson-Schill, 2006; Rende, Ramsberger, & Miyake, 2002; Troyer et al., 1997).

Although both category and letter fluency rely on all of the above-mentioned cognitive processes, there are subtle differences between the two tasks in the use of these processes. Retrieval of words on the category fluency task parallels habitual search processes (the task resembles everyday activities like organisation of shopping lists) (Azuma, 2004) and possibly relies to a greater extent on semantic memory than on executive functions. In contrast, letter fluency involves word-retrieval based on an orthographic criterion and may rely on cognitive search strategies that are generally not employed in everyday activities (Perret, 1974). It is plausible that individuals would depend largely on executive than on semantic processes involved in the task. Findings from the neural literature provide evidence in support of these possibilities by demonstrating a greater reliance on temporal and hippocampal areas (regions involved in semantic verbal memories) for category fluency, and on frontal areas (regions responsible for executive functions) for letter fluency (Baldo, Schwartz, Wilkins, & Dronkers, 2006; Birn et al., 2010; Gourovitch et al., 2000; Henry & Crawford, 2004; Tupak et al., 2012). Further, Rende, Ramsberger, and Miyake (2002) suggested that the subcomponents of working memory contribute differently to category and letter fluency performances. Their study results showed that the visuospatial sketchpad subcomponent made a key contribution to implement the visual strategies used in the category fluency task (visualizing the shelves in a supermarket), and the phonological loop played a key role in implementing the search-by-initial-letter strategy on the letter fluency task. Despite similarities between category and letter fluency, these two forms of verbal fluency can be considered dissociable and separate entities.

2.2.2. Scoring procedures for verbal fluency

The total number of correct words produced within one-minute is the most frequently used measure of verbal fluency (Benton, 1968; Brickman et al., 2005; Kemper & Sumner, 2001; Pena-Casanova et al., 2009b; Singh-Manoux et al., 2012). It has been suggested that the use of this total word score provides only a global measure of verbal ability and is not useful in distinguishing the different cognitive processes involved in verbal fluency (Fernaeus, Ostberg, Hellstrom, & Wahlund, 2008; Troyer et al., 1997). In free word recall and verbal fluency tasks, items are generated in clusters. Individuals tend to produce words from one cluster and once words are exhausted from that cluster s/he switches to the next cluster (Gruenwald & Lockhead, 1980; Wixted & Rohrer, 1994). To code this clustering aspect, Raskin, Sliwinski, and Borod (1992) introduced two variables, semantic and phonemic clusters. According to them, two consecutive words formed a semantic cluster when they belonged to the same semantic category (for example, animals in letter fluency) or subcategory (for example, farm animals or domestic animals in category fluency); and two consecutive words formed a phonemic cluster when the words had the same second phoneme or were rhymes. Raskin et al. (1992) quantified clustering using two measures: number of clusters and cluster ratio (percentage of clustered words).

Troyer, Moscovitch, and Winocur (1997) employed a similar procedure as Raskin et al. (1992) but had a more detailed set of rules to classify phonemic clusters. For category fluency (animals), the authors described subcategories (farm animals, water animals), and two or more words from a subcategory formed a cluster (farm animals: cow, goat). For letter fluency, two or more words formed a cluster when they were rhymes (sit, spit), differed by a vowel (sip, sap), had the same first two letters (sat, sank) or were homonyms (sun, son). In contrast to Raskin et al. (1992), who measured semantic and phonemic clusters for both the verbal fluency tasks, Troyer et al. (1997) focussed on using only task-consistent clustering measures (semantic clusters for category fluency and phonemic clusters for letter fluency). Troyer et al. (1997) also used an additional measure called switches which they defined as the transition from one cluster (either semantic or phonemic cluster) to another, including single words. For example, if an individual produced the following sequence of words, "(sip, sap) (sink, since), student" (words in parentheses represent clusters), then according to this scoring procedure the total number of switches produced would be two. The transitions from cluster one to cluster two, and from cluster two to the single word would be the two switches. Troyer et al. (1997) used the mean cluster size and the number of switches as measures of clustering and switching, respectively.

Further work in this area was carried out by Abwender, Swan, Bowermann, and Connolly (2001) and Lanting, Haugrud, and Crossley (2009). Abwender et al. (2001) used measures to quantify clustering and switching. Like Raskin et al. (1992), this group of researchers coded both task-consistent (phonemic clusters for letter fluency) and task-discrepant (phonemic clusters for category fluency) clusters. As opposed to Troyer et al.'s (1997) single measure of switching, Abwender et al. (2001) suggested the use of hard and cluster switch measures. They defined a hard switch as a shift between two single words (sail, sun) or a shift from a group of clustered words to a single word (sand, sang/ swim), and a cluster switch was defined as a shift between two groups of clustered words (sand, sang/swim, swan). Abwender et al. (2001) used cluster ratio (as used by Raskin, Sliwinski, & Borod, 1992), mean cluster size (as used by Troyer et al., 1997) and number of cluster words to quantify clustering, and number of hard and cluster switches to quantify switching. Lanting et al. (2009) used both Abwender et al.'s (2001) and Troyer et al.'s (1997) scoring procedures to investigate word-retrieval patterns in verbal fluency. In addition, they also measured the number of novel and repeated clusters and percentage of single and clustered words.

Thus, it is evident that the analysis of verbal fluency responses has shifted from the unitary total word count to a more multifaceted concept including an in-depth analysis of the two major components, clustering and switching. Troyer et al. (1997) suggested that clustering was a measure of verbal memory and semantic-lexical knowledge, whereas switching was related to executive functions such as cognitive flexibility and set shifting. Thus, these scoring procedures have enabled researchers to examine cognitive strategy use in verbal fluency and infer about the underlying cognitive processes. Although these procedures were a step forward in examining cognitive strategy use in verbal fluency, each of them had strengths and limitations. Raskin et al.'s (1992) method had a good inter-rater reliability for coding clusters but did not include any measure to quantify switching. Troyer et al.'s (1997) method had clear scoring instructions and good inter-rater reliabilities for both clusters and switches (Abwender et al., 2001; Troyer et al., 1997; Wadnerkar et al., 2008 June). Also, it had been reliably used in examining the effects of age (Lanting et al., 2009; Sauzeon et al., 2011; Troyer et al., 1997) and sex (Lanting et al., 2009; Wadnerkar et al., 2008 June; Weiss et al., 2003, 2006) on cognitive strategy use in healthy adults, and to differentiate clinical population from healthy controls (Gomez and White, 2006; Haugrud, Crossley, & Vrbancic, 2011; Troyer, Moscovitch, Winocur, Alexander, & Stuss, 1998a; Troyer, Moscovitch, Winocur, Leach, & Freedman, 1998b; Zhao, Guo, & Hong, 2013). However, a caveat of Troyer et al.'s (1997) scoring procedure was the method used to compute mean cluster size (Abwender et al., 2001). Troyer et al. (1997) calculated cluster size starting from the second word in a cluster. A cluster of two words was given a cluster size of one and single words were given a cluster size of zero. For example, if an individual produced '(sip, sap)', then the mean cluster size would be 1. Similarly, if another individual produced 'student, (sin, sincere, sip, sit), (sun, sum), (sat, sang), (soil, sole), stand', the cluster sizes would be 0, 3, 1, 1, 1 and 0 and the mean cluster size would be 1. Thus, it is evident that the inclusion of single words in calculation of mean cluster size might limit this procedure in efficiently distinguishing between individuals varying in performance levels. Abwender et al.'s (2001) and Lanting et al.'s (2009) scoring procedures were more detailed but were more time-consuming and cumbersome than the other procedures. Abwender et al.'s (2001) procedure also had a low inter-rater reliability for coding semantic clusters.

All the above-mentioned scoring procedures placed emphasis on coding semantic clusters either for both the tasks (Abwender et al., 2001; Raskin et al., 1992) or for only the category fluency task (Troyer et al., 1997). The applicability of semantic clusters may be problematic as it is difficult to determine the rules an individual employs in semantic clustering. For example, one participant may consider cow, cat and goat as pets, but another participant may not consider cow as a pet. Therefore, the coding of semantic clusters may differ across researchers, which would result in poor inter-rater reliability, and thereby limit its applicability in research and clinical contexts. Of the above-mentioned procedures proposed till date, Troyer et al.'s (1997) scoring technique is the most comprehensive and feasible procedure to analyse verbal fluency responses, especially in healthy older adults (the target population for the current study). Slight modifications in the scoring guidelines as adopted by Wadnerkar et al. (2008 June) (see Chapter 3 for details) could render it useful in examining the effects of age and menopause on strategy use in verbal fluency in older populations.

The above section discussed the use of clusters and switches as alternative methods to gain a deeper understanding of the cognitive processes that support verbal fluency performance. Apart from these procedures, researchers have also adopted different paradigms to analyse response patterns on verbal fluency tasks. Two more approaches that have been used include the temporal (Fernaeus et al., 2008; Sauzeon et al., 2011) and psycholinguistic methods (Forbes-McKay, Ellis, Shanks, & Venneri, 2005; Foster et al., 2008; Temple, 2002). Details on these methods are discussed in Chapter 3 of the thesis.

2.2.3. Neural correlates of verbal fluency

Advancement in technology (magnetic resonance imaging, positron emission tomography) has provided neuroscientists with an avenue to examine the neural regions that support performance on cognitive tasks such as verbal fluency. Results from these studies have enabled researchers to supplement and strengthen behavioural findings and formulate hypotheses for future work. The remainder of this section presents information about the different brain areas that are activated when performing the verbal fluency task. The effects of age and sex hormone fluctuations on these areas and their subsequent consequences on behavioural performance are discussed in sections 2.2.3 and 2.2.4, respectively.

For verbal fluency, existing evidence from neuroimaging studies suggests that overall brain activations are greater in the left than in the right hemisphere, and the major cortical areas of activation are located in the frontal and the temporal cortex (Birn et al., 2010; Fu et al., 2002; Kircher, Nagels, Kirner-veselinovic, & Krach, 2011; Nagels, Kircher, Dietsche, Backes, Marquetand, & Krug, 2012; Tupak et al., 2012; Whitney et al., 2009). Birn et al. (2010), who conducted an fMRI study, found increased activations in the left inferior frontal gyrus (IFG), the left middle frontal gyrus (MFG), the supplementary motor area (SMA), the left fusiform gyrus and the left superior parietal lobule in fluency tasks compared to automatic speech. The subcortical regions that were recruited during task performance included the brain stem, the substantia niagra, the left caudate and thalamus. Whitney et al. (2009) additionally showed activations in the anterior cingulate cortex (ACC) and concluded that the prefrontal-cingulate network played a central role in verbal fluency performance.

Evidence from the neural literature in healthy adults and in persons with brain damage suggests that there are some commonalities in brain areas that support performance on category and letter fluency tasks but subtle differences are also seen. A greater left lateralization (Tupak et al., 2012) and increased activations in the hippocampus (Gourovitch et al., 2000), left fusiform and left MFG (Birn et al., 2010) are observed for category fluency compared to letter fluency. In contrast, there are greater activations in the left premotor and left IFG during letter fluency performance (Birn et al., 2010). The left IFG is one of the major regions involved in verbal fluency, and Costafreda et al. (2006), who systematically reviewed data from 17 studies, suggested that the ventral part of the left IFG played a key role in category fluency and the dorsal part in letter fluency.

Another strand of research that has supplemented the study of neural correlates of verbal fluency is lesion studies. Category fluency is affected to a greater degree than letter fluency in patients with temporal and non-frontal lesions, whereas letter fluency is affected to a greater extent in patients with frontal lesions (Baldo et al., 2006; Henry & Crawford, 2004; Miceli, Caltagirone, Gainotti, Masullo, & Silveri, 1981; Monsch et al., 1997; Newcombe, 1969). However, findings from lesion studies remain mixed, as some investigators have reported that category and letter fluency are equally affected in patients with damage to either the frontal (Baldo & Shimamura, 1998; Schwartz & Baldo, 2001) or the temporal lobe (Loring, Meador, & Lee, 1994; Martin, Loring, Meador, & Lee, 1990).

The exact roles of the above-mentioned regions are not clear, but each of these areas has been associated with cognitive process/es that support performance on verbal fluency tasks. It is consistently reported that the frontal regions support working memory and executive demands of the task (Birn et al., 2010; Weiss et al., 2003). The superior parietal lobule and the ventral temporal regions are suggested to subserve strategic lexical and semantic search involved in the task (Birn et al., 2010). The role of the ACC remains controversial. Weiss et al. (2003) proposed that the ACC helps in word selection, error monitoring and goal directed behaviours, whereas Whitney et al.

(2009) opined that the left ACC does not underpin word selection per se but acts as a modulatory system that works in conjunction with the frontal areas and adapts to required task demands. The right anterior insula is thought to be supporting the ventral premotor area in verbal selection and in coordinating motor aspects of word generation; and the cerebellum has a general involvement in most of the cognitive functions involved in the task such as memory, language and attention (Rapoport, van Reekum, & Mayberg, 2000). The caudate, putamen support articulatory production and thalamus contributes to articulation, motor sequencing and language processing (Fu et al., 2002).

Researchers have also investigated the neural correlates of clustering and switching. Findings from behavioural, lesion and electrophysiological studies suggest a temporal cortex involvement in clustering and a frontal cortex involvement in switching (Gomez & White, 2006; Hirshorn & Thompson-Schill, 2006; Troyer et al., 1997; Troyer et al., 1998a). Thus, it can be summarised that verbal fluency involves a number of cognitive processes and recruits a large neural network for efficient performance on this task. Deficits in any of the cognitive process/es or degradation of the neural region/s because of healthy ageing or brain injury may result in deficits in behavioural performance. The next section reviews studies that have examined the effects of age on category and letter fluency. It also discusses the explanations that have been put forward to justify the presence or absence of age-related deficits in verbal fluency.

2.2.4. Effects of age on verbal fluency

Reports indicate a specific pattern of change in verbal fluency with advancing age. There is consistent evidence that older adults generate fewer exemplars than younger adults do in category fluency (Brickman et al., 2005; Kemper & Sumner, 2001; Knight, McMahon, Green, & Skeaff, 2006; Parkin & Java, 1999; Pena-Casanova et al., 2009b; Singh-Manoux et al., 2012; Troyer et al., 1997; Van der Elst et al., 2006). On the other hand, results for letter fluency remain uncertain. Some studies have found a significant age-related decline (Brickman et al., 2005; Gladsjo et al., 1999; Gordon & Kindred, 2011; Lanting et al., 2009; Pena-Casanova et al., 2009b; Ruff, Light, & Parker, 1996; Singh-Manoux et al., 2012; Steiner, Mansur, Brucki, & Nitrini, 2008; Tombaugh, Kozak, & Rees, 1999; Van der Elst et al., 2006; Zimmermann, Parente, Joanette, & Fonseca, 2014), while others show little or no change (Parkin & Java, 1999; Kemper & Sumner, 2001; Sauzeon et al., 2011; Schmitter-Edgecombe, Vesneski, & Jones, 2000; Troyer et al., 1997). In a meta-analytic review of 26 studies, Rodriguez-Aranda and Martinussen (2006) reported that letter fluency declined in later life. They analysed the data from participants aged 20 to 80 years and showed small but significant effects of age when one age decade was compared to the other (20-29 vs 30-39, 30-39 vs 40-49 and so on). Based on the analyses of their complete data set, the authors concluded that the ability to generate words on the letter fluency task declined after the age of 60 years and the rate of this decline increased after the age of 80 years.

Thus, existing literature suggests that category fluency may be more sensitive to the effects of age than letter fluency. Discrepancies in findings across studies for letter fluency may arise due to a number of reasons such as differences in sample population characteristics (such as gender, IQ, education, health status, ethnicity), sample sizes, age groups that are compared and statistical analyses of the data (Rodriguez-Aranda & Martinussen, 2006). A detailed critical analysis of the methodological differences between cross-sectional studies to which these discrepancies can be attributed is presented in Chapters 4 and 5.

Few researchers have also investigated the factors that contribute to age-related deficits in verbal fluency. Behavioural studies have researched this aspect by employing measures of word clustering and switching as proposed by Troyer et al. (1997) and time course analyses (Lanting et al., 2009; Mayr & Kliegl, 2000; Troyer et al., 1997; Sauzeon et al., 2011). Neuroimaging studies have examined this dimension by studying differences in neural activation patterns between young and old adults when performing the verbal fluency task (Meinzer et al., 2009; Nagels et al., 2012).

An age-related decline in category fluency has been associated with deficits in the switching component (Lanting et al., 2009; Troyer et al., 1997), but results for letter fluency remain uncertain. Troyer et al. (1997) showed no differences in switching ability on the letter fluency task across age groups, but Lanting et al. (2009) found that older adults produced fewer switches than younger adults did. One possible factor that could have contributed to these results is educational differences between the age groups in both the studies. Older participants had 13.2 years of mean education in both the studies. However, younger participants in Lanting et al.'s (2009) study had higher education (mean years of education: 16.1 years) than those in Troyer et al.'s study (1997) (mean years of education: 14.4 years). It is consistently reported that more years of education is associated with greater word production on verbal fluency tasks (Brickman et al., 2005; Elkadi et al., 2006; Gladsjo et al., 1999; Goral et al., 2007; Tombaugh et al., 1999; Van der Elst et al., 2006). Troyer et al. (1997) also suggested that the total number of words produced is strongly correlated with the number of switches on the letter task. The difference in years of education between the age groups was greater in Lanting et al.'s (2009) study than in Troyer et al.'s (1997). Therefore, it is plausible that the significant age effect may have been confounded with the effects of education in Lanting et al.'s (2009) study.

Similar to Lanting et al. (2009), Sauzeon et al. (2011) also found a decrease in the switching component in older adults for category and letter fluency. However, they suggested that this age-related decrease was time-dependent. Sauzeon et al. (2011) used a combination of Troyer et al.'s (1997) scoring procedure and a time course approach to analyse word-retrieval patterns. They divided the one-minute fluency responses into two equal time frames of 30 second each (T1, T2) and calculated the total number of words, number of switches and mean cluster size for each time frame. For category and letter fluency, their results showed that younger and older adults did not differ on any of the variables measured for the complete one-minute duration. However, Sauzeon et al. (2011) found that the older adults produced fewer words than younger adults in T1, and more words than younger adults in T2, irrespective of fluency type. Older adults also produced fewer switches than younger adults in T1 for both category and letter fluency, indicating that a decline in switching contributed to fewer word production in T1 in older adults. Additionally, they found that the mean cluster size was larger in older adults in T2 but only for letter fluency. This letter fluency mean cluster size in T2 was positively associated with vocabulary and negatively with processing speed measures, although these associations were not significant when controlled for age. However, age was not associated with the mean cluster size. Based on these findings, Sauzeon et al. (2011) concluded that age-related decline in processing speed in the second half of the letter fluency task was compensated by increased vocabulary levels in older adults, and this possibly masked the effects of age on the letter fluency task. Although there was a decline in the number of switches in T1 in category fluency task, there was no compensatory increase in the mean cluster size in T2. It is plausible that the participants used alternative compensatory mechanisms (other than vocabulary) to maintain their performance throughout the complete duration of the task. These results also explain why some studies do not find an effect of age on verbal fluency.

Mayr and Kliegl (2000) used a different temporal approach to explore the factors contributing to age-related decline in category fluency. They assumed that demands on the semantic processes involved in verbal fluency differs based on the recall position of the word (demands increase for words retrieved later), whereas demands on executive functions remain constant after every retrieval. Based on these assumptions they measured the inter-response interval, that is the time gap between words using a fluency task. Although Mayr and Kliegl (2000) used a different procedure to analyse word-retrieval patterns, their results were in support with previous reports. They found that a decline in non-semantic processes contributed to age-related decline in category fluency.

Decline in verbal fluency with increasing age could also be explained using the general cognitive ageing theories. According to the resource theory, it can be hypothesized that insufficient cognitive resources (working memory, attention, inhibition and processing speed) in older adults may account for a decrease in word production on verbal fluency tasks (Craik & Byrd, 1982). Alternatively, according to the processing speed theory (Salthouse, 1996), a general slowing of the component cognitive processes could result in fewer word production by older adults in the limited time duration.

As mentioned earlier, neuroimaging techniques have also been employed to investigate the factors underlying these deficits in older adults. For category fluency, it is reported that younger and older adults differ in their frontal activations (Meinzer et al., 2009; Nagels et al., 2012). A left lateralization is seen in younger adults, whereas in older adults a bilateral pattern of activation is observed. However, the role of this over-recruitment of bilateral frontal areas remains controversial. Meinzer et al. (2009) found increased activity in the right inferior and middle frontal regions in older adults, Also, these additional activations were negatively correlated with performance, indicating that greater frontal activations did not compensate for age-related decline in category fluency. On the other hand, Nagels et al. (2012) found that as age increased, activations in bilateral IFG and left ACC increased, and age was not significantly related to behavioural performance. Therefore, Nagels et al. (2012) opined that over-recruitment of these areas facilitated performance in older adults. Methodological differences between the two studies might have contributed to different findings. Firstly, younger and older participants in Meinzer et al.'s (2009) study were not matched in their behavioural performance. Therefore, we cannot be sure whether the negative association between total words and frontal activations was due to performance level or an effect of age. Secondly, Meinzer et al. (2009) compared two age groups (20-33 vs 64-88 years) and Nagels et al. (2012) considered age as a continuous variable (22-56 years). Their older adults were younger compared to the older participants in Meinzer et al.'s (2009) study, and therefore the findings may not be directly comparable.

In contrast, for letter fluency, no differences in neural activations have been found between young and old adults. Both age groups show a left lateralization and recruit similar areas in the left and right hemisphere when retrieving words on the letter fluency task (Abrahams et al., 2003; Meinzer et al., 2009). Thus, differences in brain activation patterns of neural regions supporting executive processes could be a factor contributing to age-related changes in category fluency. Furthermore, these findings support why age-related declines are evident for category but not letter fluency.

2.2.5. Sex differences in verbal fluency

Sex differences have been reported in a number of cognitive behaviours (see Miller & Halpern, 2014). It has been shown that males tend to outperform females on spatial tasks (Hyde, 2014; Linn & Petersen, 1985; Maccoby & Jacklin, 1974; Roberts & Bell, 2002; Voyer, Voyer, & Bryden, 1995), mathematical abilities and scientific reasoning (Wai, Cacchio, Putallaz, & Makel, 2010). In contrast, females perform better on tasks of fine motor skills and verbal abilities such as verbal fluency, articulation, reading, perceptual speed and accuracy (Halpern, 1992; Hyde & Linn, 1988; Kimura, 1999; Kimura & Hampson, 1994). Although a number of studies have found a sex difference in these cognitive abilities, the literature on these effects in adults remains uncertain. With particular reference to verbal fluency in adults, some studies have found a female advantage (Bolla et al., 1990; Capitani et al., 1998, 1999; Halari et al., 2005;

Pena-Casanova et al., 2009b; Weiss et al., 2003, 2006), some a male advantage (Singh-Manoux et al., 2012; Van der Elst et al., 2006) and few others have shown no differences between the sexes (Brickman et al., 2005; Tombaugh et al., 1999; Troyer et al., 1997). A clear understanding of the factors that contribute to such discrepancies has not been established, but a key factor that could be associated with such differences is hormonal status of the women sampled. Wadnerkar et al. (2008 June) investigated sex differences in verbal fluency considering the hormonal status of women in a group of young adults. They found that sex-related trends are heightened when younger women in the higher hormone states are compared to men than when women in the low hormone states are compared to men. These results indicate that sex hormone levels affect verbal fluency in young women. Women experience a major biological change in their midlife years, that is menopause, which is associated with lowered sex hormone levels. If sex hormones facilitate verbal fluency, it may be hypothesized that sex differences in older adults would also differ based on the hormonal status of women. Differences might be evident when older women having high hormone levels (premenopause) are compared to men, but the difference may not significant when women having low hormone levels (postmenopause) are compared to men. To the researchers' knowledge, there are no studies which have explored this aspect. It is also not known whether these variations in hormonal status of the women interacts with age and contributes to inconsistent effects of age on letter fluency.

The existing studies suggest that verbal fluency is affected by age and sex, but the interactive effect of these variables on this cognitive ability is under-researched. There is no consensus in findings across studies that have investigated this in detail. For example, Capitani et al. (1998) found a significant age-related decline in letter fluency in males but not in females. On the other hand, percentage change in scores in Singh-Manoux et al.'s study (2012) indicated a greater age-related decline in category and letter fluency for females. Thus, there is a need to establish the role of sex on word-finding performance in cognitive ageing studies and to study age-related trends on verbal fluency separately for men and women. The current study examines the effects of age on word-finding abilities only in women across a wide age range, 46-79 years. As discussed, an additional factor that needs consideration when examining word-finding abilities in midlife and late-life women is their menopause status and sex hormone levels. The next section (section 2.2.5) reviews literature on the effects of menopause status on verbal fluency. Before discussing this topic in detail, the relationship between hormones and cognitive behaviour across the life span is discussed in order to provide a theoretical background on how hormonal fluctuations could influence verbal fluency. Finally, the studies that have investigated the effects of hormone fluctuations during menopause on verbal fluency are reviewed.

2.2.6. Effects of sex hormone fluctuations during menopause on verbal fluency

2.2.6.1. Sex hormones and cognitive behaviour

The role of sex-steroids, especially estrogens, has been extensively studied in relation to cognitive functions in women (Berent-Spillson et al., 2012; Boss, Kang, Marcus, & Bergstrom, 2014; Hampson, 1990a, 1990b; Henderson & Popat, 2011; Hogervorst, 2013; Ryan et al., 2012; Wadnerkar et al., 2008 June). Estradiol, a form of estrogen, is primarily synthesized in the ovaries, but is also produced in bone, adipose and nervous tissues. It acts on the brain either through classical estrogen receptors (ERs) such as ERα, ERβ or membrane-associated non-classical ERs such as G protein coupled ER, Gαq protein coupled membrane ER (Arevalo, Azcoitia, & Garcia-Segura, 2015; McEwen, 2002; Micevych & Dominguez, 2009; Toran-Allerand, 2005). The estrogen receptors are widely distributed across a number of cortical and subcortical areas such as the cerebral cortex, prefrontal cortex, hippocampus, amygdala, hypothalamus, pituitary, cerebellum, midbrain and brain stem (Guyton & Hall, 2011; Sherwin, 2003, 2006; Sherwin & Henry, 2008; Shughrue & Merchenthaler, 2000; Wang, Hara, Janssen, Rapp, & Morrison, 2010). It is reported that in human females, among the cortical areas, the prefrontal cortex is the major site for estrogen action and estradiol concentration in this area is greater than in the temporal cortex and the hippocampus (Bixo, Backstrom, Winbald, & Anderson, 1995).

Estrogen mediates its neuroprotective effects on cognitive functions by either permanent or transient structural modifications, changes in neurotransmitter functioning or physiological changes in the areas that support the particular cognitive ability. Evidence for structural changes is mostly derived from studies conducted in rodents and nonhuman primates using the ovariectomy model. Animals are ovariectomized in order to mimic the menopause state (low hormone state) seen in humans. There is a decrease in dendritic spine density in the prefrontal cortex and CA1 region of the hippocampus when female rats are ovariectomized (Wallace, Luine, Arellanos, & Frankfurt, 2006). In addition, there is a decline in cognitive functions mediated by the frontal cortex and hippocampus following surgery, indicating an association between morphological alterations and cognitive functions. Treatment studies in ovariectomized rhesus monkeys have found that estrogen supplementation increases dendritic spine density of layer III pyramidal neurons in area 46 and Sp-I spines of layer I in area 46 (Hao et al., 2006; Tang et al., 2004).

Along with alterations in the structural morphology, estrogen also influences the action of neurotransmitters such as catecholaminergic, serotonergic, cholinergic and γ-aminobutyric acid (McEwen, 2002; Sherwin & Henry, 2008). The current study utilizes various word-finding tasks that rely on frontally mediated cognitive functions. Therefore, the actions of estrogen on catecholamines such as dopamine and norepinephrine are of interest to the present research as these neurotransmitters play an important role in modulating the working memory and attentional functions of the frontal cortex (Arnsten, 1997). Estrogen acts as a modulator and maintains the levels of catecholamines, thus, enabling adequate functioning of frontally-mediated cognitive behaviours. Like catecholamines, cholinergic neurotransmitters such as acetylcholine also affect memory, especially verbal memory. Estrogen helps in the production of choline acetyltransferase, an enzyme that synthesizes acetylcholine (Luine, 1985) and thus helps maintain verbal memory in healthy individuals.

The effects of estrogen on brain activities in human females have been investigated using the menstrual and menopause paradigms (*see* Maki & Resnick, 2001, *for a review*). These paradigms were used in combination with a range of functional neuroimaging studies. Studies employing the menstrual paradigm have found differences in brain activities across the menstrual cycle (Reiman, Armstrong, Matt, & Mattox, 1996a) and a general increase in brain activity with increasing estradiol levels (Dietrich et al., 2001). It is also reported that women at the follicular phase show reduced functional cerebral asymmetries compared to the menstrual phase when performing word-matching tasks (Weis et al., 2008). Evidence for estrogen action on brain activity in older women has been gathered from hormone treatment studies. It is reported that postmenopausal women show increased frontal lobe activity for verbal, spatial working memory and word-retrieval tasks following estrogen treatment (Dumas, Kutz, Naylor, Johnson, & Newhouse, 2010; Joffe et al., 2006; Shaywitz et al., 1999; Smith et al., 2006), and decreased activity in the left prefrontal cortex, ACC and MFG following hormonal suppression (Craig et al., 2007). The above reviewed literature suggests that high levels of estrogen contribute to morphological and physiological changes in the frontal cortex and hippocampus which in turn influence cognitive behaviours.

Estrogen fluctuations across the life span result in either permanent or transient changes in the brain structures and functions, which in turn give rise to sex differences in cognitive behaviours. Permanent changes in the brain structures or functions occurring during the early stages of life are termed as *organizational effects* of sex hormones. Transient changes occurring at a later stage, that is, during puberty, menstrual cycles, pregnancy and menopause, are called *activational effects* (Berenbaum, 1998; Berenbaum & Beltz, 2011; Berenbaum, Blakemore, & Bertz, 2011). The next section discusses the organizational and activational effects of sex hormones on word-finding abilities, with a major focus on activational effects during menstrual cycles and menopause.

Organizational effects

The levels of testosterone rise in the male foetus between 8 and 24 weeks of gestation prenatally and postnatally between 1 and 6 months (Smail, Reyes, Winter, & Faiman, 1981 as cited in Hines, 2003). These testosterone exposures assist in the development of masculine behaviours (such as rough play, aggression, good spatial abilities) and inhibition of female-typical behaviours (such as better verbal abilities and fine motor skills). However, if a female foetus is exposed to high levels of androgens during these critical periods, affected females exhibit male-type behaviours.

Evidence for effects of these early hormone exposures on cognition have been obtained from studies conducted in individuals in whom sex hormone levels are affected in the prenatal period. These include studies in individuals with congenital adrenal hyperplasia (CAH), children born to mothers with polycystic ovarian syndrome (PCOS) and Turners syndrome (TS). CAH occurs in both males and females. Due to genetic defects, girls with CAH have difficulties synthesizing cortisol due to 21-hydroxylase deficiency (White & Speiser, 2000). This raises the levels of adrenocorticotrophic hormone (ACTH) and androgens, leading to expression of male-type characteristics in girls with CAH. Girls with CAH excel on tasks of spatial abilities such as card rotation, mental rotation and hidden patterns compared to their sisters

(Berenbaum et al., 2011; Hampson & Rovet, 2015; Hampson, Rovet & Altmann, 1998; Resnick, Berenbaum, Gottesman, & Bouchard, 1986). Along with differences in cognitive behaviours, they also exhibit male-type characteristics on visualization, personality and sexuality (see review Auyeung, Lombardo, & Baron-Cohen, 2013). Males with CAH generally display male-typical behaviours as their age matched peers (Berenbaum et al., 2011). PCOS is an endocrine disorder and is commonly seen in females. There is an excessive exposure to androgens in the prenatal months (Norman, Dewailly, Legro, & Hichey, 2007). Like girls with CAH, girls born to mothers with PCOS show better spatial abilities than healthy age-matched females (Barry, Parekh, & Hardiman, 2013).

In TS, the second X chromosome is either absent or abnormal (Ford, Jones, Polini, de Almeida, & Briggs, 1959). The ovaries develop normally but they involute prematurely during gestation (Singh & Carr, 1966). As a result, girls with TS are exposed to low levels of estrogen from birth and there is a disruption in pubertal changes (Park, Bailey, & Cowell, 1983). Girls with TS have vocabulary knowledge equivalent to their age-matched peers, but they generate fewer words on tasks of verbal fluency tasks (Temple, 2002; Temple & Shepherd, 2012). This decline in verbal fluency has been associated with deficits in the switching component of the task (Temple, 2002), which is possibly due to reduced estrogen levels in girls with TS.

Thus, it can be summarized that females who are exposed to high levels of androgens in the early stages of development excel in cognitive behaviours for which a male-advantage has been reported (as in CAH and children born from mothers having PCOS). On the other hand, decreased exposure to estrogen in females results in suppression of female advantage on cognitive behaviours such as verbal fluency and articulation (as in TS).

Activational effects

Fluctuations in hormone levels across the life span also influence human behaviours and are termed as activational effects (Berenbaum, 1998). For example, differences in performance on verbal or spatial tasks across different phases of the menstrual cycle (menstrual, periovulatory, midluteal) or menopause (pre, peri and postmenopause) provide evidence for activational effects of sex hormones on cognitive abilities. The current study focusses on menstrual cycle and menopause-related effects on word-finding abilities in young (see Chapter 3) and older (Chapters 4-8) women, respectively. The remaining part of the section discusses these two aspects in detail.

Menstrual cycle

A regular menstrual cycle in human females ranges between 23 and 35 days. Based on hormonal fluctuations, endocrinologists have divided the menstrual cycle into four phases namely: menstrual, periovulatory, midluteal and premenstrual phases (Impey & Child, 2012). During the menstrual phase, the levels of ovarian hormones, estrogen and progesterone remain low, followed by an increase only in the level of estrogen in the periovulatory phase. Estrogen and progesterone levels are high in the midluteal phase and gradually decline in the premenstrual phase. Results from behavioural studies in young healthy women have shown that women in the high hormone phases of the menstrual cycle produce more words on verbal fluency tasks than women in the low hormone phase (Hampson, 1990a; Maki, Rich, & Rosenbaum, 2002; Wadnerkar et al., 2008 June). Although most studies indicate that high estrogen levels are associated with improved verbal fluency, conflicting results of no relationship between the two have also been found (Gordon & Lee, 1993). A detailed review on the effects of hormonal fluctuation during regular menstrual cycles on verbal fluency is presented in Chapter 3.

Menopause stages

Menopause refers to the permanent cessation of menstruation for 12 or more consecutive months. Natural menopause occurs with the cessation of follicular activity in the ovaries, whereas induced menopause results from the cessation of ovarian function following surgery or radiation therapy for cancer (World Health Organisation, 1996). Women who undergo natural menopause begin experiencing menopausal symptoms from the age of 45 years, an average. The Stage of Reproductive Aging Workshop (STRAW +10) (Harlow et al., 2012) system classifies women into three major groups based on reproductive aging: reproductive, menopausal transition and postmenopause. Women in the reproductive stages are otherwise referred to as premenopausal (from puberty to menopause transition). Premenopausal women have regular menstrual cycles, but there may be subtle changes in blood flow and length with increase in age. Menopausal transition refers to the period from the beginning of variability in the menstrual cycle to the final menstrual period (FMP). The primary clinical symptom reported at this stage is irregularity in the menstrual cycles. According to STRAW+10, the menopausal transition is divided into early and late phases. Women in the early stages experience a delay of greater than 7 days between two consecutive cycles and women in the late stages have a delay or amenorrhea of greater than 60 days. Postmenopause refers to the period from the FMP, for the remaining lifespan. Postmenopausal women are also classified into two stages depending on the time since menopause: early (zero to six years postmenopause) and late postmenopause (greater than six years postmenopause).

A change in hormone levels, including gonadotropins (follicle stimulating hormone: FSH; luteinizing hormone: LH), gonadal steroids (estrogen, progesterone, testosterone), peptides (inhibins A and B) and anti-Mullerian hormone (AMH) is seen during the different stages of menopause (Burger, Dudley, Robertson, & Dennerstein, 2002; Burger, Hale, Robertson, & Dennerstein, 2007). FSH and LH levels increase during perimenopause and remain at high levels postmenopause. The levels of inhibin B decline as FSH levels increase in the perimenopause stage. At postmenopause, estrogen levels decrease by 50% of the concentration seen premenopause but levels of testosterone remain unaffected (Burger et al., 2002).

This decrease in the level of estrogen has been associated with cognitive changes experienced during menopause transition and postmenopause (Hogervorst, 2013). Psychoendocrinologists have investigated the effects of menopause on a number of cognitive behaviours such as spatial ability, verbal memory (immediate and delayed), executive functions, working memory and processing speed (Barrett-Connor & Goodman-Gruen, 1999; den Heijer et al., 2003; Drake et al., 2000; Fuh et al., 2006; Henderson, Dudley, Guthrie, Burger, & Dennerstein, 2003; Herlitz et al., 2007; Kok et al., 2006; Luetters et al., 2007; Ryan et al., 2012; Weber et al., 2013). Despite some progress in this field, the primary focus has been on episodic memory and research on word-finding abilities remains fragmented and limited. Therefore, the current study examines the effects of menopause on word-finding abilities using the verbal fluency and verbal naming tasks. The next section reviews available studies that have investigated the effects of changing level of sex hormones during menopause on verbal fluency and menopause-related effects on naming are discussed in section 2.3.5.

2.2.6.2. Effects of sex hormone fluctuations in menopause on verbal fluency

Menopause-related effects on verbal fluency have been studied using both cross-sectional and longitudinal-research designs. Findings from cross-sectional studies are mixed. It is reported that women across stages of menopause do not differ in category fluency (Fuh et al., 2003; Lokken & Ferraro, 2006; Weber et al., 2013; Weber, Maki, & McDermott, 2014). In contrast, premenopausal women produce more words than peri and postmenopausal women on the letter fluency task (Berent-Spillson et al., 2012, controlled for age), although contradictory reports of no significant differences across menopause stages have also been published (Herlitz et al., 2007; Lokken & Ferraro, 2006; Weber et al., 2013). Berent-Spillson et al. (2012), who found a significant effect of menopause stage on letter fluency, further strengthened their results by demonstrating a positive relationship between the total number words produced and estrogen levels. Additionally, they found greater activations in the bilateral inferior frontal cortex, the left prefrontal cortex and the left temporal pole in postmenopausal women, and these activations were negatively associated with estradiol and positively with FSH levels. These results indicate that as hormone levels decrease following menopause, word production in letter fluency decreases. Also, postmenopausal women show greater frontal and temporal activations during task performance, although it cannot be clearly established whether these additional activations have a compensatory or inhibitory effect. Although Berent-Spillson et al. (2012) found a positive association between estradiol and verbal fluency, the other studies which also measured hormone levels did not find a significant association between estrogen and verbal fluency performance (Herlitz et al., 2007; Weber et al., 2013), again adding to inconsistencies across the literature.

Likewise, in longitudinal research, results for the effects of menopause stage on verbal fluency are not consistent. Two studies which followed women transitioning from pre to peri or postmenopause stages found declines in category (Fuh et al., 2006; Thilers et al., 2010) and letter (Thilers et al., 2010) fluency. Fuh et al.'s (2006) longitudinal data showed that premenopausal women who transitioned from pre to perimenopause in an interval of 18 months generated 1.3 items fewer on the second testing session. In another longitudinal study, Laughlin et al. (2010) examined verbal fluency performance of postmenopausal women two times in a span of four years. Their findings showed that women who had high levels of endogenous estrogen at baseline worsened in category fluency after four years, but postmenopausal women with low levels of estrogen at baseline did not. These above-mentioned studies indicate that lowered estrogen levels post menopause have deleterious effects on verbal fluency. However, Ryan et al. (2012) did not find a significant association between estrogen levels and category fluency in postmenopausal women, but their data showed a weak positive association with testosterone to estradiol ratio.

Thus, cross-sectional findings suggest that category fluency is not affected by menopause stage, but results for letter fluency remain inconsistent. Differences in findings for letter fluency might have arisen because of variations in sample population characteristics, menopause stage groupings, sample sizes and test materials used. A detailed critical analysis is presented in Chapter 4. Weber, Maki, and McDermott (2014), who conducted a meta-analysis of cross-sectional studies, concluded that only letter fluency deteriorated in the postmenopause stage compared to perimenopausal women. It is well known that age at menopause for women living in the developing countries differs from those living in the developed countries (Castelo-Branco et al., 2006; Gold, 2011; McCarthy, 1994; Samil & Wishnuwardhani, 1994; Wasti et al., 1993). Differences in reproductive characteristics across women can also differentially affect cognitive outcomes in late life. All the three studies included in Weber et al.'s (2014) meta-analysis were conducted in the USA. Therefore, the findings of the meta-analysis are only applicable to these populations and cannot be generalized to all women. Results from longitudinal research on the effects of menopause on category and letter fluency also remain inconclusive. Of the above-mentioned longitudinal studies, only one study examined menopause effects on letter fluency (Thilers et al., 2010) and the remaining three used a category task (Fuh et al., 2006; Laughlin et al., 2010; Ryan et al., 2012). Differences in results between Fuh et al.'s (2006) and Ryan et al.'s (2012) studies may be due to differences in research designs. Fuh et al. (2006) followed up women from the pre to perimenopause stage, whereas Ryan et al. (2012) examined the association between estrogen levels and verbal fluency performance only in postmenopausal women. The current review reflects the paucity of cross-sectional and longitudinal research that have investigated the effects of menopause status or reduced estrogen levels post menopause on verbal fluency, indicating the need for future studies.

Another strand of research that provides evidence for the relationships between estrogen level and cognitive functions in midlife women are hormone treatment studies. Until 2004, the effects of hormone supplementation in arresting cognitive decline and dementia in postmenopausal women remained conflicting. Results from case-control (Henderson, Paganini-Hill, Emanuel, Dunn, & Buckwalter, 1994; Waring et al., 1999) and prospective studies (Jacobs et al., 1998; Kawas et al., 1997; Tang et al., 1996) suggested a positive benefit of hormone therapy on cognitive functions, but evidence from observational (Barret-Connor & Kritz-Silverstein, 1993; Matthews, Cauley, Yaffe, & Zmuda, 1999) and clinical trials (Henderson et al., 2000; Mulnard et al., 2000; Wang et al., 2000) found no beneficial effects of treatment. In order to resolve these inconsistencies, a large controlled long-term randomised clinical trial, the Women's Health Initiative Memory Study (WHIMS), was initiated in the USA in 1998 (Shumaker et al., 1998). This clinical trial examined the effects of hormone therapy on dementia and the results indicated that estrogen therapy in combination with progestin was associated with increased risk for probable dementia in postmenopausal women aged 65 years and older (Shumaker et al., 2003; Shumaker et al., 2004). The outcomes of the study raised concerns about the use of hormone therapy in postmenopausal women. Although it was one of the largest clinical trials carried out in this area, it had some limitations. One of the most compelling justifications that were provided for the failure of the WHIMS to show a positive benefit of hormone treatment on cognition was the age of the participants. Women in the study were too old when the treatment was initiated. Therefore, the results cannot be generalized to the younger population (aged less than 65 years) when hormone therapy is generally initiated (Connelly, Richardson, & Platt, 2000). Additionally, women in the treatment group also had a higher prevalence of hypertension compared to women in the control group. Hypertension has been associated with cognitive decline (Albert et al., 2009; Brady, Spiro III, & Gaziano, 2005) and therefore, it cannot be confirmed that the emergence of dementia was an effect of hormone treatment per se. Maki (2006) reviewed basic science, observational and randomized clinical trial studies conducted in women in the menopausal transition and suggested that hormone therapy may have a positive effect on cognition, especially verbal memory in the early stages of menopausal transition. A recent meta-analysis from the Cochrane database involving 42,830 women concluded that hormone therapy should not be prescribed to older postmenopausal women, in order to delay cognitive decline or to reduce the risk of dementia as seen in AD (Marjoribanks, Farquhar, Roberts, & Lethaby, 2012). However, there were not enough studies to make conclusive statements on the effects of hormone therapy on cognition in younger women (aged less than 65 years).

With particular reference to verbal fluency, the effects of hormone therapy on this cognitive ability remain unconfirmed. Mixed findings have been reported in younger postmenopausal women. Some researchers have found that women taking hormone replacement therapy perform better than non-users on verbal fluency tasks (Kugaya et al., 2003), whilst others have reported no significant differences between users and non-users (Dunkin et al., 2005; Kocoska-Maras et al., 2011; Maki, Gast, Vieweg, Burriss, & Yaffe, 2007; Wolf, Heinrich, Hanstein, & Kirschbaum, 2005). Moreover, Grady et al. (2002) showed that non-users performed better than the treatment group. Dis-concordance among studies and no consensus among researchers may arise due to a number of factors such as differences in the type of hormone therapy prescribed, mode of administration, dosage and treatment duration. Heterogeneity among women may also contribute to discrepant findings across studies. Women across studies may differ in their reproductive characteristics such as age at menopause, type of menopause, prior use of hormone based medications and fertility status, which in turn may affect the outcomes of the studies (see Chapter 5 for details). Although the benefits of hormone replacement therapy on verbal fluency in young postmenopausal women remains unclear, most of the studies conducted in older women report no significant effects of hormone replacement therapy on verbal fluency (Almeida et al., 2006; Lethaby, Hogervorst, Richards, Yesufu, & Yaffe, 2008; Resnick et al., 2006, 2009; Pefanco et al., 2007; Viscoli et al., 2005; Yaffe et al., 2006). A meta-analytic review by Henderson & Popat (2011) concluded that there were no significant effects of estrogen treatment on verbal fluency in both younger (45-55 years) and older (>65 years) postmenopausal women.

Thus, the relationship between estrogen and verbal fluency in midlife and late-life women remains unclear. Current findings, from studies that have compared young women across menopause stages and treatment studies, indicate that there may be a positive relationship between estrogen levels and verbal fluency in younger postmenopausal women. However, majority of the research in older women suggest no relationship between the two. These results reflect that the effects of sex hormone levels on cognition may be age-dependent. Researchers who have investigated this dimension in relation with hormone therapy suggest that estrogen treatment has a neuroprotective effect on cognition only when treatment is administered closer to the time of menopause (Gibbs, 2010; Maki, 2006; Resnick & Henderson, 2002; Sherwin, 2005, 2007, 2012; Sherwin & Henry, 2008). These findings gave rise to the critical period hypothesis and support for this comes from basic neuroscience, animal and human studies. Estrogen replacement therapy increases the dendritic synaptic density in the hippocampus in young ovariectomized rats, but not in old rats (Adams, Shah, Janssen, & Morrison, 2001). It is also seen that hormonal treatment is more effective in increasing synaptic density when initiated closer to the time of ovariectomy (Gibbs, 2000; Silva, Mello, Freymuller, Haider, & Baracat, 2003). Further, Daniel, Hulst, & Berbling (2006) found that 12 to 17 month old rats improved in their working memory performance when treatment was initiated immediately after ovariectomy than if it was delayed by five months. Similar, improvements in spatial working memory have also been found in nonhuman primates such as rhesus monkey (Lacreuse, Wilson, & Herndon, 2002; Rapp, Morrison, & Roberts, 2003). Research in humans also indicates improvement in cognitive functions and reduced risk of AD when treatment is initiated in the menopausal transition and closer to the time of menopause (Gibbs, 2010; Matthews, Cauley, Yaffe, & Zmuda, 1999; Zandi et al., 2002). There is prolonged absence to the exposure of sex hormones in longer-term menopausal women. This makes the neurons less responsive to estrogen treatment, thereby giving rise to a critical period wherein the neuroprotective effects of estrogen on cognition are observed (Sherwin & Henry, 2008).

Thus, evidence from exogenous hormone supplementation studies indicates that there may be a critical period when hormone treatment is effective. However, not many researchers have investigated whether cognitive functions differ based on time since menopause. The two studies that examined this aspect concluded that women across postmenopause stages (recent versus longer-term) do not differ in verbal fluency performance (Elsabagh, Hartley, & File, 2007: Henderson et al., 2013).

2.3. Verbal naming

2.3.1. Types of verbal naming tasks and cognitive processes involved in verbal naming

Naming refers to the appropriate selection and production of the target word with ease and accuracy (Lezak et al., 2004). This cognitive ability can be tested through visual (picture naming) or auditory (naming-to-auditory-definitions) modalities. The most frequently used format in everyday clinical assessments is the picture naming test where the test stimuli consists of pictures of common objects (Boston Naming Test, BNT, Kaplan, Goodglass, & Weintraub, 1983) or action verbs (Action Naming Test, ANT, Obler & Albert, 1979). Participants are shown a line drawing of an object and are instructed to say the most suitable or common name for it. If a participant is unable to name it, the examiner provides a semantic or phonemic cue to aid retrieval. Standardized tests such as the BNT (Kaplan et al., 1983) or the Graded Naming Test (GNT) (McKenna & Warrington, 1980) comprise of target words graded according to difficulty levels. Easier items appear in the beginning of the list and the most difficult ones are tested at the end. Researchers have also developed sets of picture stimuli of target words varying in their lexical characteristics such as name agreement, image agreement, familiarity and visual complexity (Snodgrass & Vanderwart, 1980).

Alternatively, verbal naming can also be examined using the naming-to-auditory-definitions task, which requires listening to a definition and retrieving the word that best fits the definition. This task has primarily been used in the neuropsychological literature to investigate the tip of the tongue (TOT) phenomenon in healthy adults (Brown & McNeill, 1966; Burke, MacKay, Worthley, & Wade, 1991; Harley & Bown, 1998), naming deficits in temporal lobe epilepsy patients (Bell, Seidenberg, Hermann, & Douville, 2003; Hamberger, Goodman, Perrine, & Tamny, 2001; Hamberger & Seidel, 2003; Hamberger, Seidel, Goodman, Perrine, & McKhann, 2003; Hamberger &

Tamny, 1999) and modality-specific naming deficits in patients with aphasia (Druks & Shallice, 2000). Stimulus items on naming to definitions tasks are classified either based on word types such as abstract nouns, object names, adjectives and verbs, place names and famous people (Burke et al., 1991) or lexical factors such as frequency and neighbourhood density (Harley & Bown, 1998). Compared to picture naming, the naming-to-definition task has been infrequently used in the cognitive ageing literature. The auditory naming task is representative of everyday discourse and Hamberger and Siedel (2003) found that performance on this task, but not on picture naming, was correlated with subjective complaints of word-finding difficulties. Therefore, this task can be considered an ecologically valid measure of naming and as such, it could be helpful to be more frequently used in neuropsychological assessments of naming abilities. The current study makes use of both the formats in order to obtain a comprehensive profile of naming abilities in midlife and late-life women.

Efficient word-retrieval in picture naming is dependent on a number of processes such as sensory-perceptual processing, activation of conceptual-semantic information, lexical access and articulatory movements (Burke & Graham, 2012; Dell, Schwartz, Martin, Saffran, & Gagnon, 1997; Levelt et al., 1991; Levelt, Roelofs, & Meyer, 1999). Similarly, naming-to-auditory-definitions also involve similar cognitive processes as picture naming, but there are differences between the two. The naming-to-auditory-definitions task relies on input from the auditory modality, whereas in picture naming a visual stimulus triggers word production. Retrieving words on the naming-to-auditory-definitions task may place greater demands on working memory because the individual needs to remember the complete definition to retrieve the target word. On the other hand, picture naming may depend on working memory to a lesser extent because of the availability of the stimulus item all through the response period. The naming-to-auditory-definitions task also involves sentence processing, a complex cognitive ability, which is not the case in picture naming.

2.3.2. Scoring procedures for verbal naming

The number of total correct responses given by the participant is the most commonly used measure on naming tests. Some researchers have also used latency times (Gordon & Kindred, 2011; Gordon & Kurczek, 2014; Mortensen, Meyer, & Humphreys, 2006; Thomas, Fozard, & Waugh, 1977; Tsang & Lee, 2003) and error types as measures of naming performance (Dell et al., 1997; Levelt et al., 1999). One of the prominent error classificatory systems was given by Dell, Schwartz, Martin, Saffran, and Gagnon (1997) which was based on an interactive model of word production proposed by them. The current study employs this system to classify errors on the picture naming task. Prior to discussing the error types, the model is briefly outlined to have a clear understanding of different stages of word-retrieval and to determine the source of the error.

The model proposes that interaction between three layers, a semantic, word (also called the lemma) and a phoneme layer, results in word production. The semantic layer contains conceptual information, the lemma layer represents information about the grammatical structure and the phoneme layer contains information about the phonemes and phonological frame of the pictured object. The authors assume that each object has 10 units in the semantic layer and these units are connected to the word layer by excitatory bidirectional connections. When an individual sees a picture, all the 10 units in the semantic layer are equally activated. There is both top-down and bottom-up processing and lemma and phoneme selections receive a positive feedback. The semantic layer receives feedback from the word layer and the word layer from the phonological layer. During lemma access, both semantic and phonological neighbours of the target word are activated and this step of retrieval concludes by selection of the most highly activated noun in a picture naming task. The next step involves the phonological access and the selected lemma receives maximum activation than its competitors. Neighbouring words other than the target word may be activated at this stage due to the presence of bidirectional connections. Finally, the most highly activated phonemes are selected and placed in the phonological frame. According to this model, there is only one phonological frame, single-syllable consonant-vowel-consonant (cvc) words. Thus, the most activated onset consonant, vowel and coda are selected and the word phonemes are placed in the phonological frame. Each phoneme receives activation, and it is then translated to the correct articulatory code. The target word is then finally produced. The model assumes that there are no inhibitory connections and the strength of the connection is determined by learning and recent exposure with the target words.

Error at any stage of retrieval can contribute to word-finding difficulties. Dell et al. (1997) classified errors into five types: semantic, formal, mixed semantic and formal, unrelated word errors, and non-words or neologisms. A *semantic error* occurs when words that share conceptual semantic information are produced (mop for broom). These errors are due to lemma access deficits. A *form related error* (tomb for broom) occurs due to deficit in lemma or phonological access. If it occurs due to an error in lemma access, then the incorrect response produced follows the same grammatical category as that of the intended word. However, if this is not the case, then the form-related error is due to a deficit in phonological access. For example, in a picture naming task, if a participant produces 'tomb' for 'broom' then it is a form-related error due to a deficit in lexical access as both the words have the same phonological frame and belong to the same syntactic category (noun). On the other hand, if an individual produces 'whom' for 'broom', then it is an error due to inaccurate phonological access as the words have the same phonological frame, but differ on the grammatical category. The third category of errors consists of *mixed semantic and formal errors*, for example producing 'brush' for 'broom'. The fourth category compromises of *unrelated errors*, for example producing 'crush' for 'broom'. These errors occur due to difficulties at the lemma level. 'Crush' is a distant relation of 'brush' and 'brush' is semantically related to 'broom'. Therefore, it is possible that during activation of the word 'broom', the word 'crush' would have been incorrectly selected, thus resulting in a naming error. An unrelated error could also result because of an error only in phonological access, or because of faulty programming at both levels. The last type of errors as explained by Dell et al.'s (1997) model was *non-words or neologisms* (producing 'brog' for 'broom'). These errors mostly arise due to deficits in phonological access. Classifying errors has been found useful to determine the level at which the naming deficit occurs.

2.3.3. Neural correlates of verbal naming

Picture naming, like verbal fluency, activates a large neural network and is primarily dependent on left hemisphere regions (Abrahams et al., 2003; Baldo, Arevalo, Patterson, & Dronkers, 2013; Indefrey & Levelt, 2000, 2004). It activates more regions in the left hemisphere than in the right (Indefrey, 2011; Indefrey & Levelt, 2000), and each of these regions supports a cognitive process that underlies picture naming performance. The areas of activation in the left hemisphere include the posterior inferior frontal gyrus, ventral precentral gyrus, supplementary motor area, mid and posterior superior and middle temporal gyri, posterior temporal fusiform gyrus, anterior insula, thalamus, and medial cerebellum. In the right hemisphere, activations are seen in the mid superior temporal gyrus, medial and lateral cerebellum, and supplementary motor area. As described earlier, picture naming involves a number of cognitive processes such as conceptual preparation, lexical selection, lexical retrieval, phonological processing and articulation. The left middle temporal gyrus has been associated with the conceptual preparation and the lexical selection stages of naming. The left anterior insula, Wernicke's area and the right supplementary motor area (SMA) support lexical word form retrieval and the inferior frontal gyrus (that is, BA 44, Broca's area) has been related to phonological processing and syllabification. The articulation processes are primarily regulated by the left precentral gyrus, left thalamus and cerebellum, and the bilateral superior temporal gyri supports self-monitoring of responses (Indefrey & Levelt, 2000).

Like picture naming, naming-to-auditory-definitions also recruit a large neural network. Evidence for the neural regions involved in auditory naming has mostly been obtained from studies conducted in patients with temporal lobe epilepsy. Naming-to-auditory-definitions deficits have a greater sensitivity than picture naming deficits to distinguish patients with left temporal lobe lesions from healthy controls (Bell et al., 2003; Hamberger & Seidel, 2003; Hamberger & Tamny, 1999), indicating a greater contribution of this region for efficient performance on this task. Findings from lesion studies also suggest that different parts of the temporal lobe contribute differentially to performance on picture naming and naming-to-auditory-definitions tasks. The posterior lobe is found to be involved in both the tasks, but the anterior temporal lobe supports performance only on the naming-to-auditory-definitions task (Hamberger et al., 2001; Messas, Mansur, & Castro, 2008).

In summary, the two frequently used formats to test naming abilities include picture naming and naming-to-auditory-definitions. Accuracy is the most common measure of verbal naming, although the latency measure has also received some attention. Performance on these tasks involves semantic and executive processes and requires activation of a large neural network in the brain. Deficits in any of these processes or atrophy or lesions to the brain areas supporting naming performance can affect this cognitive ability. The next section discusses the effects of age on verbal naming.

2.3.4. Effects of age on verbal naming

Older adults often complain of difficulties recalling names of objects and an increase in TOT frequency. These subjective reports of age-related naming deficits have been substantiated by objective neuropsychological test results that indicate an age-related decline in naming ability.

Kave et al. (2010) found that picture naming ability across the lifespan fits both a linear and a curvilinear quadratic model. The linear model suggests a general pattern of increase in the scores from childhood and the curvilinear model indicates that this increase in the early years is followed by a late life fall. The majority of experimental studies have shown that picture naming accuracy declines with advancing age (Albert, Heller, & Milberg, 1988; Bowles, Obler, & Albert, 1987; Feyereisen, 1997; Goral et al., 2007; Gordon & Kurczek, 2014; Gordon & Kindred, 2011; LaBarge, Edwards, & Knesevich, 1986; MacKay, Connor, Albert, & Obler, 2002; Neils et al., 1995; Tsang & Lee, 2003; Van Gorp, Satz, Kiersch, & Henry, 1986; Welch et al., 1996; Worrall, Yiu, Hickson, & Barnett, 1995; Zec, Markwell, Burkett, & Larsen, 2005). However, there are studies which do not support this view. A few researchers have found no significant differences between younger and older adults (Cruice, Worrall, & Hickson, 2000; Wierenga et al., 2008), and a small number of literature sources provide evidence that older adults perform better than younger adults do (Brown & Nix, 1996; Schmitter-Edgecombe et al., 2000).

Along with inconsistencies for the effects of age on naming abilities, another aspect that remains controversial in this field is the age at which the decline begins. Feyereisen (1997) in a meta-analytic review of 11 studies concluded that age-related decline in picture naming is seen only after the age of 70 years. Similar findings have also been reported by several other researchers (Albert et al., 1988; Van Gorp et al., 1986; Welch et al., 1996; Zec et al., 2005). In contrast, researchers from the Cambridge

Centre for Ageing and Neuroscience (Cam-Can, 2010, June) have shown that picture naming accuracy declined with increase in age across the whole period (20-100 years).

A second measure that has been used to quantify picture naming ability is the latency time. In one of the earliest studies, Thomas, Fozard, and Waugh (1977) compared the mean latency scores from 60 healthy males in the age range of 25-74 years. As expected, their results showed that older adults took longer to give accurate responses than younger adults. In order to determine the factors contributing to increased latency times in older adults, Thomas et al. (1977) measured naming latencies in primed and un-primed conditions and by repeating the same task again. These various alternations decreased the age effect but did not entirely eliminate it and therefore, led the authors to conclude that age effects in naming latency are a consequence of slowing of lexical access, perceptual and motor processes. Similar findings of longer response latencies in older adults have also been reported by many others (Mortensen et al., 2006; Tsang & Lee, 2003). However, Gordon & Kindred (2011) found no significant effects of age on picture naming latency.

Discrepant age-related findings across studies may arise due to differences in several factors such as sample population characteristics (see Chapter 5 for details), tests used, scoring procedures and statistical analyses (Goulet, Ska, & Kahn, 1994) (see Chapter 4 for detailed discussion on these factors). An alternative factor that could contribute to nonsignificant findings is the small size of decrement in naming with advancing age (Connor et al., 2004; Zec et al., 2005). A decline of only two percentage points per decade was observed by Connor et al. (2004) and therefore, studies with small sample sizes may have insufficient power to detect significant effects. Moreover, differences in research designs (cross-sectional versus longitudinal) may also lead to discrepancies. For example, Cruice et al. (2000) examined naming ability using both cross-sectional and longitudinal designs. They found a small significant association between age and naming accuracy only in the cross-sectional study. Longitudinal studies that examine the effects of age on naming ability are susceptible to practice effects. Participants become familiar with the items and shorter duration between repeated assessments may contribute to practice effects, thus masking possible age-related decrease in the scores. Differences in familiarity with items could also attribute to discrepancies in results. Schmitter-Edgecombe, Vesneski, and Jones (2000) examined picture naming ability across three age groups (young, 18-22 years; young-old, 58-74 years; old-old, 75-93 years). Their study failed to show the expected age-related decline in naming and found that the two older groups obtained higher scores than the youngest age group, controlled for the effects of education. The BNT was published in 1983, and therefore older adults were more familiar with four items on the task (yoke, trellis, palette and abacus) than the younger adults. This in turn contributed to higher accuracy scores in the older groups.

The current study utilized an additional task, naming-to-auditory-definitions, to investigate naming abilities. In the cognitive ageing literature, this task has mostly been used to examine TOT errors. Burke, MacKay, Worthley, and Wade (1991) compared young and old participants on a naming-to-definitions task using 100 low-frequency stimuli which were classified into five categories (abstract nouns, object names, adjectives and verbs, place names, famous people). They recorded the number of “know”, “don’t know” and “TOT” responses produced. Their results showed that older adults experienced more TOTs than younger adults for names of famous people, indicating greater word-retrieval difficulties in older adults for specific word categories. Similar findings of increase in TOT frequency with advancing age has also been reported by other researchers (see Mortensen et al., 2006).

In summary, the existing literature suggests a decline in naming accuracy (although results for picture naming accuracy remain inconsistent) and an increase in latency with increase in age. A number of explanations and theories have been proposed to identify the factors that contribute to naming deficits in older adults. Differences in the use of underlying cognitive processes and brain activations have been related to these deficits. The remaining part of this section discusses this in detail.

The Cattell-Horn theory (Cattell, 1971; Horn & Cattell, 1967), one of the most influential models of intelligence, classifies intelligence as crystallised (Gc) and fluid (Gf) intelligence. According to this theory, vocabulary knowledge is considered as an example of crystallised ability, whereas cognitive functions such as reasoning, concept formation and problem solving refer to fluid intelligence. The Cattell-Horn theory suggests that crystallised intelligence remains unaffected by age because of continuous exposure and new learning (Catell, 1987). Similarly, these findings have been replicated by other researchers who suggest that older adults perform at par with the younger adults on tests of vocabulary knowledge (Bowles & Salthouse, 2008; Kave & Halamish, 2015; Kave & Yafe, 2014; Kemper & Sumner, 2001; Verhaegen, 2003). Thus, it can be speculated that difficulties in accessing word forms from the store (fluid intelligence) and not deficits in the store itself (crystallised intelligence) contributes to naming difficulties in older adults.

Naming deficits and increase in TOT's with age have also been explained from a psycholinguistic perspective. It is suggested that difficulties in mapping the lexical form onto the phonological features leads to increased occurrence of TOTs (Burke & MacKay, 1997). The speaker retains the ability to describe and produce words related to the target word and can give the correct number of syllables, but s/he is unable to retrieve the word completely. Burke et al. (1991) proposed the Transmission Deficit Hypothesis (TDH) to explain this phenomenon. The TDH was developed as an application of the Node Structure Theory (NST) to cognitive ageing (MacKay, 1987). NST is a localist and connectionist model. Like Dell et al.'s (1997) model, it states that there are three distinct systems, semantic, phonological and muscle movement, which interact during word production. Each system consists of a vast number of nodes which are organized in a hierarchical manner. The semantic system represents conceptual and lexical information of words and consists of the propositional and lexical nodes. The phonological system represents sound structure and consists of the syllable, phonological compound, phonological and feature nodes. The muscle movement system contains information about the articulatory movements. According to this model, during word production tasks such as picture naming or naming-to-definitions, top-down processing is involved. Priming and activation are the core components and word production depends on the amount and speed with which priming spreads across the different nodes. It is suggested that frequent use of words strengthens the connection between the nodes and increases priming transmission. During naming, priming starts at the semantic level and diverges to the different phonological nodes. However, these connections are weakened with progressing age and there is a delay in transmission. The TDH suggests that difficulty in accessing phonological representations in older adults due to weakened connections contributes to naming failures. Thus, this theory also suggests that a deficit in lexical access, and not in the semantic store, underlies naming difficulties in older adults.

The neural literature also supports that naming deficits in older adults occur due to access deficits. Wirenga et al. (2008) showed that older adults activated a larger frontal network than younger adults during picture naming, despite having equivalent naming accuracy. They also demonstrated a bilateral pattern of activation (increased activations in right inferior frontal gyrus and anterior cingulate) in older adults, rather than a left lateralization, which was seen in the younger group. However, no differences were noted in activation patterns of the fusiform gyrus. Abrahams et al. (2003) reported similar findings and additionally, found increased activations in the middle frontal gyrus

(MFG) in older adults. As described earlier, the frontal cortex has been associated with executive functions and the temporal structures with semantic memory. Therefore, this evidence supports that change in activation patterns of frontal regions may contribute to naming deficits in older adults.

Apart from these above-mentioned theories, a generalized slowing of all the cognitive components may also contribute to naming errors (Salthouse, 1996). For the picture naming task, the assumption of a generalized cognitive slowing has received support from Thomas et al.'s (1977) study who found that longer latencies in older adults was not because of lexical access deficit alone, but also due to difficulties in perceptual and motor processes involved in the task. It is well established that with increase in age there are difficulties in visual and auditory processing (Fozard & Gordon-Salant, 2001). Therefore, a compromise in the sensory-perceptual processing might also contribute to naming difficulties.

Despite three decades of research, it is not clearly established whether picture naming ability declines with advancing age in healthy adults. Studies investigating the effect of age on naming ability using the naming-to-auditory-definitions task are also limited. Furthermore, the age at which this decline begins and the reasons underlying these deficits are unclear. The role of sex in determining naming performance in older adults is under-researched and results across studies that have investigated this dimension remain inconsistent. Some researchers have reported that men have higher accuracy scores than women (Hall, Vo, Johnson, Wiechmann, & Bryant, 2012, Connor et al., 2004, Ivnik et al., 1996; Lansing, Ivnik, Cullum, & Randolph, 1999; Tombaugh & Hubley, 1997; Welch et al., 1996), and some others have found no sex differences (Cruice et al., 2000; LaBarge et al., 1986; Welch et al., 1996; Zec, Burkett, Markwell & Larsen, 2007a, 2007b). The reasons underlying these discrepancies across studies are not very well understood and it is not known whether men and women show similar rates of age-related decline in naming abilities. As discussed in the verbal fluency section (section 2.2.5), discrepancies in sex effects in older adults could be related to menopause status and hormone levels of the women studied. The following section reviews available evidence on the effects of fluctuating hormone levels during menopause on verbal naming.

2.3.5. Effects of sex hormone fluctuations during menopause on verbal naming

The literature review on the effects of ovarian hormones on verbal fluency in midlife women revealed a field of work that remains inconsistent and fragmented. Similarly, the effects of fluctuating hormone levels during menopause on picture naming are not well-documented. Ryan et al. (2012) examined the association between picture naming performance and endogenous sex hormone levels in younger postmenopausal women aged 56-67 years using both cross-sectional and longitudinal research designs. Cross-sectional results indicated that higher scores on the BNT were associated with high levels of total and free estradiol after controlling for age, education, age of menopause and depressive symptoms. On the other hand, a low testosterone to estradiol ratio was associated with higher BNT scores. These findings suggest that a decline in endogenous level of sex hormones post menopause might have a detrimental effect on naming abilities. In contrast to this cross-sectional finding, their longitudinal data showed different results. They found that high levels of free testosterone relative to estradiol was now associated with better performance on semantic memory (BNT and category fluency) after a period of two years. This led the authors to conclude that the effects of sex hormone fluctuations during menopause on naming abilities are activational and not organizational. Ceiling effect on BNT restricts the improvement of scores over two years which may have contributed to different findings across time. The hormone levels were also measured only at baseline and not at follow-up after two years. Therefore, it is not definite whether women continued to have same levels of sex hormones after a period of two years, and whether their hormone levels after two years would have correlated with performance.

In contrast, Drake et al. (2000) showed no significant associations between sex hormones and picture naming after controlling for age, education, depression and hormone replacement therapy use in an older group of postmenopausal women with a mean age of 78.8 years (Drake et al., 2000). As already discussed in the verbal fluency section, these discrepancies in associations may be related to the age of the individual. Other methodological differences that could have contributed to discrepancies are sample size and inter-subject variations. Drake et al.'s (2000) study had a smaller sample size of 39 participants with a wider age range (65-91 years), whereas Ryan et al. (2012) recruited 148 participants aged 56-67 years. It is possible that Drake et al.'s (2000) study lacked sufficient power to detect the subtle effects of estrogen on naming. Ryan et al. (2012) included only women who had experienced natural menopause, whereas Drake et al. (2000) did not state the type of menopause of the participants. Therefore, the study findings may not be directly comparable. Results from the Early versus Late Intervention Trial (ELITE) provided evidence in support of the above-mentioned studies (Henderson et al., 2013). This study found a positive association between estrogen levels and naming performance only in the recent menopausal group, possibly suggesting that estrogen fluctuations affect naming abilities only in younger postmenopausal women.

Most of the studies conducted in women taking hormone replacement therapy report no effect of intervention on picture naming abilities. Until 2002, none of the experimental studies investigated the effects of estrogen treatment on picture naming (see Zec & Trivedi, 2002 for a review). Of the four observational studies which examined this cognitive ability, only Jacobs et al. (1998) found that participants who had ever used estrogen replacement therapy had higher scores on picture naming than those who had never done so. The other three studies reported no positive benefits of hormonal treatment on picture naming (Maki & Resnick, 2000; Resnick, Maki, Golski, Kraut, & Zondermann, 1998; Verghese et al., 2000). Thus, these studies highlighted that estrogen therapy did not influence either performance on picture naming in young (Resnick et al., 1998) or older postmenopausal women (Maki & Resnick, 2000; Verghese et al., 2000). In line with previous reports, some later studies have also found no effects of hormone treatment on picture naming in younger and older postmenopausal women (Buckwalter, Crooks, Robins, & Pettiti, 2004; Grady et al., 2002; Lethaby, Hogervorst, Richards, Yesufu, & Yaffe, 2008; Pefanco et al., 2007; Shaywitz et al., 2003; Viscoli et al., 2005; Yaffe et al., 2006).

Considering the existing evidence from research that have investigated the effects of endogenous hormone levels at midlife and exogenous hormone supplementation on naming, the association between estrogen levels and naming ability in midlife women remains unconfirmed. The current review also suggests that relatively little work has been undertaken to explore the effects of hormone fluctuations during menopause on picture naming. Moreover, the results from the few studies that have been conducted also remain conflicting, thus requiring further investigation in this area. Additionally, there are no studies which have considered the naming-to-auditory-definitions task when investigating the relationship between naming performance and sex hormone levels in midlife and late-life women.

Summary

The two most commonly used tasks to examine word-finding abilities are verbal fluency and verbal naming. Efficient performance on these tasks requires an intact semantic memory and search strategies to access this semantic store. The role of age and menopause in determining word-retrieval on these tasks has not been confirmed yet and the reasons that underlie discrepancies across studies in the documented literature are unclear. It is also unknown as to which dependent measure on these tasks is most sensitive to the subtle effects of age and menopause in healthy midlife and late-life women. These factors drive the motivation to conduct further research in this area. Thus, the present study investigates the effects of age and menopause on these cognitive abilities in a group of women aged 46-79 years. Aspects of the work are also dedicated to understanding how best to assess and analyse effects on task performance and strategy use. The next chapter focusses on examining the effects of hormone fluctuation across menstrual cycle phases in young healthy women on verbal fluency. This pilot study was undertaken to determine the measures that are most sensitive to detect the effects of hormonal fluctuation on verbal fluency, which is a core task of the primary study.

Chapter 3

Effects of menstrual cyclicity on verbal fluency in young healthy women

3.1. Introduction

The verbal fluency test is an important component of neuropsychological batteries assessing word production (Lezak et al., 2004). Performance on verbal fluency tasks has been widely used as a measure of lexical or semantic memory (Bokat & Goldberg, 2003; Neill, Gurvich, & Rossell, 2014), and executive functions (Fitzpatrick, Gilbert, & Serpell, 2013; Kemper & McDowd, 2012; Rende et al., 2002). In the psychoendocrinological literature, it has been utilised to probe the organizational (Resnick, Berenbaum, Gottesman, & Bouchard, 1986; Temple, 2002; Temple & Shepherd, 2012) and activational effects of sex hormones on verbal functioning (Hampson, 1990a, 1990b; Maki et al., 2002; Ryan et al., 2012; Wadnerkar et al., 2008 June). As mentioned in Chapter 2, activational effects of ovarian hormones in humans can be studied by comparing women across phases of the menstrual cycle or across stages of menopause. This data mining study uses the menstrual cycle model to examine the effects of fluctuating hormone levels on verbal fluency in a group of young healthy women. As background to the study, the next section reviews the endocrinology of the menstrual cycle and the effects of menstrual phase on verbal fluency performance.

3.2. Menstrual cycle phases and their effects on verbal fluency

In human females, an important reproductive event that marks sexual maturity is the onset of menstruation which occurs on a monthly basis. A single menstrual cycle ranges between 23 and 35 days with an average of 28 days (Impey & Child, 2012). The menstrual cycle is regulated by five hormones, namely, gonadotrophin-releasing hormone (GnRH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), estrogen and progesterone. The hypothalamus secretes GnRH which in turn regulates the production of anterior pituitary gland hormones FSH and LH. FSH and LH further regulate estrogen and progesterone production, which are primarily secreted by the ovaries (Erlanger, Kutner, & Jacobs, 1999; Ledger, 2012). Hormonal and biological changes occurring across the menstrual cycle have been classified by endocrinologists into four phases: menstrual, periovulatory or proliferative, midluteal or secretory and premenstrual (Ledger, 2012; Impey & Child, 2012).

The menstrual phase consists of days 1 to 4 of the cycle. It is marked by the shedding of the outer two layers of the endometrium and menstrual bleeding. Levels of estrogen and progesterone remain low during menstruation. The periovulatory phase covers days 5 to 13, that is, leading up to ovulation on day 14. There is maximum growth of the endometrium and an increase in the level of estrogen. Progesterone continues to remain at a low level. Post-ovulation there is a slight decrease in the estrogen level. The midluteal stage comprises the period between days 14 to 24. Progesterone reaches its peak at day 22 of the cycle alongside a second peak in estrogen. Days 24 to 28 are referred to as the premenstrual phase and levels of estrogen and progesterone decline gradually and the cycle restarts.

Classification of the menstrual cycle into these different phases has provided a paradigm for psychologists to study the relationship between ovarian hormones, behaviour and cognition in perceptual, motor, verbal and spatial domains (Gordon & Lee, 1993; Hampson, 1990a, 1990b; Kimura & Hampson, 1994). The effects of ovarian hormone fluctuations during the menstrual cycle on verbal fluency have been studied using between subject (Hampson, 1990a; Wadnerkar et al., 2008 June) and repeated measure designs (Gordon & Lee, 1993; Hampson, 1990a; Maki et al., 2002). It is reported that women at the midluteal phase (high estrogen & progesterone) produce more words compared to women at the menstrual phase (low estrogen & progesterone) on verbal fluency tasks (Hampson, 1990a; Maki et al., 2002; Wadnerkar et al., 2008 June). Maki et al. (2002) also found a positive association between measured estrogen levels, but not progesterone levels, and total number of words produced on category and letter fluency tasks; thus, strengthening the facilitative effects of estrogen on verbal fluency. In contrast, Gordon and Lee (1993) showed that women across the menstrual phases did not differ in verbal fluency. Although Maki et al. (2002) suggested that estrogen alone facilitates verbal fluency, similar findings were not reported by other researchers. Studies that compared women at the high estrogen periovulatory phase with women at low hormone states such as at the menstrual phase or women on oral contraceptives or women with amenorrhea for at least 180 days did not reveal greater word production in the periovulatory group (Gordon & Lee, 1993; Hampson, 1990b). Similarly, women at the periovulatory phase do not differ in verbal fluency from women at the midluteal phase (high estrogen and progesterone) (Gordon & Lee, 1993).

Of the four above-mentioned studies that compared verbal fluency in women across menstrual and midluteal phases, two reported a midluteal enhancement (Hampson, 1990a; Maki et al., 2002), one reported a similar trend (Wadnerkar et al., 2008 June) and the other showed no differences between the two groups (Gordon & Lee, 1993). Hampson (1990a) and Maki et al. (2002) employed a repeated measure design and used a composite verbal fluency score to evaluate group performances. In contrast, Wadnerkar et al. (2008 June) used a cross-sectional design and measured the total number of words produced on a letter fluency task. Although there were differences in study designs, menstrual phase effects were found, thereby strengthening the presence of phase effects on verbal fluency. The reason why Gordon and Lee (1993), who used a similar study design as Hampson (1990a) and Maki et al. (2002), did not find significant effects of menstrual phase on verbal fluency is unclear. Gordon and Lee (1993) commented that intra-subject differences may have contributed to discrepancies in the results across studies. Hampson (1990a) and Maki et al. (2002) used a composite score of only verbal fluency tasks, whereas Gordon et al. (1993)

employed a composite score which included performance on verbal fluency and tests of perception and recall of auditory sequences. This could have also contributed to the discrepant findings. Thus, the effect of menstrual phase on verbal fluency remains unconfirmed because of the limited number of studies and inconsistent findings across them. Consequently, further examination of this area is warranted including the differential effects of each of the ovarian hormones (estrogen and progesterone) on verbal fluency.

3.3. Scoring procedures for analysing verbal fluency responses

Verbal fluency is multidimensional in nature and involves a number of cognitive processes such as verbal semantic memory, working memory, planning, organization, shifting, updating and self-monitoring. The effects of hormonal fluctuations across menstrual phases on these processes are uncertain because of the very limited number of studies that have investigated this dimension. The most sensitive data analysis procedures that could be employed to study these effects are also unclear. In the literature on cognitive ageing, a number of approaches have been used to investigate the effects of age on the cognitive processes underlying verbal fluency. These approaches include analysis of word clustering and switching (Lanting et al., 2009; Sauzeon et al., 2011; Troyer et al., 1997), temporal production of words (Sauzeon et al., 2011) and linguistic-feature analysis of the produced words (Forbes-McKay et al., 2005). These additional analyses have supplemented the traditional measure of total number of words and have aided understanding of the particular processes that are affected by age or age-related disorders such as Alzheimer's disease (AD). In the psychoendocrinological literature, studies have used the Troyer et al.'s (1997) method to analyse cognitive strategy use in verbal fluency (Temple, 2002; Wadnerkar et al., 2008 June), but no work has been conducted using the time course and linguistic approaches. The current study uses a combination of all three approaches to investigate the effects of menstrual phase on cognitive processes underlying verbal fluency. The remainder of this section reviews these approaches and the advantages of using them in a study of this kind.

The most widely adopted measure of verbal fluency is total word count (Benton, 1968; Brickman et al., 2005; Kemper & Sumner, 2001; Singh-Manoux et al., 2012). Considering the hybrid nature of the task, this use of the total word score has been questioned and different measures have been considered to investigate the cognitive processes involved in verbal fluency. The most widely used, Troyer et al.'s (1997) analysis, employs two additional measures: clustering as a measure of semantic verbal memory and switching as a measure of executive functions. This approach has been adopted in menstrual cycle research in healthy women (Wadnerkar et al., 2008 June) and in clinical populations such as in girls with Turner's syndrome (TS), who have low levels of ovarian hormones (Temple, 2002). Findings from these studies indicate that low hormone states are associated with a decrease in the switching component, suggesting a decline in executive functions at low hormone states. Wadnerkar et al. (2008 June), who studied women across the menstrual phases in addition to men, found that cognitive strategy use was phase-dependent. The total number of words generated was associated with mean cluster size but not number of switches in low hormone states such as women at the menstrual phase and men; whereas a strong relationship between total number of words and number of switches was found in women at the high hormone midluteal phase. These findings suggest that use of Troyer et al.'s (1997) approach could help to distinguish cognitive strategy use across menstrual cycle phases and draw inferences on the cognitive processes that may be affected by cycle phase.

Another available method that is rarely used in response analysis of verbal fluency is the temporal approach. The temporal dynamics of word-retrieval were first studied by Bousefield and Sedgewick (1944) (as cited in Wixted & Rohrer, 1994) who reported that the quickest recall and highest rate of word production takes place in the initial time interval in a free recall task. Additionally, words are produced in spurts or clusters of semantically related words. This temporal clustering of words on a free recall task was further investigated in detail by Gruenwald and Lockhead (1980). They carried out a study in which university students were asked to produce as many words as possible from a semantic category (animals/birds/food/cold food) for 15 minutes. As expected, their results confirmed a decrease in the number of words generated over time. For the clustering measures, Gruenwald and Lockhead (1980) found that the number of clusters decreased over time but cluster size remained constant. The above-mentioned studies pioneered the field of temporal analysis of free recall and shed light on the use of clustering over time in verbal fluency. In recent years, a slightly different temporal procedure has gained attention. Researchers have spliced the total output into six 10 second (Fernaeus et al., 2008) or two 30 second time intervals (Sauzeon et al., 2011) and investigated word production across time. This temporal analysis procedure has been shown to be sensitive to subtle differences in memory impairments between individuals with AD, mild cognitive impairment (MCI) and subjective cognitive impairment (SCI) (Fernaeus et al., 2008). Sauzeon et al. (2011) also found differences in word production across the time frames between younger and older adults, which were not revealed in the total words score (see Chapter 2 for details). Taken together, the findings from the temporal studies indicate that this analysis procedure could be useful in determining the subtle effects of menstrual phase on verbal fluency.

A third approach, that has been gaining interest over the recent years, is to analyse the content of the fluency performance. In this method, researchers study the lexical characteristics of the words produced such as frequency, age of acquisition, concreteness, familiarity and word length. The effects of these variables on word-retrieval has been extensively studied in picture naming tasks both in healthy adults and in persons with aphasia (Bonin, Peereman, Malardier, Meot, & Chalard, 2003; Colombo

& Burani, 2001; Ellis & Morrison, 1998; Gilhooly & Logie, 1980; Khwaileh, Body, & Herbert, 2014; Snodgrass & Vanderwart, 1980), but little attention has been paid to content analysis of verbal fluency responses (Forbes-McKay et al., 2005; Foster et al., 2008; Temple, 2002). This may have been the case because the lexical characteristics of words on picture naming test items can be experimentally controlled which is not possible for the output from verbal fluency tasks. Reviewing all variables was beyond the scope of the present project and therefore, three lexical characteristics, frequency, word length and imageability, were studied. As mentioned above, word-retrieval on verbal fluency tasks involves semantic memory and lexical access. Evidence from picture naming studies suggests that frequency (Brysbaert, 1996; Oldfield & Wingfield, 1965) and word length (Santiago, MacKay, Palma, & Rho, 2000) are predictors of lexical access and imageability reflects the semantic aspect of word-retrieval (Nickels & Howard, 1995). Therefore, to investigate which of these processes are primarily affected by menstrual phase, these three lexical characteristics were chosen. This phase is a pilot study for data analysis of verbal fluency, which is one of the core word-finding tasks for the primary study that investigates the effects of age and menopause on word-finding abilities. The main study is focussed on older adults and existing evidence suggests that lexical access deficits contribute to word-finding difficulties in older adults (see Chapter 2 for details). This provided an additional rationale to include measures of frequency and word length in the present study.

The frequency rating of a word refers to how often the word occurs in spoken or written samples of a language (Hernandez-Munoz, Izura, & Ellis, 2006). Word frequency effects were first proposed by Oldfield and Wingfield (1965), who found that the frequency of the target object affects the latency time of retrieval: high frequency words are easier to retrieve than low frequency words. Although this variable has gained a lot of attention in the picture naming literature (Jescheniak & Levelt, 1994; Levelt, Roelofs, & Meyer, 1999), not many researchers have investigated the role of frequency in word-retrieval on a verbal fluency task. Hernandez-Munoz et al. (2006) showed a trend for high frequency words to be produced in the earlier time intervals on a word-generation task in healthy adults. However, two studies that investigated frequency effects on the verbal fluency task in clinical populations did not reveal a high frequency effect. Foster et al. (2008) used the letter fluency task and found that the average frequency of words produced by patients with Parkinson's disease (PD), who predominantly have frontal lobe impairments, was lower than the frequency of words produced by healthy controls. They attributed this finding to an increase in the spreading activation in the lexico-semantic network as a consequence of dopamine depletion. Similarly, Temple (2002) found that girls with TS produced a larger proportion of low frequency words than their age-matched peers. Temple suggested that this might have occurred because of differences in the internal storage structure or increased access to low frequency words or different lexical access processes. Thus, the role of frequency in word-retrieval on verbal fluency tasks remains unconfirmed.

The second variable of focus in the current study was word length. Word length has been shown to be a predictor of naming speed in people with brain damage (Morrison, Ellis, & Quinlan, 1992), but its effects on healthy speakers' word production as assessed by naming tasks remains unclear. Some have suggested that word length significantly affects naming speed (Bates et al., 2003; Roelofs et al., 2002), whereas others report no effects (Bonin et al., 2003; Severens, Van Lommel, Ratinckx, & Hartsuiker, 2005). The role of word length in determining word-retrieval on verbal fluency tasks is limited. Forbes-McKay, Ellis, Shanks, and Venneri (2005) used a category fluency task and found that patients with AD produced shorter words than healthy controls, indicating that individuals with lexical access difficulties have difficulty accessing a wide range of words varying in length.

The third variable that was considered in this study was imageability. Imageability of a word refers to the ease with which it can evoke a mental image (Hernandez-Munoz et al., 2006). For example, the word "convocation" has a low imageability rating (151 on a rating scale ranging from 100-700; MRC Psycholinguistic Database) compared to "flower" (618). Both the items are picturable, but it is much easier to generate a mental image of a flower than of convocation. The verbal fluency task may provide a better model to discriminate imageability effects on lexical retrieval than picture naming tasks, which mostly include items with high imageability.

In summary, the above literature suggests that each of the analysis procedures (Troyer et al.'s (1997), temporal and linguistic-feature analyses) have contributed to investigations of the cognitive processes underlying verbal fluency in healthy controls and in detecting subtle differences in performance across different populations based on age, brain damage and hormone status. The use of these approaches in differentiating verbal fluency performance in women across menstrual phases remains under-researched, thus providing the motivation to examine this in detail in the current study.

3.4. Research aims and hypotheses

The present study aimed to extend the findings of Wadnerkar et al. (2008 June) to a broader age range of women (from 20-25 to 20-30 years) and to examine differences in verbal fluency performance at the periovulatory stage from the menstrual and midluteal stages. It also aimed to investigate the effects of menstrual phase on underlying cognitive strategy use (switching and clustering) and to determine the measure most sensitive to phase effects.

It was hypothesized that performance on total word production and switching would vary as a function of menstrual cycle phase. More words were predicted in the high hormone (periovulatory and midluteal) phases than in the low hormone phase (menstrual) (Hampson, 1990a; Maki et al., 2002; Wadnerkar et al., 2008 June). It was also predicted that women in the high hormone phases would switch more frequently compared to women in the low hormone phase. Mean cluster size was expected to remain unaffected by phase changes (Wadnerkar et al., 2008 June). It was expected that comparison of verbal fluency performance of women in the periovulatory and midluteal phases would differentiate the effects of estrogen and progesterone on letter fluency. If estrogen alone had a facilitative effect on verbal fluency (Maki et al., 2002), women in the periovulatory stage would produce more words and switches. On the other hand, if both estrogen and progesterone have a role, then women in the midluteal phase would perform better on these two measures. It was also predicted that the association between total words and switches would be stronger in the high hormone periovulatory and midluteal phases.

For the time course analysis (see section 3.5.3), it was predicted that patterns of word production would differ as a function of time with the majority of words being produced in the first 20 second interval (Fernaeus et al., 2008). The number of switches on the letter task has been shown to be positively associated with total number of words (Troyer et al., 1997). Therefore, it was predicted that a higher number of switches would be produced in the initial time intervals. Based on prior evidence (Gruenwald & Lockhead, 1980), it was also hypothesized that cluster size would remain constant over time. If sex hormones facilitate frontally-mediated executive functions, then it could be hypothesized that women in the periovulatory and midluteal groups would produce more words and switches than women in the menstrual group, and this finding may be accentuated in the initial time frames.

For the linguistic-feature analysis (see section 3.5.3), it was hypothesized that all women would produce words with higher frequency, higher imageability and shorter length (mono or bisyllabic) in the initial 20 second interval. Once the access to high frequency and short items is exhausted, participants would be more likely to produce words with lower frequency, lower imageability and greater length. Word frequency and word length are predictors of lexical access. Therefore, it was hypothesized that women in the menstrual phase would produce words with higher frequency, higher imageability and shorter length than women in the other two phases.

3.5. Methods

3.5.1. Sample

Speech samples of 20 healthy women in the age range of 20-30 years (M_{age} = 25.24 ± 0.74 years) were used for this study. This is a data mining study and therefore, pre-existing data from Hormones, Speech and Related Behaviour study were analysed (Cowell, Ledger, Wadnerkar, Skilling, & Whiteside, 2011). The study had ethical approval from the Department of Human Communication Sciences Research Ethics Review Panel, The University of Sheffield. The participants were recruited from The University of Sheffield and the local community. All women reported a history of regular menstrual cycles. In the larger study, a whole range of speech and languages measures was studied of which the verbal fluency task was chosen for the present analysis. A repeated measures design was employed for key speech and language tasks such that women were tested on three sessions for all measures of speech except for verbal fluency due to the potential for practice effects on the second and third session of testing. A cross-sectional design was deemed more suitable for this measure to remove the possibility of confounding interactions between learned strategy and hormone effects.

All participants were right handed ($M \pm SEM$: 29.71 ± 1.23), as measured by the behavioural test battery designed by Cowell and published in Wadnerkar et al. (2008). The estimated mean IQ score on the 2-test form of Wechsler's Abbreviated Scale of Intelligence (Wechsler, 1999) was 117.43 ± 2.05. All participants were English speakers and acquired English before the age of six. They were free from injuries, illnesses, and medications that could affect reproductive health, behaviour and brain function. They had not used any hormonal based medication such as oral contraceptives, implants or patches at least one year prior to the start of the study. They had not been pregnant or lactating in the past one year. All participants had regular menstrual cycles, with a mean cycle length of 29.20 ± 0.96 days. The participants reported that they had reached the age at menarche between 9 and 15 years ($M_{\text{age at menarche}}$: 12.81 ± 0.32 years).

For the first test session, women were classified into menstrual (days 2-5, low estrogen and progesterone), periovulatory (days 8-11, high estrogen and low progesterone) and midluteal (days 18-25) phases based on a calendar method. The letter fluency task was administered in the first testing session to all women. The cycle phase on the first test session was counter-balanced across women such that there were seven women in the menstrual phase, six in the periovulatory and seven in the midluteal phase.

3.5.2. Task administration

The letter fluency task was administered. The letter task was chosen because of higher inter-rater reliability in coding switches and clusters on this task than on the category task (see Chapter 2 for details). Total word production in letter fluency is associated with estrogen levels (Maki et al., 2002) and use of cognitive strategies on this task is reported to be phase-dependent (Wadnerkar et al., 2008 June). This provided an additional rationale to use this task.

Participants were asked generate as many words as possible beginning with the letters F, A and S for one-minute each. They were instructed not to produce any proper nouns. Responses were audio recorded using a Marantz Portable Professional Solid State Recorder.

3.5.3. Data analysis

The data were analysed to calculate the total number of words, number of switches and mean cluster size using the adapted Troyer's method (Troyer et al., 1997; Wadnerkar, 2008; Wadnerkar et al., 2008 June). Two adaptations were incorporated. First, single words (cluster size of zero) were not included in the mean cluster size measure. Second, transitions between single words that fell between clusters were considered as switches. Transition from a cluster to a single word was also considered as a switch. However, in contrast Troyer et al. (1997) also included the transitions between single words before the first cluster and after the final cluster as switches. Thus, the following guidelines were used to score the responses. The total words included correct responses minus errors and repetitions. Proper nouns were classified as errors as it was a rule violation. In this study, words generated by the addition of suffixes were excluded from the total count (for example, if sending followed send, sending was not counted). Two or more words formed a cluster if they shared the same first two letters (sell, sent), were rhymes (sand, stand), differed by a single vowel sound (sat, set) or were homonyms (sun, son). Cluster words were counted from the second word in the cluster. For example, if a cluster contained three words, then the number of cluster words was two. The mean cluster size was the total number of cluster words divided by the total number of clusters. Words between any two clusters were counted as switches. Errors and repetitions were included in the cluster and switch count. It has been shown that total word production differs across letters (Borkowski et al., 1967; Tombaugh et al., 1999; Wadnerkar, 2008); therefore analyses were conducted with the letters F, A and S serving as an independent variable rather than using a combined score.

Time course analysis for the data was performed using the PRAAT software (Boersma & Weenink, 2011). A text grid file was created for each sound file and the responses were divided into three equal 20 second time frames (T1, T2, T3). The total number of words, number of switches and mean cluster size were calculated for each time frame.

The data were also analysed using the linguistic-feature approach. The three variables of interest were frequency, word length and imageability. The British National Corpus (BNC) web at Lancaster University[1] was used to rate word frequency. BNC is a collection of 100 million words, representing a cross section of words used for spoken and written tasks in British English. The letter task required verbal production of words and therefore, only the spoken frequency rating (frequency rating per million words) was considered in the present study. The MRC Psycholinguistic Database Version 2 (Coltheart, 1981), a computer resource, was used to measure word length and rate imageability of the produced words. The MRC database contains 150837 words and information on lexical characteristics of the words such as frequency, length, imageability and age-of-acquisition. However, information on all the linguistic properties is not available for every word. Word length was measured as the number of syllables in each word. The norms for imageability rating in the MRC database have been derived by merging the normative data from Gilhooly and Logie (1980), Pavio, Yuille, and Madigan (1968) and Toglia and Battig's (1978) studies. The ratings range from 100-700. Pavio et al. (1968) used a 7 point rating scale (1 = words arousing images with great difficulty or not at all; 7 = words arousing images readily) to establish norms for imageability ratings. Each rating was further multiplied by 100 in order to obtain an imageability rating ranging between 100 and 700.

[1] British National Corpus (n.d.). BNC*web* (CQP- Edition). Available at http://bncweb.lancs.ac.uk/cgi-binbncXML/BNCquery.pl?theQuery=search&urlTest=yes [accessed on 15.11.2011]

Mean frequencies and word length were calculated for each time interval (T1, T2, T3) separately for each letter (F, A, S). Imageability ratings were missing for more than 50% of the data and due to time constraints it was not possible to develop a new rating scale. Therefore, this variable was dropped in the final analysis.

3.5.4. Inter and Intra-rater correlations

The data for 12 participants were analysed by two raters (RM and PEC) and inter-rater reliability was computed for total number of words, number of switches and mean cluster size according to Troyer et al.'s (1997) method. Pearson correlations ranged from $r = .95$ to $r = .99$ (p-values < .01) for all the dependent variables. Rater 1 (RM) also analysed the responses at two different time points for six participants. The time difference between the two ratings was approximately three months. Similarly, within-rater values for Pearson correlations ranged from $r = .90$ to $r = 1.00$ (p-values < .01). These results are consistent with findings by earlier researchers who have reported that this scoring procedure has a high degree of inter and intra-rater reliability (Abwender et al., 2001; Troyer et al., 1997; Wadnerkar, 2008; Wadnerkar et al., 2008 June).

3.6. Results

3.6.1. Adapted Troyer method analysis (Troyer et al., 1997; Wadnerkar, 2008; Wadnerkar et al., 2008 June)

The effects of Menstrual Phase for the total number of words, number of switches and mean cluster size were studied using ANOVAs with Letter (F, A, S) as the repeated measure and Phase (menstrual, periovulatory, midluteal) as the between group factor.

There was no significant effect of Phase for the total number of words, but a significant effect of Letter was seen, $F(2, 34) = 8.87$, $p = .001$. Post hoc paired t-tests with Bonferroni correction ($\alpha = .05/3 = .017$) revealed significant differences in the total number of words produced between the letters F and S, $t(19) = -2.76$, $p = .012$, and the letters A and S, $t(19) = -4.24$, $p < .001$, but not between the letters F and A. The highest number of total words was produced with S (see Table 3.1). Letter x Phase interaction was not significant. A main effect of Phase was significant for the mean cluster size, $F(2, 17) = 4.77$, $p = .023$, but not for switches. Post hoc independent *t*-tests with Bonferroni corrections ($\alpha = .05/3 = .017$) showed that women in the midluteal phase had a larger mean cluster size than women in the menstrual phase, $t(12) = -2.88$, $p = .014$ (see Table 3.1 last row). There were no significant effects of Letter and Letter x Phase for the number of switches and mean cluster size.

Table 3.1

Means (± SEM) for total number of words, number of switches and mean cluster size for the letter fluency task as a function of letter and menstrual phase. The scores averaged across letters are presented in the bottom row. LEP: Low estrogen and progesterone, Menstrual phase, n = 7; HELP: High estrogen and low progesterone, Periovulatory phase, n = 6; HEP: High estrogen and progesterone, Midluteal phase, n = 7

	Dependent variable								
	Total number of words			Number of switches			Mean cluster size		
Letter	LEP	HELP	HEP	LEP	HELP	HEP	LEP	HELP	HEP
F	16.29	23.33	17.29	2.71	7.50	4.00	1.31	1.70	1.61
	(1.80)	(3.52)	(1.17)	(0.94)	(2.62)	(0.76)	(0.15)	(0.30)	(0.20)
A	17.29	17.67	16.29	4.86	4.50	3.43	1.07	1.58	1.62
	(3.02)	(2.08)	(2.11)	(1.83)	(2.05)	(1.04)	(0.04)	(0.14)	(0.21)
S	19.71	23.83	20.86	5.29	4.83	5.86	1.33	1.53	1.76
	(1.38)	(2.71)	(1.86)	(1.17)	(0.87)	(1.44)	(0.18)	(0.21)	(0.20)
Mean (F, A, S)	17.76	21.61	18.14	4.29	5.61	4.43	1.24	1.60	1.66
	(1.86)	(2.66)	(1.45)	(0.70)	(1.14)	(0.41)	(0.09)	(0.11)	(0.12)

Spearman's rank correlations were conducted to study the interrelationships between the total number of words, number of switches and mean cluster size (average of the three letters was considered for each variable). Correlations were examined separately for each of the three groups (menstrual, periovulatory and midluteal). The results are presented in Table 3.2. In the menstrual phase, the magnitude of correlation between the total number of words and the mean cluster size was stronger compared to the correlation between total words and switches. A similar trend was seen in the midluteal group, although the direction of association was negative in this group. However, in the periovulatory phase, the magnitude of correlation was stronger between total words and switches than between total words and mean cluster size. The two statistically significant correlations were the associations between switches and total words in periovulatory group and cluster size and total words in the menstrual group.

Table 3.2

Correlations between the total number of words and the number of switches and mean cluster size as a function of menstrual cycle phase

Menstrual cycle phase	*n*	Total number of words/Number of switches	Total number of words/Mean cluster size
Menstrual phase	7	.56	.88**
Peri-ovulatory phase	6	.94**	-.26
Midluteal phase	7	-.28	-.60

* $p < .05$, ** $p < .01$

3.6.2. Time course analysis

The effects of Time and Phase for the total number of words, number of switches and mean cluster size were examined using ANOVA with Letter (F, A, S) and Time (T1, T2, T3) as repeated measures and Phase (menstrual, periovulatory, midluteal) as the between group factor. Separate ANOVAs were conducted for each dependent variable. The descriptive statistics are summarised in Table 3.3 and are collapsed across letters. The mean values obtained for the above-mentioned dependent variables across letters are provided in Appendix 1.

3.6.2.1. Total number of words

There was no significant effect of Phase for the total number of words. A main effect of Letter was significant, $F(2, 34) = 8.87$, $p = .001$, and the post hoc results showed that the number of words produced with letter S was greater than those produced with letters F and A (see section 3.6.1 for details). There was a significant effect of Time for the total number of words, $F(2, 34) = 87.41$, $p < .001$. Further, post hoc paired *t*-tests with Bonferroni corrections ($\alpha = .05/3 = .017$) revealed that significantly more words were produced in T1 than in T2, $t(19) = 9.53$, $p < .001$, and in T3, $t(19) = 10.85$, $p < .001$. The number of words produced in T2 was slightly higher than in T3, but this difference was not statistically significant. Overall, the total number of words produced decreased from T1 to T3 (see Table 3.3). Time x Phase showed a nonsignificant trend, $F(4, 34) = 1.91$, $p = .132$. Post hoc univariate ANOVAs were conducted and the results showed a nonsignificant trend of Phase for the total number of words only in T1, $F(2, 17) = 3.04$, $p = .074$. Women in the periovulatory group produced the highest number of words followed by the midluteal and menstrual groups (see Table 3.3, first column).

3.6.2.2. Number of switches and mean cluster size

There were no significant effects of Phase for the number of switches and mean cluster size. A main effect of Time was significant for the number of switches, $F(2, 34) = 15.82$, $p < .001$, but not for mean cluster size. Post hoc paired *t*-tests with Bonferroni corrections ($\alpha = .05/3 = .017$) confirmed that the number of switches produced in T3 differed significantly from those produced in T1, $t(19) = 4.88$, $p < .001$, and in T2, $t(19) = 6.96$, $p < .001$. Switches in T1 and T2 did not differ significantly. Switches were highest in T1 and T2 (T1 ≈ T2 > T3) (see Table 3.3, bottom row data). The effects of Letter or additional interaction effects were not significant for switches or mean cluster size.

Table 3.3

Means (± SEM) for total number of words, number of switches and mean cluster size across T1, T2 and T3 for the letter fluency task as a function of menstrual cycle phase. The mean values are averaged across letters (F, A, S)

		Dependent variable								
		Total number of words			Number of switches			Mean cluster size		
Menstrual cycle phase	*n*	T1	T2	T3	T1	T2	T3	T1	T2	T3
Menstrual phase	7	7.95	5.14	4.67	1.81	1.76	0.71	1.09	1.01	0.91
		(0.56)	(0.77)	(0.68)	(0.32)	(0.45)	(0.28)	(0.08)	(0.27)	(0.24)
Periovulatory phase	6	10.44	5.56	5.61	2.61	2.11	0.89	1.55	1.60	1.16
		(0.94)	(0.94)	(0.91)	(0.77)	(0.37)	(0.27)	(0.12)	(0.30)	(0.29)
Midluteal phase	7	8.76	5.24	4.14	1.81	2.00	0.62	1.49	1.32	1.63
		(0.65)	(0.73)	(0.60)	(0.28)	(0.21)	(0.13)	(0.23)	(0.34)	(0.29)
Mean	20	8.98	5.30	4.77	2.05	1.95	0.73	1.37	1.29	1.24
		(0.45)	(0.44)	(0.42)	(0.27)	(0.20)	(0.13)	(0.10)	(0.18)	(0.17)

Spearman's correlations were conducted to study the interrelationships between total number of words and strategy use across time. The analyses were carried out separately for the three menstrual cycle phases (see Table 3.4). The correlations indicated that associations between total number of words, number of switches and mean cluster size differed across menstrual phases and time. In the menstrual group, there were strong positive associations between total number of words and switches in the latter two time intervals (T2, T3), but moderate to strong associations were found between total words and mean cluster size across all time intervals. In contrast in the periovulatory group, there were strong positive associations between total number of words and switches across all the time frames, and a negative strong association was found between total words and mean cluster size only in the first time frame. For women in the midluteal group, a strong significant association was found between total number of words and mean cluster size in T2.

Table 3.4

Correlations between the total number of words and number of switches and mean cluster size across T1, T2 and T3 as a function of menstrual cycle phase

Menstrual phase	*n*	Time frame	Total number of words/ Number of switches	Total number of words/ Mean cluster size
Menstrual phase	7	T1	.07	.50
		T2	.78*	.60
		T3	.62	.83*
Periovulatory phase	6	T1	.84*	-.60
		T2	.97**	.03
		T3	.65	.16
Midluteal phase	7	T1	.45	-.71
		T2	-.25	.79*
		T3	.06	.26

* $p < .05$, ** $p < .01$

3.6.3. Linguistic-feature analysis

The effects of Letter, Time and Phase for the frequency and length of words were studied using ANOVAs with Letter (F, A, S) and Time (T1, T2, T3) as repeated measures and Phase as the between group factor. Separate ANOVAs were performed for each dependent variable.

There was a significant effect of Letter[2], $F(2, 34) = 9.22$, $p = .001$, for the word frequency. Post hoc paired t-tests showed a significant difference between letters F and A, $t(19) = -3.21$, $p = .005$, and between letters A and S, $t(19) = 3.14$, $p = .005$, but not between A and S. The mean frequency of words produced with the letter A was higher than those produced for the letters F and S (see Table 3.5). Time and Phase effects were not significant. No significant interactions were observed.

A main effect of Letter was significant for word length, $F(2, 34) = 55.68$, $p < .001$. Post hoc paired t-tests with Bonferroni corrections ($\alpha = .05/3 = .017$) indicated a significant difference between letters F and A, $t(19) = -10.66$, $p < .001$, and between A and S, $t(19) = 7.47$, $p < .001$. Words produced with the letter A were longer than those produced with F and S. A main effect of Time, $F(2, 34) = 3.49$, $p = .042$, was also observed. Words produced in T3 were longer than those produced in T1 and T2 but these differences did not hold up to Bonferroni corrections. No significant effects of Phase or additional interactions were seen. The mean scores are presented in Table 3.5.

[2]Mauchly's test of sphericity was significant, $\chi2(2) = 49.24$, $p < .001$. The Greenhouse-Geisser correction also showed a significant difference across letters for the word frequency, $F(1.024, 17.401) = 9.22$, $p = .007$.

Table 3.5

Means (± SEM) for frequency and length of words produced on the letter fluency task as a function of letter, time and menstrual cycle phase. LEP: Low estrogen and progesterone, Menstrual phase, HELP: High estrogen and low progesterone, Periovulatory phase, HEP: High estrogen and progesterone, Midluteal phase

		Frequency			Length (in syllables)		
Letter	Time frame	LEP (*n* = 7)	HELP (*n* = 6)	HEP (*n* = 7)	LEP (*n* = 7)	HELP (*n* = 6)	HEP (*n* = 7)
F	T1	56.71	51.26	72.78	1.59	1.40	1.39
		(10.69)	(14.18)	(22.39)	(0.12)	(0.12)	(0.14)
	T2	152.21	25.52	27.89	1.19	1.29	1.95
		(79.69)	(5.30)	(15.25)	(0.23)	(0.12)	(0.21)
	T3	25.63	99.51	44.68	1.66	1.45	1.74
		(13.98)	(61.25)	(23.59)	(0.17)	(0.13)	(0.32)
A	T1	24.88	550.17	452.55	2.41	2.34	2.36
		(9.67)	(440.77)	(368.97)	(0.19)	(0.15)	(0.23)
	T2	1042.11	725.28	609.70	1.75	2.07	2.81
		(879.07)	(268.37)	(596.05)	(0.33)	(0.29)	(0.25)
	T3	276.96	543.88	1102.02	2.51	2.83	2.75
		(246.58)	(374.84)	(924.06)	(0.30)	(0.39)	(0.26)
S	T1	65.46	52.43	21.00	1.59	1.34	1.76
		(15.17)	(12.16)	(2.44)	(0.05)	(0.13)	(0.15)
	T2	100.86	111.05	81.16	1.67	1.46	1.49
		(59.13)	(46.60)	(45.52)	(0.12)	(0.16)	(0.12)
	T3	116.21	31.71	61.76	1.55	1.73	1.61
		(76.74)	(13.74)	(28.83)	(0.21)	(0.25)	(0.23)

3.7. Discussion

The overarching aim of this pilot study was to examine the effects of menstrual phase on verbal fluency and to determine the measure which is most sensitive to hormonal fluctuations. The results of the study partly supported previous findings, which have shown greater word production in women in the high hormone phases (Hampson, 1990a; Maki et al., 2002; Wadnerkar et al., 2008 June). Women in the periovulatory and midluteal groups produced more words than women in the menstrual group, but these differences were not statistically significant. This project was cross-sectional in nature and the results are in line with the cross-sectional findings of Hampson (1990a) and Wadnerkar et al. (2008 June), who also reported nonsignificant phase-related trend for the total number of words produced on verbal fluency tasks.

A secondary aim of the study was to differentiate the effects of estrogen and progesterone on verbal fluency, and this was investigated by including women in the periovulatory group. The findings of the current study showed a trend for women in the periovulatory phase to produce more words compared to women in the midluteal phase. These findings indicate that probably estrogen alone facilitates letter fluency and progesterone has an inhibitory effect on this task (Maki et al., 2002). If progesterone did not have any effect on the letter fluency task, then women in the midluteal phase would have obtained similar scores as in the periovulatory phase. However, this was not the case, suggesting an inhibitory role of progesterone on verbal fluency.

Verbal fluency is multifactorial in nature and involves a number of cognitive processes (Shao, Janse, Visser, & Meyer, 2014; Troyer et al., 1997). In the literature, these processes have been examined using measures such as clustering (as a measure of semantic verbal memory) and switching (as a measure of executive processes), in addition to the total word count (Lanting et al., 2009; Sauzeon et al., 2011; Troyer et al., 1997; Wadnerkar et al., 2008 June). The current study also employed these two measures and found that women across the menstrual phases did not differ in cognitive strategy use. However, some interesting correlation patterns were noted. The relationships between total words and cognitive strategies (switching and clustering) were found to be phase-dependent. The correlation between the total number of words and the mean cluster size was stronger than that between the total words and the switches in the menstrual and midluteal phases. On the other hand, a very strong relationship was seen between total number of words and switches in the periovulatory group. These findings support Wadnerkar et al.'s (2008 June) study on healthy women, who also found a strong association between total words and mean cluster size in low hormone phases (women in the menstrual phase and men) and a strong association between total words and switches in the high hormone phase. Reduced use of switching has also been reported in girls with TS who have low levels of estrogen (Temple, 2002). Thus, the findings indicate that high estrogen levels in the periovulatory phase may have a beneficial effect on switching which in turn affects overall performance.

Additionally, word production and cognitive strategy use on the letter fluency task across the one-minute duration were investigated using the time course approach. The findings replicated previous research of greater word production in the initial stages of recall (Graesser & Mandler, 1978; Fernaeus et al., 2008; Zimmermann et al., 2014). More words were produced in the first 20 second of the task. The results also showed that all women switched more in the first 40 second; and in line with previous studies, the mean cluster size remained constant over time (Graesser & Mandler, 1978; Gruenwald & Lockhead, 1980). There was also a marginal interaction between time and menstrual phase for the total number of words. Women in the periovulatory phase produced more words in comparison to women in the other two groups but only in T1

(0-20 seconds). This greater word production in T1 was associated with a heightened use of switching. This finding suggests a possible role of hormonal mediation as a function of menstrual phase in determining word production.

The letter fluency task is primarily thought to be frontally-governed and support for this hypothesis comes from behavioural (Baldo et al., 2006; Martin, Wiggs, Lalonde, & Mack, 1994; Troyer et al., 1997) and neuroimaging studies (Baldo et al., 2006; Birn et al., 2010; Costafreda et al., 2006). Switching on letter fluency is also thought to rely on a function of the frontal cortex, whereas clustering is associated with the functions of the temporal cortex (Troyer et al., 1997). Existing evidence suggests that the prefrontal cortex is a major site for estrogen action in the female brain (Bixo et al., 1995; Keenan, Ezzat, Ginsburg, & Moore,, 2001) and high levels of estrogen have also been associated with greater word production on letter fluency tasks (Berent-Spillson et al., 2012; Maki et al., 2002). It is likely that high estrogen levels at the periovulatory phase may have a facilitative effect on frontally-mediated functions such as the letter fluency task and switching. This in turn would have led to a stronger association between switching and word production at the periovulatory phase.

The current study also examined the content of verbal fluency performance, that is, word frequency and word length. Word frequency and word length remained stable across the time intervals. These findings receive support from Hernandez-Munoz et al.'s (2006) study which reported that word frequency and word length did not significantly predict word production across time on a category fluency task. Women across the menstrual phases also did not differ in the lexical characteristics of the produced words. It is possible that these parameters may not be sensitive enough to detect the subtle changes in lexical access that may occur across menstrual phases. Not finding a significant effect for any of the measures (total words, number of switches, mean cluster size, frequency and word length) could also be because of a combination of the subtle effects of menstrual cycle phases and the small sample size.

Summary

The current study showed no significant differences in letter fluency performance across phases of the menstrual cycle in young women aged 20-30 years. The mean scores revealed a phase-related trend with better performance in women at the periovulatory phase than women at the menstrual and midluteal phases. The time course analysis, which was studied for the first time in relation with menstrual cycle effects, indicated that word generation differed across the time intervals T1, T2 and T3. This provided insights into the use of different cognitive processes over the typical one-minute period of verbal fluency tasks. Women in the periovulatory phase tended to produce more words in the initial stages of recall compared to women in the menstrual and midluteal phases, and this optimized word production was associated with a greater use of the switching strategy in the periovulatory phase.

Thus, the study highlights the importance of using a combined approach to investigate the effects of ovarian hormone fluctuations across menstrual phases on verbal fluency. The use of word clustering and switching measures, along with the time course approach was particularly helpful in distinguishing subtle differences in performance between women in the high and low hormones states of the menstrual cycle. Therefore, it can be suggested that these approaches might be useful for examining verbal fluency performance and cognitive strategy use across menopause stages when hormonal fluctuations are seen. Sauzeon et al. (2011) suggested that age group differences in verbal fluency are evident in more fine-grained analysis of verbal fluency responses such as time course analysis. Word production and cognitive strategy use were found to be time-dependent in the current study. Thus, it could be predicted that the time course analyses may provide evidence of differences in word production and cognitive strategy use between younger and older adults across the one-minute period. Decline in verbal fluency in older adults has mostly been related to lexical access deficits. Although the linguistic-feature approach did not supplement our understanding of lexical access abilities in this group of young women, it may be helpful in discriminating content of fluency performance across young and old adults. Hence, the adapted Troyer's method (Troyer et al., 1997; Wadnerkar, 2008; Wadnerkar et al., 2008 June) word clustering and switching, temporal analysis, and linguistic-feature (frequency and word length) will be used in the primary study that examines the effects of age and menopause on verbal fluency.

Chapter 4

Methodology for phase II study which investigates word-finding abilities in healthy midlife and late-life women

4.1. Introduction

Women in their midlife and late life often experience word-finding difficulties and these difficulties have been associated with menopause status and age. The effect of menopause on word-finding abilities remains unclear. Little attention has been paid to study these effects and to the researcher's knowledge, there are only five cross-sectional studies that have compared women across stages of menopause. Among these studies, only one reported a significant effect of menopause stage, with postmenopausal women producing fewer words in comparison to premenopausal women on verbal fluency tasks (Berent-Spillson et al., 2012). The remaining studies showed no differences between menopause stages in verbal fluency (Fuh et al., 2003; Herlitz et al., 2007; Lokken & Ferraro, 2006; Weber et al., 2013). A number of methodological differences could explain these discrepancies across studies. Classification of women into different menopause stages varied between the studies. Berent-Spillson et al. (2012) compared women across three stages (pre, peri, postmenopause; aged 42-61 years), whereas Weber et al. (2013) compared women across four stages (late reproductive, 41-53 years; early transition, 40-55 years; late transition, 42-56 years; younger postmenopausal, 44-60 years). Lokken and Ferraro (2006) also used a four-stage classification (young pre, 18-22 years, older pre, 35-48 years, postmenopausal not using hormone therapy, 42-67 years; postmenopausal women using hormone therapy, 45-61 years), but the groups differed from that of Weber et al.'s (2013) study. There were also differences in the education levels of women across studies. Participants in Weber et al.'s (2013) study had a mean education of 16 years, whereas the mean education levels in the other studies ranged between 13.5 and 14.5 years (Berent-Spillson et al., 2012; Herlitz et al., 2007; Lokken & Ferraoro, 2006).

Women also differed in the type of menopause they had experienced. For example, both Berent-Spillson et al. (2012) and Lokken & Ferraro (2006) included women with natural and surgical menopause, but Weber et al. (2013) included only women with natural menopause. Women with surgical menopause experience a sudden decline in estrogen levels and therefore, are at a greater risk for cognitive impairments and dementia than women with natural menopause (Rocca, Grossardt, Shuster, & Stewart, 2012; Settnes, Andreasen, & Jorgensen, 2005). Inclusion of surgically menopausal women in Berent-Spillson et al.'s (2012) study might have affected the results. It could be argued that Lokken & Ferraro (2006) also included surgically menopausal women, yet did not report significant differences. These two studies differed on two factors. First, as seen above, there were differences in grouping of women by menopause status. Second, women in different menopause stages in Lokken & Ferraoro's (2006) study were matched for education but not in Berent-Spillson et al.'s (2012) study. It has been reported that education is associated with verbal fluency performance (Brickman et al., 2005; Elkadi et al., 2006; Gladsjo et al., 1999; Tombaugh et al., 1999; Van der Elst et al., 2006). Postmenopausal women in Berent-Spillson et al.'s (2012) study had fewer years of education than the other two groups. Therefore, it is not entirely clear whether Berent-Spillson et al.'s (2012) study findings were affected by the lower education levels in postmenopausal women. The three studies that did not report a significant effect of menopause on verbal fluency controlled for the effects of education (Herlitz et al., 2007; Lokken & Ferraro, 2006; Weber et al., 2013), whereas Berent-Spillson et al. (2012) who found a significant effect did not.

These findings highlight the importance of having well matched comparison groups on demographic variables such as education and IQ in cross-sectional research. Additionally, none of the studies included detailed information on reproductive history of the participants such as age at menarche, parity, age at first childbirth and number of children. These markers have been associated with verbal fluency and naming performance in midlife and late-life women (see Chapter 5 for details). Variations in reproductive histories results in differences in cumulative hormone exposure across the lifespan and thereby, may also contribute to discrepant findings among studies.

The impact of age on word-finding abilities has been studied extensively using verbal fluency and naming tasks. Numerous studies suggest an age-related decline in category fluency (Brickman et al., 2005; Kemper & Sumner, 2001; Parkin & Java, 1999; Troyer et al., 1997; Van der Elst et al., 2006), letter fluency (Brickman et al., 2005; Gladsjo et al., 1999; Gordon & Kindred, 2011; Lanting et al., 2009; Lucas et al., 2005; Pena-Casanova et al., 2009b; Ruff et al., 1996; Singh-Manoux et al., 2012; Steiner et al., 2008; Tombaugh et al., 1999; Van der Elst et al., 2006; Zimmermann et al., 2014) and picture naming (Albert et al., 1988; Bowles et al., 1987; Feyereisen, 1997; Goral et al., 2007; Gordon & Kindred, 2011; Gordon & Kurczek, 2014; Kave et al., 2010; MacKay et al., 2002, 2005). However, contradictory reports of no significant change in category fluency (Sauzeon et al., 2011), letter fluency (Parkin & Java, 1999; Kemper & Sumner, 2001; Sauzeon et al., 2011; Schmitter-Edgecombe et al., 2000; Troyer et al., 1997) and picture naming (Cruice et al., 2000; Wierenga et al., 2008) with increasing age have also been published. As seen in the menopause literature, these differences could result because of methodological differences. Study samples differ on demographic characteristics such as participants' age, years of education, and verbal IQ. For example, there is little consensus among researchers for the age ranges to be considered. Some have examined verbal fluency across a wide age range (20-80 years) (Brickman et al., 2005), whereas others have investigated age differences using a comparison of two distinct age groups (e.g., 22 versus 70 years) (Sauzeon et al., 2011). High levels of education and verbal IQ are associated with better performance on verbal fluency tasks (Brickman et al., 2005; Elkadi et al., 2006; Gladsjo et al., 1999; Goral et al., 2007; Tombaugh et al., 1999; Van der Elst et al., 2006) and verbal naming tasks (Connor et al., 2004; Elkadi et al., 2006; Neils et al., 1995; Pena-Casanova et al., 2009a; Tsang & Lee, 2003; Welch et al., 1996). Therefore, to compare findings across studies, it is essential that participants have similar levels of education and IQ. In addition, to study the independent effects of age in cross-sectional studies, it is essential that subjects across age-based comparison groups are matched on these demographics. In the present literature, matching comparison groups on education remains a challenge because older adults generally have had less access to education. For example, in the UK the school leaving age increased from 14 to 16 years between 1918 and 1972 (Bolton, 2012). Thus, individuals born before 1918 would have had access to fewer years of education compared to those born in the later cohorts. Investigations which found significant effects of age on word-finding ability might have used study designs that were confounded by differences in education levels across the groups.

Alternatively, differences in the test material used could also contribute to discrepant results. For example, Brickman et al. (2005) used the animals category fluency task and found a significant difference. However, Sauzeon et al. (2011), who used the supermarket category, did not find a significant effect of age for category fluency. Word production has been found to differ across categories because of unequal difficulty levels across conditions (Amunts et al., 2004; Nagels et al., 2012). Thus, this difference would have possibly contributed to discrepant findings between the two studies. As discussed above and in Chapter 2, hormonal status could also contribute to discrepancies between studies examining the effects of age on word-finding abilities. For example, a sample containing a higher percentage of premenopausal women may show an age-related difference in word-finding abilities but not a sample containing a greater percentage of postmenopausal women in the younger groups. No studies in the literature on cognitive ageing have considered menopause status when examining age effects on word-finding abilities.

The above review indicates a number of gaps and inconsistencies in relation to the effects of menopause and age on word-finding abilities in women. Primarily, a clear understanding of menopause on this cognitive ability remains limited in the context of age effects, which are also inconsistent. The most sensitive dependent measure to examine age and menopause effects has also not been confirmed. For verbal fluency, most researchers focus on using total words and on naming tasks, they use the accuracy of responses as the dependent variable. As outlined in Chapter 3 and in previous studies, the subtle effects of ovarian hormones on verbal fluency are evident on finer measures such as clustering and switching (Temple, 2002; Wadnerkar, 2008; Wadnerkar et al., 2008 June). Similar accounts have been published in the cognitive ageing literature (Sauzeon et al., 2011), although findings remain unconfirmed due to differences in results and the limited number of studies that have researched this aspect (Lanting et al., 2009; Troyer et al., 1997). Cognitive strategy use in verbal fluency has never been explored in the menopause literature and the effect of age on cognitive strategy use remains inconsistent. This provides an opportunity to conduct further research on the key cognitive elements of word-finding. Further, little is known about the relationships between reproductive markers such as age at menarche, parity, number of children, age at menopause, number of reproductive years and word-finding ability.

The present investigation was conducted to address these concerns and build on earlier findings. The study was designed to address these issues at four different levels: test battery development, sensitive customized scoring procedures, sample recruitment and statistical modelling for comparisons across age or menopause groups. The current chapter focusses on the first three in detail. The screening and interview questionnaires and test battery (tasks and scoring procedures), which were developed as part of the thesis, are mentioned in section 4.2. Section 4.3 gives details about the study sample and the selection criteria used. The procedural details of data collection are explained in section 4.4. The statistical approaches and models that were used to investigate the effects of age and menopause on word-finding abilities are discussed in the data analyses chapters (Chapters 5, 6, 7, 8).

4.2. Development of screening and interview questionnaires and test battery

4.2.1. Screening and interview questionnaires

The screening and interview questionnaires (see Appendix 2a) were adapted from earlier forms developed for a research programme on Hormones, Speech and Related Behaviour (Cowell, Ledger, Wadnerkar, Skilling, & Whiteside, 2011; Wadnerkar, Cowell, & Whiteside, 2006; Whiteside, Hanson, & Cowell, 2004). The screening questionnaire was used to support participant selection and to obtain basic information about background health and reproductive status. It consisted of 15 questions which focused on demographic details (age, language spoken, country of residence), medical history (current and past medical illnesses, surgeries, medications) and reproductive history (length and regularity of menstrual cycle, last date of menstruation, delay or absence or irregularity of menstrual cycles, pregnancy status for the past one year). An email version of the screening form was prepared (see Appendix 2a) and sent out to participants who could not be reached over the telephone. The interview questionnaire was designed to collect detailed information on education, handedness and history of any medical conditions. The participants were asked for their highest level of education, and the number of years of education was used for future analysis. Continuing adult education was not included. Information regarding past and current substance abuse was also obtained. The participants were also asked if there was any history of head injury and if they had received a diagnosis of and treatment for psychological, movement, cognitive and speech and language disorders. Information regarding their self-perception of current cognitive difficulties was also gathered. Detailed information on the number and age at pregnancies (full-term, miscarriages and abortions) and number of biological children was also collected. This information on the demographic and reproductive characteristics of the sample was used to match comparison groups and to study the role of these factors in word-finding abilities.

4.2.2. Test Battery

4.2.2.1. Rationale for development of test battery and choice of tasks

The primary aim of the thesis was to examine change in word-finding abilities with age and menopause. The interrelated effects of age and menopause on measures of word-finding were considered in the design of the study at several levels, including test battery development. Word-finding abilities are often tested using verbal fluency or naming tasks. In order to obtain a comprehensive profile of this cognitive ability, a test battery including both verbal fluency and verbal naming tasks was developed. This enabled the researcher to explore the aspects of word-finding that were primarily affected or stable with age and menopause status (see Table 4.1). The choice of the tasks was based on two principles. First, tasks that had previously been shown to be sensitive to age, sex and hormone fluctuations across menopause stages (verbal fluency, picture naming) were chosen. Second, the tasks were considered from a neuropsychological perspective in terms of underlying neurocognitive processes. Although all the chosen tasks (category fluency, letter fluency, continuous series task, picture naming and naming-to-auditory-definitions) measured word-finding ability, each task relied differently on the underlying neurocognitive processes. For example, the category task relies on semantic memory to a greater extent than on executive processes and vice-versa for the letter task (see Chapter 2). Continuous-series (C-series) task is similar to verbal fluency tasks but relies to a greater extent on working memory than category fluency. The two naming tasks also differed in the cognitive processes involved. Picture naming assesses naming performance in the visual modality and naming-to-auditory definitions in the auditory modality. The naming-to-auditory-definitions task also requires sentence processing which is not the case in picture naming (see Chapter 2 for details). The frequently used neuropsychological tasks of category fluency, letter fluency and picture naming were used to compare findings with the results from current literature on age and menopause-related changes in word-finding abilities. Additional experimental tasks such as the C-series and the naming-to-auditory-definitions were incorporated to further investigate higher-order cognitive functions underlying word-retrieval. The test battery also included measures to match age or menopause groups on IQ and these are discussed in the next subsection.

4.2.2.2. Baseline measures

The two-subtest form (vocabulary & matrix reasoning) of Wechsler's Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) was administered to provide measures for verbal and non-verbal IQ. Wechsler's Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) and Wechsler's Adult Intelligence Scale (WAIS; Wechsler, 1958) are commonly used to estimate verbal and non-verbal intelligence (Bowles & Salthouse, 2008; Gong et al., 2005; Verhaegen, 2003). Vocabulary knowledge can be measured by various test formats such as multiple-choice synonym or antonym tests, picture naming and word definitions. The effects of age on vocabulary are evident in spoken word definition tasks, as they require an individual to find the right words for the definition, which is not the case in multiple-choice tests (Verhaegen, 2003). Therefore, the spoken word definition from the WASI was deemed suitable to be used in this study. The matrix-reasoning subtask was included to explore age and menopause effects, if any, in the non-verbal domain.

The vocabulary subtask consisted of 42 items. The first four items were pictures and the rest 38, words (nouns, verbs and adjectives). Administration and scoring followed the same guidelines as in the test manual. Participants were orally and visually presented with the stimulus item and were instructed to give the meaning of each word. Responses were audio recorded using a Marantz Portable Professional Solid State Recorder (Marantz PMD 670). The responses were scored after data collection. The maximum score that could be obtained on this task was 80.

The matrix reasoning subtask consisted of 32 items. The participants were shown a matrix with a missing item and asked to indicate the option (from a choice of five) that fitted the best. Administration and scoring guidelines described in the WASI manual were followed. The examiner simultaneously scored while testing. The maximum score on this subtask was 32.

The raw scores were converted into verbal and non-verbal T scores. The full scale IQ was estimated by calculating the sum of the T scores for both the tasks and scaling with the standardized IQ equivalents.

4.2.2.3. Word-finding tasks

Verbal fluency

Verbal fluency is used extensively in neuropsychological assessments of verbal functioning. It provides a measure of the speed and ease with which words can be retrieved. Researchers have used it in various forms to measure semantic memory, lexical memory and executive functions. Three versions of verbal fluency (category fluency, letter fluency, C-series task) were employed in the present study. Each type differed from the other on the type of cognitive load required to perform the task and the neural systems associated with performance. The order of administration was the category fluency task followed by the letter fluency task and the C-series task for all 78 participants.

Category Fluency

Participants were asked to generate as many words as possible in one minute from the semantic categories of animals, fruits and vehicles (Newcombe, 1969; Troster et al., 1998; Troyer et al., 1997). They were instructed not to produce brand names in the category of vehicles. A fixed order of administration was used. Responses were scored for the total number of correct words produced, repetitions and errors. Repetitions reflect an inability to self-monitor already retrieved responses and therefore, were not included in the total word count. Errors such as production of proper names (e.g., saying Ferrari, Volkswagen) were excluded as it was a rule violation.

Letter fluency

The participants were asked to generate as many words as possible in a minute beginning with a specific letter (F, A, S) (Benton, 1968; Benton, Hamsher, & Sivan, 1994). They were instructed not to produce any proper nouns. Responses were scored for the total number of words, number of switches and mean cluster size using the adapted Troyer's method (Troyer et al., 1997; Wadnerkar, 2008; Wadnerkar et al., 2008 June) (see Chapter 3 for details). Repetitions and errors were excluded from the total word count but were included for calculating the number of switches and the mean cluster size. For example, for the letter 'S' if the participant produced psychology or celebrate, then these were considered as errors and not included in the total count. Inflected words were also not included in the total count. For example, if a participant produced smear, smears, smeared, smearing, then only the first word that was produced was considered in the total word count but not the others.

The letter fluency responses were also analysed using the temporal and linguistic procedures that were described in Chapter 3. The time course approach was sensitive in detecting effects of menstrual cycle phase on verbal fluency in younger women (see Chapter 3). Therefore, it was used in the current analysis to detect effects of hormonal fluctuations during menopause on word-retrieval in midlife and late-life women. In brief, PRAAT (Boersma & Weenink, 2011) was used to divide a one-minute fluency sample into three 20 second time intervals T1, T2 and T3. The time intervals were manually marked at 20 and 40 seconds and a text grid file was created for each speech sample. The variables studied in the temporal analysis were the total number of words, the number of switches and the mean cluster size for each time interval. The linguistic-feature analysis involved two dependent variables, frequency and word length (number of syllables). The Lancaster web version of the British National Corpus[3] was used to determine the frequency of the words produced. The word length was obtained from the MRC Psycholinguistic Database (Coltheart, 1981) and the examiner calculated the word length for the response items which were not available from the database.

---

[3] British National Corpus (n.d.). BNC*web* (CQP- Edition). Available at http://bncweb.lancs.ac.uk/cgi-binbncXML/BNCquery.pl?theQuery=search&urlTest=yes [accessed on 15.11.2011]

C-series task (Gurd, 1995)

Prior to administration of the C-series task, participants were asked to complete the overlearned sequence (OS) task. This task served as a baseline for age-related effects on motor speech production and was used for calculation of switch cost which is described later in this section. The OS task included four categories, that is, numbers, letters of the alphabet, months of the year and days of the week. The task required the participants to recite the days of the week beginning from Monday to Sunday until the examiner asked them to stop at the end of one minute. They were instructed to start over again after each sequence was completed. The same procedure was followed for the letters and months. For numbers, participants were instructed to count numbers until the researcher asked them to stop. The C-series task was administered after the OS task. In this task, participants were asked to generate words from two or more categories alternatively. They were allowed to repeat once all the words from that category had been produced. For example, if the participant was asked to name the letters of the alphabet and numbers, then the expected response would be A, 1, B, 2, C, 3, ….., Z, 26, A, 27, B, 28 and so on. All participants were given an example prior to administration of the actual tasks. The task was adapted from Gurd's (1995) study and participants were instructed to alternate between categories in a fixed order. In the present study, each subtask used one minute as the time limit in contrast to the Gurd's (1995) task which was stopped after 23 iterations had been produced.

The subtasks included were:

2-category series: Letters of the alphabet, Numbers (A, 1)

3-category series: Letters of the alphabet, Numbers, Months (A, 1, January)

4-category series: Letters of the alphabet, Numbers, Months, Days of the week (A, 1, January, Monday)

All participants completed the subtasks in the same order (2-series followed by 3 and 4 series) so that the task load increased hierarchically.

For the OS task, number of syllables per second and number of words per second were calculated. For the C-series tasks, switch rates and switch costs were computed in the same manner as outlined in Gurd and Cowell (2015). Switch rate was the number of words per second for each of the series. Switch cost was calculated as the difference between the switch rate and mean pre-task baseline rate (for those two or three or four categories), expressed as a percentage of the total mean switch rate per category. The detailed scoring is explained in Chapter 6. Further analysis included classifying the errors as within-task errors (e.g., F being produced instead of D), between-task errors (e.g., January being produced instead of 1) and other errors (e.g., repetitions, omissions).

<u>Data collection</u>

Verbal fluency, overlearned sequences and C-series tasks were timed using a stop watch during administration. A digital Marantz Portable Professional Solid State Recorder (Marantz PMD 670) was used for recording responses. The audio files were stored as .wav files in a 16-bit format.

Naming

The second part of the test battery involved testing verbal naming abilities. The tasks used in the current study were picture naming and naming-to-auditory-definitions.

<u>Picture Naming</u>

All participants were administered the Boston Naming Test (BNT) to examine visual confrontation naming abilities (Kaplan et al., 1983). The test contains 60 pictures graded according to increasing levels of difficulty. Test administration and scoring were conducted as described in the BNT manual. The two dependent measures were total number of correct responses and mean latency time. The guidelines state that for adults, testing can begin with item 30. However, for this study all 60 items were administered as the secondary aim was to investigate latency times. The procedure used to measure latencies was initially piloted with a volunteer prior to data collection by using video and audio recording of the responses. In order to record latency time, the pages of the test booklet were turned in a manner so that an audible sound could be produced and recorded by the digital audio recorder. Audio cues were satisfactory for marking response latencies in PRAAT, therefore video recording was not further used in the main study. This pilot study volunteer did not take part in the main study. Latency was operationalized as the time interval between the audio cue of a page being turned and the verbal response being provided for the item. In order to mark the boundaries for response latency in the audio recordings, the *SpeCT*- The Speech Corpus Toolkit for Praat script to mark pauses (Mietta, 2011a) was used and the accuracy of the boundaries was checked manually by the researcher. The latencies were then obtained by using *SpeCT* script to calculate segment durations (Mietta, 2011b). The mean latency time for the correct responses was considered for further comparisons across age or menopause groups. Responses were also coded for error types. Errors were categorized as semantic (*setsquare* for *protractor*, *a mathematical instrument to measure angles* for *protractor*), phonological (*projector* for *protractor*), mixed (*badger* for *beaver*) and no-responses.

<u>*Naming-to-auditory-definitions*</u>

For this task, the definitions of 60 target words by Harley and Bown (1998) were used. Their stimulus set was graded on the high to low frequency scale and by neighbourhood density (N, high and low neighbourhood density). Half of the words on the list were high frequency (frequency of at least 100 per million, with a mean of 270.3) and the remaining were low frequency (less than 9 per million, with a mean of

4.5). The high and low frequency words in Harley and Bown's (1998) list were further divided into items with high and low N values. The N statistic refers to orthographic neighborhood density and correlates highly with phonological neighborhood density (Coltheart, Davelaar, Jonasson, & Besner, 1977). This has been defined as "the number of different English words that can be produced by considering each letter position in a word and substituting all the other letters in the alphabet for the target letter" (Harley & Bown, 1998, pp. 154). For example, among high frequency words "ball" has a high N value, whereas "answer" has a very low N value. The number of words that can be produced by replacing the first letter in ball (for example, mall, tall, call, fall, hall) is higher than the number of words that can be produced by replacing the first alphabet in answer (zero in this case). Half of the items had N value ranging between 10 and 29, while the other half had no close neighbors. Thus, the stimuli consisted of four lists of definitions with target words in four categories (high frequency, high N value (HFHN); high frequency, low N value (HFLN); low frequency, high N value (LFHN); low frequency, low N value (LFLN). An example from the HFHN list was "A spherical or nearly spherical object, especially one used in games" (Harley & Bown, 1998, pp 171). The expected response for this definition was ball.

The procedure, below, was followed for developing the technical aspects of the naming-to-auditory-definitions task. Stimulus sentences were recorded by a native female British-English speaker by using a digital audio recorder. The audio files were trimmed to remove any extraneous noise by using the Audacity software[4]. These audio files were then integrated into the DMDX (Forster & Forster, 2003) script which was prepared by following the guidelines outlined in the DMDX introductory tutorial (Darcy, 2010). The presentation of the sentence definition stimuli was delivered using

[4]Audacity software [Version 2.0.5] [Computer program]. Retrieved from https://code.google.com/archive/p/audacity/downloads

DMDX software on a 17” screen laptop. Definitions were presented binaurally by using a headset with an integral microphone (Velleman HSM 12, Velleman Inc., USA) which was set 5 cm away from the participant’s mouth to record responses. During presentation of the stimuli, the computer screen remained blank. Each response served as a vocal trigger for the DMDX timer to register response latency. The DMDX programme is sensitive to non-verbal vocal sounds, therefore the participants were instructed not to produce any filler sounds such as ah or um or er.

The following instructions were given:

“Now you are going to hear definition of a word through the headphones. Listen carefully and produce the word that has been defined after the sound file has played completely. Give the best option that you think is the target answer. This is a computer based recorder and hence cannot differentiate between spoken words and other sounds. Therefore, please do not produce any fillers such as ‘aah, um, er’ while responding. Do not breathe heavily or produce any loud lip smacking or throat clearing sounds or noises if possible”.

The order of administration was HFHN followed by HFLN, LFHN and LFLN. This order of presentation was chosen because high frequency (Oldfield & Wingfield, 1965) and high neighbourhood density words (Harley & Bown, 1998; Vitevitch, 2002) are easily retrieved than low frequency and low neighbourhood density words on naming tasks. The 60 stimulus sentences were administered to all participants using the same order of presentation. A rest period was given after presentations of the first two stimulus sets to avoid cognitive fatigue. The maximum time that was available to provide an appropriate target response after the stimulus had been played was 15 seconds. No feedback was given regarding the correctness or incorrectness of the responses. The program recorded a sound file and latency for each response. The responses were transcribed and analysed for accuracy as correct, incorrect or no response. Synonyms were classified as correct responses. Responses which were synonyms and were also part of the stimulus sentence were coded as incorrect. Latency was measured as the time gap between the end of the test stimulus sentence and the onset of the spoken word. Latency times were obtained automatically through DMDX or marked manually by the researcher for items that triggered a response in the program because of extraneous noise (see Chapter 7 for details). Mean latency for correct responses for each of the stimulus sets was computed and used for further statistical analysis.

4.3. Sample selection and participant characteristics

4.3.1. Sample stratification

A cross-sectional research design was employed whereby participants were grouped by age and menopause stages. To examine effects of age on word-finding abilities, participants were classified into three groups, 46-55 years (Group I), 56-65 years (Group II) and 70-79 years (Group III). The literature suggests that age-related effects are primarily seen after the age of 70 years (Feyereisen, 1997). Therefore, the present study focused on recruiting women aged between 70 and 79 years and did not consider women between the ages of 66 and 69 years. This approach was also taken because of practical and temporal constraints. Women experience menopause in their late 40s and early 50s, with 51 years being the average age at menopause in the UK (National Health Service, 2015, November 12). To study the effects of menopause on word-finding abilities, Group I women, who were within the same age decade, were further classified as a function of menopause status (pre, peri, and postmenopause).

4.3.2. Participants

The participants for the study were recruited from University staff volunteers through email advertisements. Advertisements were also posted on university notice boards and the University Third Age website and magazine, and circulated at local churches, women's groups such as the Sheffield City Council Women's Network, Menopause Matters, Sheffield Feminist network, and women's lunch or sewing or reading clubs. These clubs were identified from the resources available at the Sheffield Central Library or through social contacts of other participants who volunteered for the study.

The research protocol was approved by the Department of Human Communication Sciences Research Ethics Review Panel, The University of Sheffield (see Appendix 2b). An information sheet was sent out to interested volunteers and telephone screening was completed by using the questionnaire described above in order to determine volunteers' eligibility. Volunteers having any history of major illnesses that could affect their cognitive functioning were excluded from the present study. Women who had been pregnant or lactating in the past one year were also excluded as increased estrogen, progesterone levels are seen during pregnancy (Oats, Abraham, & Llewellyn-Jones, 2010), and estrogen levels decline to low levels after childbirth and during lactation. Participants were also excluded if they were on antidepressants or thyroxin medication at the time of the study. Use of any form of hormone-based medications such as oral contraceptives, hormonally based contraceptive implants, patches and estrogen or hormone replacement therapy at the time of the study was also employed as an exclusion criterion. However, participants who had used hormone therapy prior to one year of data collection were included. Women with premature menopause before the age of 40 years (American Society for Reproductive Medicine, n.d.) or surgical menopause which involved hysterectomy with bilateral oophorectomy were not included. Women who had had hysterectomy but had one or both of the ovaries preserved were included because the ovaries still continue to produce ovarian hormones until the menopause stage is reached.

In total 130 participants were screened and 84 participants fulfilled the study criteria. From the screened volunteers, 46 did not meet the criteria: 14 were taking thyroxin medication, 9 were taking some form of hormone based medication, 7 were using antidepressant medication, 6 had total hysterectomy with ovariectomy, 1 had menopause following treatment for breast cancer, 1 woman had diabetes, 1 had been lactating in the past one year and the remaining 7 had a combination of these health issues. Of the 84 participants who were eligible for the study, two participants were excluded from the final study sample as one reported of having a learning disability and another reported depression. Four more participants dropped out after the screening interview due to personal reasons. A total of 78 participants were included in the final study sample. Participants were classified into three age groups: Group I, 46-55 years (n = 32), Group II, 56-65 years (n = 24) and Group III, 70-79 years (n = 22).

Background information for each age group is summarized below. Detailed analyses of the demographic and reproductive characteristics of participants are described in Chapter 5.

4.3.2.1. Group I (46-55 years)

Thirty-two participants were included in this age group. Thirty participants had British English as their native language and lived in Sheffield or nearby areas. One of the participants in the premenopausal subgroup was a North American English speaker who had lived in England for nearly 27 years. One participant in the postmenopausal group was born in Pakistan and had moved to England at the age of 4 years and used

British English as her primary language of communication at home and work. Women in this age group were further categorized into premenopause, perimenopause and postmenopause stages. The classification into different stages was based on self-reports of menstrual cycle characteristics. This information was obtained during the telephone screening. The categorization into different stages of menopause was based on classification guidelines from Stages of Reproductive Ageing Workshop +10 (STRAW +10) (Harlow et al., 2012) and World Health Organization (1996). Women in the premenopause stage had regular cycles every month, although some of them experienced subtle changes in the flow and cycle length. Nine participants were classified as premenopausal. In the perimenopause group (n = 11), women experienced irregularity in cycle occurrence. For this study sample, delay between two consecutive cycles ranged between six weeks to seven months, and the women had been experiencing these symptoms for at least one year (maximum of six years). The postmenopause group comprised of women who had had a permanent cessation of menstruation for 12 consecutive months (n = 12). None of the participants had a history of hysterectomy. All postmenopausal women in this age group (n = 12) had experienced natural menopause. In the pre and postmenopause groups, none of the participants were taking any form of hormone based medication at the time of the study nor had been past users. One woman in the perimenopause group had used hormone replacement therapy before two years eight months prior to commencement of the study for a period of eight months.

4.3.2.2. Group II (56-65 years)

Twenty-four women were included in this age group. All were native speakers of British English and lived in Sheffield or nearby areas. All women in this group were postmenopausal. Twenty-three had experienced menopause without hysterectomy. One participant aged 64 years had had a hysterectomy without oophorectomy at the age of 43. She had not used any form of hormone based medications such as hormone replacement therapy following the surgery. In this group, three participants had used hormone replacement therapy for time periods ranging between six months to two and half years, two more participants had used mirena coil and/or estrogen patch for a period of five to six years, and one had used hormone based medication for the treatment of fibroids for a period of six years. All women had ceased hormone use for at least one year prior to taking part in the study.

The complete test battery was administered to 23 women. One participant was excluded from the naming-to-auditory-definitions task as she reported age-related hearing loss.

4.3.2.3. Group III (70-79 years)

Twenty-two women were included in this age group. Twenty participants were native speakers of British English and lived in Sheffield or nearby areas. One participant had Armenian as her native language but had moved to England and had started learning English from 6 years of age. She reported that she was fluent in English, not Armenian, and used English as her primary language. A second participant had German as her first language but had lived in England for more than 50 years. Eighteen out of 22 women had experienced menopause without hysterectomy. Three women had undergone hysterectomies without oophorectomy. Of the three women with hysterectomies, two had taken hormone replacement therapy. One participant aged 74 years had had a hysterectomy with unilateral oophorectomy at the age of 43. She had used hormone replacement therapy for a period of six years. Three other participants in the group had also taken hormone replacement therapy ranging between 10 and 13 years. All women had ceased hormone use for at least one year prior to taking part in the study.

Women with controlled hypertension and cholesterol levels were included in the study as these metabolic conditions are common in this age group. The complete test battery was administered to 21 women. One participant was excluded from the naming-to-auditory-definitions task due to reported age-related hearing loss.

4.4. Procedure

Eligible women who met the study criteria were invited to the Department of Human Communication Sciences to complete the test battery. The testing was conducted in a quiet room in a single session, which lasted for 1.5 to 2 hours. All the participants were briefed about the study and informed written consent was taken. Data collection began by reviewing the items from the screening form and administering the interview questionnaire (Cowell et al., 2011; Wadnerkar et al., 2006; Whiteside et al., 2004). The interview was followed by the Edinburgh Handedness Inventory (Oldfield, 1971). Participants then completed category and letter fluency tasks. Next, the OS and the C-series tasks were administered. The four tasks were carried out in a fixed order. Participants were allowed a break of five minutes to avoid fatigue. Naming tasks followed verbal fluency tasks so that naming items would not prime word production in verbal fluency. The naming-to-auditory-definitions task was then administered and a second rest period of five to ten minutes was given before completion of the remaining tasks. Next, participants completed the picture naming task and vocabulary and matrix reasoning subtests of WASI (Wechsler, 1999).

The next three chapters discuss the results obtained for the demographic and reproductive characteristics of the sample (Chapter 5) and the effects of age and menopause on verbal fluency (Chapter 6) and verbal naming (Chapter 7).

Table 4.1

Test battery for examining word-finding abilities in midlife and late-life women aged 46-79 years

---

Demographic and reproductive measures

- Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999)
    a. Vocabulary and Matrix reasoning subtasks
- Years of Education- Interview Questionnaire (Cowell et al., 2011; Wadnerkar et al., 2006; Whiteside et al., 2004)
- Reproductive Characteristics- Screening and Interview Questionnaires (Cowell et al., 2011; Wadnerkar et al., 2006; Whiteside et al., 2004)

Word-finding tasks

- Verbal Fluency

    a. Category Fluency- Animals, Fruits, Vehicles (Newcombe, 1969; Troster et al., 1998; Troyer et al., 1997)

    b. Letter Fluency - F, A, S (Benton, 1968; Benton, Hamsher, & Sivan, 1994)

    c. Continuous Series (C-series task) (Gurd, 1995)

    - Series 1: Numbers, Letters of the Alphabet
    - Series 2: Numbers, Letters of the Alphabet, Months
    - Series 3: Numbers, Letters of the Alphabet, Months, Days

    Baseline task for C-series task: Overlearned Sequences (Numbers, Letters of the Alphabet, Months, Days)

- Verbal Naming

    a. Picture Naming- Boston Naming Test (Kaplan et al., 1983)

    b. Naming-to-auditory-definitions (Harley & Bown's, 1998 stimuli)

Chapter 5

Sample demographic and reproductive characteristics

5.1. Introduction

The effects of age and menopause on word-finding abilities remain conflicting because of discrepant findings across studies. As discussed in Chapters 2 and 4, these discrepancies arise because of differences in sample population characteristics, sample sizes, tests used, scoring procedures and statistical analyses. Chapter 5 addresses the issue of sample population characteristics (demographic and reproductive characteristics) and their relation with inconsistent findings in cross-sectional studies. Chapter 5 also reports and discusses the demographic and reproductive characteristics of the present study sample.

Performance on word-finding tasks is associated with demographic and reproductive characteristics of an individual. Therefore, differences in these factors across studies might contribute to discrepancies in results of studies examining the effects of age and menopause on word-finding abilities. Similarly, dissimilarities in sample population characteristics across comparison groups in a cross-sectional study could also affect the results. Especially in cross-sectional cognitive ageing studies, these differences are likely to appear because women are studied from different birth cohorts. For example, in the UK, the minimum school leaving age increased from 14 to 15 in 1947 and from 15 to 16 in 1972, an indication that the older cohorts would have had access to fewer years of education than the younger cohorts (Bolton, 2012). Also, the average age of childbearing has been increasing since 1975 till date (Briggs, 2014). This suggests that the younger cohorts would have a later age at childbirth than the older cohorts. Therefore, to arrive at consistent findings for the effects of age on word-finding abilities, it is essential to match age groups on demographic and reproductive characteristics. Additionally, it is also important to study the interactive effects of demographic and reproductive characteristics on word-finding abilities.

The present study design was cross-sectional and information on demographic characteristics and reproductive markers was collected for three main reasons. The first reason was to verify whether the study sample was representative of the general population from which the participants were recruited. The second reason was to match the comparison groups on these variables (this is the focus of the current chapter) and the third reason was to study the relationships between these variables and word-finding measures (discussed in Chapters 6, 7, 8). The current chapter reviews studies that have examined the effects of demographic (education, IQ) and reproductive characteristics (age at menarche, menstrual cycle length, age at first childbirth, number of children, age at menopause, number of years since menopause and reproductive years) on word-finding abilities. There is little evidence of an association between these variables and word-finding performance and therefore, the above-mentioned factors were chosen to supplement previous literature and explore novel relationships. Additionally, the reproductive markers were selected because they reflect change in hormone levels across the lifespan.

5.2. Relationships between demographic, reproductive variables and word-finding abilities

5.2.1. Effects of education, IQ on word-finding abilities

The relationship between education and word-finding ability has received some attention, whereas few researchers have investigated the effects of IQ on this cognitive ability. It is reported that education is positively associated with performance on verbal fluency (Brickman et al., 2005; Elkadi et al., 2006; Gladsjo et al., 1999; Goral et al., 2007; Tombaugh et al., 1999; Van der Elst et al., 2006) and verbal naming tasks

(Connor et al., 2004; Elkadi et al., 2006; Neils et al., 1995; Pena-Casanova et al., 2009a; Tsang & Lee, 2003; Welch et al., 1996). Individuals with more years of education generate a greater number of words on verbal fluency tasks and have higher accuracy scores on naming tasks than those with fewer years of education. Like education, higher IQ is also associated with better word-finding abilities. The 1946 British cohort study showed that both education attained by 26 years of age and cognitive ability measured at the ages of 8 and 26 years were positively correlated with verbal fluency performance at midlife (at the age of 53) (Hatch, Feinstein, Link, Wadsworth, & Richards, 2007). Steinberg, Bieliauskas, Smith, Langellotti, and Ivnik (2005), who measured full scale IQ using the WAIS-R test (Wechsler, 1987), also found that letter fluency was associated with both IQ and education, although more strongly with IQ. Bolla, Lindgren, Bonaccorsy, and Bleecker (1990) published contradictory findings. They reported that verbal IQ and not education was a significant predictor of verbal fluency performance after controlling for the effects of age and sex. Discrepancies in findings between Steinberg et al. (2005) and Bolla et al. (1990) may have occurred because of differences in the manner IQ was measured in both the studies. Steinberg et al. (2005) used the full scale IQ measure from WAIS-R (Wechsler, 1987), whereas Bolla et al. (1990) used the raw scores from the vocabulary subtask of WAIS-R to measure IQ. It is also possible that multicollinearity issues (strong association between IQ and education) in regression models might have also contributed to such a finding in Bolla et al.'s (1990) study.

Although there is some evidence that education levels and IQ affect word-finding performance, it is not clear whether these demographic variables interact with age to influence verbal fluency or verbal naming across the lifespan. For example, existing literature suggests that both education and age are significant predictors of verbal fluency performance (Gladsjo et al., 1999; Tombaugh et al., 1999), but differential age-related decline in verbal fluency based on education levels has not been confirmed yet (Brickman et al., 2005; Kempler, Teng, Dick, Taussig, & Davis, 1998). Not all cross-sectional studies in the literature on cognitive ageing and psychoendocrinology have investigated the relationships between age, education, IQ and word-finding measures or controlled for their effects by matching comparison groups on these variables. As specified earlier, in cross-sectional studies older cohorts tend to have fewer years of education than younger cohorts mostly due to differences in access to education over the years. These differences in education may contribute to better performance by younger adults on word-finding tasks which otherwise may not be seen in groups matched for education levels.

Similar issues have been observed in the menopause literature. For example, Berent-Spillson et al. (2012) showed a significant effect of menopause stage on verbal fluency performance whereas other researchers (Herlitz et al., 2007; Lokken & Ferraro, 2006; Weber et al., 2013) did not. Berent-Spillson et al. (2012) did not control for the effects of education but the others did. Moreover, the premenopausal women in Berent-Spillson et al.'s (2012) study had more years of education than the postmenopausal women. Therefore, one cannot be sure whether the finding of a significant effect of menopause stage on verbal fluency was confounded by effects of education.

5.2.2. Effects of reproductive markers on word-finding and other cognitive abilities

The effects of reproductive history on word-finding abilities have been relatively less studied. The reproductive history of a woman determines the cumulative hormone exposure across her lifetime. Women vary substantially in their reproductive histories, and therefore this can result in differences in cumulative hormone exposure across individuals. There is evidence that increased lifetime exposure to estrogen is associated with better global cognitive functioning as measured by the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) (Smith et al., 1999) and a lower risk of Alzheimer's disease (AD) (Fox, Berzuini, & Knapp, 2013). Therefore, it could be predicted that women varying in reproductive histories would differ in their cognitive abilities. Also, age- or menopause-related cognitive declines may differ among women varying in these characteristics. The following subsections discuss important reproductive events (puberty, pregnancy, menopause) in a woman's lifetime. Each subsection first outlines the hormonal changes that occur during an event and then discusses the relationship of the respective marker with word-finding performance. Literature in this area is very sparse, and therefore studies that have investigated the effects of these reproductive markers on other cognitive abilities and onset of AD were also reviewed. This was undertaken in order to formulate hypotheses about the associations between reproductive markers and word-finding performance.

5.2.2.1. Puberty (age at menarche)

Low levels of estrogen and progesterone are secreted by the ovaries up to 8 years of age. A slow rise is seen in these levels followed by a rapid increase at the age of 11 (Edmonds, 2012). Girls typically reach puberty and begin their menstrual cycles between 8.5 and 13.3 years of age (Edmonds, 2012). From puberty till perimenopause, menstrual cycles occur on a monthly basis with the cycle length ranging from 23 to 35 days (Impey & Child, 2012).

A marker of hormone changes at puberty is the age at menarche with the average age at menarche in the UK at 12.7 years (Morris, Jones, Schoemaker, Ashworth, Swerdlow, 2011). An earlier age at menarche is associated with early onset of ovulatory cycles (Vihko & Apter, 1984) and higher estradiol levels in adulthood (Apter, Reinila, & Vihko, 1989; Bernstein, Pike, Ross, & Henderson, 1991). The existing literature shows that a later age at menarche is correlated with lower performance on tasks of visual memory (as measured by Benton's visual retention test; Benton, 1965) and psychomotor speed (Trail Making Test A & B; Reitan, 1958) after correcting for age, education, depressive symptoms, marital status, caffeine intake, physical inabilities and comorbidity (Ryan et al., 2009). It has also been found that a later age at menarche is associated with low scores on global cognition as measured by MMSE (Smith et al., 1999) and an increased risk of AD (Paganini-Hill & Henderson, 1994). These findings suggest that a later hormone exposure at puberty increases the risk of cognitive impairments and AD.

The studies reviewed above provide evidence for neuroprotective effects of an early age at menarche on cognition. However, contradictory results of no significant associations between age at menarche and global cognition, verbal fluency, verbal memory, executive functions (Ryan et al., 2009), verbal naming (Smith et al., 1999) or AD risk (Fox et al., 2013) have also been published. Thus, the role of age at menarche in shaping cognitive performance in later life remains inconclusive.

5.2.2.2. Pregnancy (parity, number of children and age at first childbirth)

In the reproductive years, pregnancy is another salient phase of variation in ovarian hormone exposure for many women. The placenta is the main source of estrogen during pregnancy and of the three types of estrogen, estrone (E1), estradiol (E2) and estriol (E3), it produces more E3. E3 levels rise gradually throughout pregnancy. The level of progesterone also increases linearly from the 35th day of gestation until the end of term (Oats et al., 2010). Following the birth of the child, hormone levels decline abruptly and remain at low levels until the end of lactation. Parous women tend to have shorter cycle lengths and, after controlling for cycle length, it is found that estrogen levels in parous women are 22% lower than those in nulliparous women (Bernstein et al., 1985). With reference to the role of parity in cognition, no relationship between parity and cognition has been found in healthy postmenopausal women (Ryan et al., 2009; Smith et al., 1999). However, it has been indicated that parous women are at an increased AD risk than nulliparous women (Ptok, Barkow, & Heun, 2002).

The number of children a woman has also affects hormone levels. Women with four or more children have lower estrogen levels than women with one child (Chubak et al., 2004), an indication that women with more children may be at a greater risk of cognitive decline. Colucci et al. (2006) reported that women with three or more pregnancies are at three-fold increased risk of AD than nulliparous women. An increase in the number of pregnancies has also been associated with an early onset of AD (Colucci et al., 2006; Sobow & Kloszewska, 2004). Dunkin et al. (2005) reported a positive weak correlation between number of children and executive functioning in postmenopausal women who were treated with estrogen. As stated earlier, women with more children have lower estrogen levels than women with fewer children, and therefore supplementing them with additional estrogen, as mentioned in the above study, may have affected their executive functions positively. However, Ryan et al. (2009) found no relationship between the number of children and cognitive abilities (global cognition, verbal fluency, verbal memory, executive functions, and visual memory) in postmenopausal women with no dementia; thus, giving rise to inconsistencies on the role of this reproductive marker in cognition.

Another marker that has been utilized to represent reproductive status is age at first childbirth. Women with later age at first childbirth remain in the nulliparous high hormone exposure state for a longer time than women with younger age at first childbirth. Therefore, it might be predicted that women with a later age at first childbirth may have better cognitive abilities than women with an earlier age at childbirth. These assumptions receive support from a prospective cohort study which showed that women with an age at first childbirth between 21 and 29 years obtained better scores on the MMSE and produced more words on verbal fluency tasks in later life than women who had had a child before 21 years (Ryan et al., 2009). Similarly, Fox et al. (2013) found that women with a pregnancy after the age of 21 years were at a lower risk of AD than women who gave birth earlier, after controlling for age, education and family history of dementia. Increased hormone exposure linked to later age of first childbirth may offset the negative effects of age and menopause later in life and hence, delay cognitive decline.

5.2.2.3. Menopause (age at menopause, number of years since menopause and reproductive years)

The onset of menopause marks a major reproductive event in midlife years. Women begin to experience changes in frequency and regularity of menstrual cycles. Estrogen levels decrease in the perimenopausal stage and continue to decline postmenopause (Burger et al., 2002, 2007). A later age at menopause is associated with more years of exposure to ovarian hormones. The positive benefits of this increased hormone exposure have been demonstrated on global cognition with higher scores on MMSE (Lebrun et al., 2005; McLay, Maki, & Lyketsos, 2003), lesser decline in executive functions (Ryan et al., 2009) and later onset of AD (Sobow & Kloszewska, 2004). Sobow and Kloszewska (2004) showed that with every increase of two years in menopausal age, the onset of AD was delayed by one year. However, a few researchers have also found no correlation between age at menopause and cognitive abilities such global cognition, visual memory and processing speed (Ryan et al., 2009) or increased risk and earlier onset of AD (Colucci et al., 2006; Fox et al., 2013; Paganini-Hill & Henderson, 1994).

Women who have been in the postmenopause stage for more than 20 years have lower estradiol than women within 4 years of menopause (Chubak et al., 2004). Therefore, number of years since menopause may be a predictor of cognitive performance in later life. The effect of this variable on cognition remains unclear. As discussed in Chapter 2, time since menopause does not affect verbal fluency and naming abilities in postmenopausal women (Elsabagh et al., 2006; Henderson et al., 2013). In contrast, evidence from treatment studies suggests that recent menopausal women exhibit improvements in their cognitive abilities but not longer-term menopausal women (Dunkin et al., 2005; Matthews et al., 1999), an indication that estrogen exerts it protective effects on cognition only in younger menopausal women.

The number of reproductive years is yet another useful way to indirectly estimate endogenous hormone exposure. It is often measured by subtracting the age at menarche from the age at menopause. The higher the number of reproductive years, the greater is the estimated duration of hormone exposure. For example, consider two individuals who achieved menarche at the age of 12 and 14 years respectively, and then experienced menopause at the age of 52 years. If reproductive activity and exogenous hormone exposures are the same in both of them, then cumulative hormone exposure may be greater in the woman who experienced an earlier menarche. It has been reported that the number of reproductive years is positively correlated with performance on verbal fluency (Ryan et al., 2009) and negatively correlated with AD risk (Fox et al., 2013). Every additional increase of a month in the reproductive span decreases AD risk by 0.45%. However, conflicting trends have also been noted, with some researchers finding a higher number of reproductive years being associated with a greater risk of dementia (Geerlings et al., 2001). The prospective Rotterdam cohort study (Geerlings et al., 2001), carried out in naturally postmenopausal women with apolipoprotein E4 genotype, found that women with a reproductive period of 34-36 years were at 1.56 times greater risk of AD than women with a reproductive period of less than 34 years. Similarly, women with reproductive periods of 37-39 years and greater than 39 years were at 1.64 and 1.78 times higher risk respectively, compared to women with reproductive periods of 34 years. Yet, others reported no association between the number of reproductive years and the risk of dementia (Colucci et al., 2006).

There has been some progress in understanding the relationships between reproductive markers, cognitive abilities and AD onset but results remain fragmented. Similarly, research investigating the effects of reproductive markers on word-finding performance is limited. Another aspect of the research that requires more work is the method used to quantify the reproductive markers used in the investigation of hormone effects on cognitive abilities. Most researchers have concentrated on examining the effect of individual reproductive markers on cognitive abilities, although some investigators have also employed cumulative measures. Smith et al. (1999) devised an Index of Estrogen Exposure (IEE) based on a combination of markers that increased hormone exposures such as nulliparity, later age at menopause, duration of estrogen replacement therapy, and postmenopausal weight, and a set of markers that decreased hormone exposures such as later age at menarche and more years since menopause. They found that as the IEE index increased, global cognitive functioning and verbal attention increased. Hesson (2012) used a very similar measure, the Index of Cumulative Estrogen Exposure (ICEE), and showed that women with higher cumulative estrogen exposure performed better on tests of prospective memory. The differences between the ICEE (Hesson, 2012) and the IEE (Smith et al., 1999) were that the ICEE used body mass index instead of postmenopausal body weight and also included duration of breast feeding, whereas the IEE did not. Fox et al. (2013) also used a cumulative measure of hormone exposure to investigate AD risk in a cohort of British women and found that greater hormone exposure was associated with decreased AD risk. These studies indicate that a cumulative measure might be helpful in investigating the role of reproductive history on late-life cognition. The current study initially focusses on studying the effects of the reproductive markers individually. A composite approach is explored in Chapter 8.

The cross-sectional studies that have examined the effects of age and menopause on word-finding abilities have not fully explored the relationships between reproductive markers and word-finding performance. This provides the motivation for the current study to examine the interactive effects of these variables with age and menopause in determining word-finding performance. The available literature suggests that more years of education, higher IQ, later age at first childbirth (greater than 21 years), later age at menopause and greater number of reproductive years are associated with better performance on verbal fluency, but no association has been shown with age at menarche or parity. Based on this evidence, it was predicted that women with the above listed characteristics may show a slower rate of age-related cognitive decline than women with lower levels of education, lower IQ, younger age at first childbirth, earlier age at menopause and shorter reproductive spans. The following sections report the demographic and reproductive characteristics of the current study sample. The associations between these variables and word-finding are reported in Chapters 6 and 7. Whether age-related decline in word-finding varies across women differing on these characteristics is discussed in Chapter 8. The next section provides details on the methods that were used to gather information on demographic and reproductive characteristics for the current study sample.

5.3. Methods

5.3.1. Sample

Data from 78 healthy women in three age groups were collected: Group I (*n* = 32; 46-55 years), Group II (*n* = 24; 56- 65 years) and Group III (*n* = 22; 70-79 years). The first age group was subdivided as a function of menopause status (pre: *n* = 9, peri: *n* = 11, post: *n* = 12). All women in Groups II and III were postmenopausal.

5.3.2. Tests administered and data collection

Vocabulary and non-verbal reasoning levels were assessed using the vocabulary and matrix reasoning subtasks of the WASI (Wechsler, 1999). Vocabulary and non-verbal reasoning T scores were computed. Full Scale IQ was estimated by combining the T scores obtained on the subtasks and scaling them to standardized IQ equivalents.

Information on demographic characteristics and reproductive markers was collected using questionnaires. Past researchers have generally gathered information on reproductive markers by using similar forms of self-report (Henderson et al., 2003; Xu et al., 2005). It has been found that 75-90% of women accurately recall their age at menarche and age at menopause (Bean, Leeper, Wallace, Sherman, & Jagger, 1979). There is a high concordance rate (82%) between self-reports and medical reports on oophorectomy status (Kritz-Silverstein & Barrett-Connor, 2002). Therefore, the questionnaire-based procedure was deemed suitable for the present study to collect data on demographic characteristics (age, years of education) and reproductive markers (age at menarche, menstrual cycle length, age at first childbirth, number of children, age at menopause, number of years since menopause and reproductive years) as described in Chapter 4. The screening questionnaire was administered over the telephone prior to inviting participants to complete the main study. The more detailed interview questionnaire was administered on the day of testing.

Age, age at menarche, age at first childbirth, age at menopause, number of years since menopause and reproductive years were recorded in years. Education was measured as the number of years spent in formal education. Menstrual cycle length was counted in number of days. Reported cycle history prior to entering the peri and postmenopause stages was used to determine menstrual cycle lengths for these groups of women. The current study included five women who had undergone hysterectomies. It was not possible to obtain data on ovarian function cessation in this group of women through their verbal reports and therefore, the age at menopause may not be accurate. A method that has been used to estimate the age at menopause for such women is the average age at menopause for women in the group who have had no hysterectomy (Kritz-Silverstein & Barrett-Connor, 2002). The age at menopause for women with a history of hysterectomy was estimated similarly in this study. Number of years since menopause was calculated by subtracting the age at menopause from the chronological age. The number of reproductive years was computed by subtracting the age at menarche from the age at menopause.

5.3.3. Statistical analysis

To study trends in the data and to verify whether the sample groups were representative of published population statistics, the means and standard errors were computed for each age and menopause group. A series of ANOVAs was used to investigate how well matched the groups were on demographic and reproductive characteristics. Groups were defined by Age (46-55, 56-65, 70-79 years) and Menopause status (pre, peri, postmenopause) on the demographic and reproductive characteristics. The ANOVAs were conducted separately for Age group and Menopause stage comparisons. Pearson correlations were used to examine the relationships among demographic and reproductive variables.

5.4. Results

5.4.1. Comparison of demographic characteristics and reproductive markers across the three age groups (46-55, 56-65, 70-79 years)

ANOVAs were conducted using the Demographic characteristics or the Reproductive markers as dependent variables and Age group as the independent variable in order to compare women across the three groups.

5.4.1.1. Demographic characteristics

Age

The mean ages (± *SEM*) for Group I (46-55), Group II (56-65) and Group III (70-79) were 51.27 (0.43), 60.89 (0.60) and 74.16 (0.61) years respectively.

Years of education

Women across the Age groups differed on number of years of education, $F(2, 75) = 4.73$, $p = .012$. Post hoc independent *t*-tests with Bonferroni correction ($\alpha = .05/3 = .017$) showed that women in Group I had more years of education than women aged 70-79 years, $t(52) = 3.15$, $p = .003$. Women in Group II did not differ from Groups I and III on this variable (see Table 5.1).

FSIQ, Vocabulary T score, Matrix reasoning T score

The FSIQ was comparable across the three Age groups, $F(2, 75) = 2.19$, $p = .119$. There were no significant differences between the groups on the vocabulary subtask of WASI, $F(2, 75) = 0.63$, $p = .536$, but a main effect of Age group was seen for the matrix reasoning T score, $F(2, 75) = 7.02$, $p = .002$. From the mean scores, it is evident that scores were higher in the older groups (see Table 5.1). Post hoc independent *t*-tests with Bonferroni correction ($\alpha = .05/3 = .017$) showed that women in

Group I had lower scores than women in Group III, $t(52) = -3.67$, $p = .001$. Women in Group II did not statistically differ from Groups I and III on matrix reasoning.

To examine the relationships between IQ scores, years of education and age, Pearson correlations were conducted. In line with the ANOVA results, correlations showed that age was significantly associated with matrix reasoning, but not with FSIQ or vocabulary (see Table 5.2). Matrix reasoning T scores increased with age. An increase in the number of years of education was related to higher FSIQ and vocabulary but not matrix reasoning T scores. The relationship of FSIQ with vocabulary and matrix reasoning T scores was also examined. Analyses revealed that matrix reasoning had a stronger correlation with FSIQ than vocabulary.

Table 5.2

Correlations between FSIQ, vocabulary T score, matrix reasoning T score, years of education and age (N = 78)

	FSIQ	Vocabulary T score	Matrix reasoning T score
Age	.20	-.15	.37**
Years of education	.32**	.40**	.14
FSIQ	-	.66**	.83**

** $p < .01$.

Table 5.1

Means (± SEM) for demographic characteristics and reproductive markers as a function of age group

		Group I (46-55 years) (*n* = 32)	Group II (56-65 years) (*n* = 24)	Group III (70-79 years) (*n* = 22)
Demographic	Age (in years)	51.27 (0.43)	60.89 (0.60)	74.16 (0.61)
	Years of education (in years)	17.41 (0.43)	16.67 (0.52)	15.36 (0.46)
	FSIQ	119.06 (1.28)	120.79 (1.45)	123.27 (1.58)
	Vocabulary T score	62.84 (0.83)	62.25 (0.95)	61.45 (0.83)
	Matrix reasoning T score	58.88 (0.92)	61.13 (1.07)	64.59 (1.32)
	Laterality quotient for right-handers	92.96 (+60 to +100) (*n* = 27)	91.30 (+50 to +100) (*n* = 23)	92.63 (+70 to +100) (*n* = 19)
	Laterality quotient for left-handers*	-93.33 (-100 to -60) (*n* = 3)	-	-60.00 (-60 to -60) (*n* = 1)
	Laterality quotient for ambidextrous participants	10.00 (-20 to +40) (*n* = 2)	0.00 (0 to 0) (*n* = 1)	5.00 (-30 to +40) (*n* = 2)
Reproductive	Age at menarche (in years)	12.79 (0.21)	13.05 (0.31)	13.32 (0.27)
	Length of menstrual cycle (in days)	27.97 (0.43)	27.75 (0.35)	28.55 (0.21)
	Number of children**	1.75 (0.23) (*n* = 32)	2.00 (0.19) (*n* = 24)	2.62 (0.27) (*n* = 21)
		2.33 (0.19) (*n* = 24)	2.09 (0.18) (*n* = 23)	2.62 (0.27) (*n* = 21)
	Age at first childbirth (in years)	28.21 (0.89) (*n* = 24)	30.35 (1.09) (*n* = 23)	23.62 (0.81) (*n* = 21)
	Age at menopause (in years)***	50.33 (0.69) (*n* = 12)	53.00 (0.52) (*n* = 24)	50.06 (0.72) (*n* = 22)
		50.33 (0.69) (*n* = 12)	53.00 (0.55) (*n* = 23)	50.06 (0.88) (*n* = 18)
	Number of years since menopause (in years)***	2.65 (0.47) (*n* = 12)	7.85 (0.68) (*n* = 24)	24.02 (1.14) (*n* = 22)
		2.65 (0.47) (*n* = 12)	7.71 (0.70) (*n* = 23)	24.12 (1.36) (*n* = 18)
	Number of reproductive years (in years)***	37.75 (0.78) (*n* = 12)	39.84 (0.60) (*n* =24)	36.70 (0.80) (*n* = 22)
		37.75 (0.78) (*n* = 12)	39.92 (0.62) (*n* =23)	36.73 (0.96) (*n* = 18)

Note. *There were no left handed participants in Group II (56-65 years). Values in parentheses for laterality quotient represent the range of scores **The upper row represents the mean for number of children including women with and without children and the lower row represents the mean only for women with a child/children. In Group III, one woman who reported not having any children because of infertility was excluded from this analysis. ***The upper rows represent the means for age at menopause, number of years since menopause and reproductive years when the data were analysed including women with and without hysterectomies. The lower row represents the means after women with hysterectomies were excluded.

5.4.1.2. Reproductive markers

Age at menarche and length of menstrual cycle

For the age at menarche, there was no significant difference between the Age groups, $F(2, 75) = 1.09$, $p = .343$. As evident from the mean scores (see Table 5.1), women in Group III had only a slightly higher age at menarche compared to the other two groups. In the total sample, the age range of menarche varied from 10 to 16 years. Length of menstrual cycle was comparable across the three groups, $F(2, 75) = 1.07$, $p = .348$. The mean (± *SEM*) cycle length for all women was 28.06 (± 0.22) days.

Age at first childbirth and number of children

The study sample included women who had and did not have children. To compare women across Age groups on the age at first childbirth, women who had no children were excluded. This resulted in a sample of 68 participants. There was a significant difference between the Age groups, $F(2, 65) = 12.77$, $p < .001$. Post hoc independent *t*-tests with Bonferroni correction showed that women in Group III had a significantly lower age at first childbirth compared to women in Group I, $t(43) = -3.77$, $p < .001$, and Group II, $t(42) = -4.89$, $p < .001$. Groups I and II did not differ significantly.

Out of 78 participants, one woman in Group III reported not having any children due to infertility. This participant was excluded for purposes of analysing the data for number of children. Women across the three Age groups varied in the number of children they had, $F(2, 74) = 3.49$, $p = .035$. From the mean scores, it is evident that the number of children increased between the older and younger age groups (see Table 5.1), but this did not survive a Bonferroni correction. The number of children in Groups I and II ranged from 0 to 4 and in Group III ranged from 1 to 6, supporting the previously described result that women in the oldest group had more children. When women who had no children were excluded from the sample (n = 68), there was no significant difference across the Age groups on this variable, $F(2, 65) = 1.53$, $p = .225$.

Age at menopause and number of years since menopause

As mentioned above, the study sample included five women who had undergone hysterectomies. Analyses were done by both excluding and including these women in the sample. When women with hysterectomies were excluded, differences across Age groups for the age at menopause was significant, $F(2, 50) = 5.81$, $p = .005$. Post hoc independent t-tests with Bonferroni corrections showed that women in Group II had a higher age at menopause than women in Group I, $t(33) = 2.94$, $p = .006$, and in Group III, $t(39) = 2.96$, $p = .005$. Women in Groups I and III did not differ. Age group differences remained the same when the data were analysed including women with hysterectomies.

For postmenopausal women, ANOVA[5] showed a significant difference between Age groups on number of years since menopause when the data were analysed after excluding women with hysterectomies, $F(2, 50) = 121.70$, $p < .001$. Post hoc independent t-tests revealed significant differences between Groups I and II, $t(33) = -4.92$, $p < .001$, Groups I and III[6], $t(28) = -12.46$, $p < .001$, and Groups II and III[7], $t(39) = -11.40$, $p < .001$. The mean number of years since menopause increased from Groups I to III (see Table 5.1). The findings remained the same when women with hysterectomies were included in the sample.

---

[5] Levene's test was significant, $F(2, 50) = 7.57$, $p = .001$. Welch's test, $F(2, 31.246) = 114.08$, $p < .001$, indicated a statistically significant difference across the groups for the number of years since menopause.

[6] The assumption of equal variances was violated and Levene's test was significant ($p = .002$). The statistical results with the assumption of unequal variances also showed significant differences between these two groups for the number of years since menopause, $t(20.796) = -14.89$, $p < .001$.

[7] The assumption of equal variances was violated and Levene's test was significant ($p = .024$). The statistical results with the assumption of unequal variances also showed significant differences between these two groups for the number of years since menopause, $t(25.710) = -10.70$, $p < .001$.

Number of reproductive years in postmenopausal women

When women with hysterectomies were excluded, the three Age groups differed significantly on this reproductive marker, $F(2, 50) = 4.86$, $p = .012$. Post hoc independent *t*-tests with Bonferroni correction ($\alpha = .05/3 = .017$) showed a significant difference between Groups II and III, $t(39) = 2.90$, $p = .006$, but Group I did not vary from Groups II and III. Participants in Group II had comparatively greater number of reproductive years than the others (see Table 5.1). The results remained the same after including women with hysterectomies.

In summary, women across Age groups were matched on vocabulary T score, age at menarche and menstrual cycle length. They differed in the number of years of education, matrix reasoning, age at first childbirth, number of children, age at menopause, number of years since menopause and reproductive years.

5.4.2. Comparison of demographic characteristics and reproductive markers across menopause stages (46-55 years, pre, peri and postmenopause)

To compare women across menopause stages, ANOVAs with Demographic or Reproductive variables as the dependent measure and Menopause stage as the between group factor were conducted.

5.4.2.1. Demographic characteristics

Age

In Group I (46-55 years), women across the three stages of menopause differed significantly on Age, $F(2, 29) = 8.61$, $p = .001$. Post hoc independent *t*-tests with Bonferroni correction ($\alpha = .05/3 = .017$) showed that women in the postmenopausal group were significantly older than premenopausal women[8], $t(19) = 4.36$, $p < .001$.

[8] The assumption of equal variances was violated and Levene's test was significant ($p = .019$). However, the statistical results with the assumption of unequal variances also showed significant differences between these two groups on age, $t(16.680) = -4.77$, $p < .001$.

Perimenopausal women did not differ significantly in age from the other two groups (see Table 5.3).

Years of education

The number of years of education was comparable across women in the three stages of menopause, $F(2, 29) = 0.47$, $p = .630$ (see Table 5.3).

FSIQ, Vocabulary T score, Matrix reasoning T score

Women across menopause stages did not differ significantly on FSIQ (see Table 5.3), $F(2, 29) = 0.25$, $p = .785$, vocabulary T score[9], $F(2, 29) = 1.55$, $p = .230$ or matrix reasoning T score, $F(2, 29) = 1.88$, $p = .171$.

5.4.2.2 Reproductive markers

Age at menarche and length of menstrual cycle

Women across menopause stages did not differ on the age at menarche, $F(2, 29) = 0.33$, $p = .721$ (see Table 5.3) or length of menstrual cycle, $F(2, 29) = 0.59$, $p = .561$. All women had a mean (± *SEM*) cycle length of 27.97 (± 0.43) days.

Age at first childbirth and number of children

Nulliparous women were excluded from the analysis when comparing women on the age at first childbirth. This resulted in a sample of 24 participants. There was no significant difference between women across menopause stages on the age at first childbirth, $F(2, 21) = 0.17$, $p = .844$. For the number of children, data from all women were considered ($n = 32$) and the analysis showed no significant differences between women in different menopause stages[10], $F(2, 29) = 0.56$, $p = .578$. However, when women without children were excluded, women across the stages of menopause varied

---

[9] The levene's test was significant, $F(2, 29) = 3.57$, $p = .041$. Welch's test showed no significant differences between the groups on vocabulary T score, $F(2, 16.757) = 1.10$, $p = .355$.

[10] Levene's test was significant, $F(2, 29) = 3.54$, $p = .042$. However, the results from the Welch's test also showed no significant differences across the menopause stages for the number of children, $F(2, 16.865) = .39$, $p = .683$

on the number of children, $F(2, 21) = 4.84$, $p = .019$. Post hoc independent *t*-tests showed that premenopausal women had more children than perimenopausal women, $t(14) = 2.94$, $p = .011$. Postmenopausal women did not vary from pre and perimenopausal women on this variable. In summary, women across menopause stages were well matched on IQ, education and reproductive events but differed on age.

Table 5.3

Means (± SEM) for demographic characteristics and reproductive markers as a function of menopause stage, aged 46-55 years

		Premenopause (n = 9)	Perimenopause (n = 11)	Postmenopause (n = 12)
Demographic	Age (in years)	49.37 (0.37)	50.97 (0.66)	52.98 (0.66)
	Years of education (in years)	17.67 (0.90)	16.82 (0.86)	17.75 (0.55)
	Full Scale IQ	119.11 (2.82)	117.91 (1.89)	120.08 (2.21)
	Vocabulary T score	60.56 (2.00)	63.55 (1.36)	63.92 (1.00)
	Matrix reasoning T score	61.22 (1.36)	56.82 (1.55)	59.00 (1.61)
	Laterality quotient for right-handers	87.50 (+60 to +100) (n = 8)	93.33 (+70 to +100) (n = 9)	97.00 (+80 to +100) (n = 10)
	Laterality quotient for left-handers	-100.00 (-100 to +100) (n = 1)	-	-90.00 (-100 to -80) (n = 2)
	Laterality quotient for ambidextrous participants*	-	10.00 (-20 to +40) (n = 2)	-
Reproductive	Age at menarche (in years)	13.01 (0.53)	12.82 (0.30)	12.58 (0.31)
	Length of menstrual cycle (in days)	28.72 (0.66)	27.68 (0.58)	27.67 (0.90)
	Number of children**	2.11 (0.59) (n = 9)	1.73 (0.27) (n = 11)	1.50 (0.36) (n = 12)
		3.17 (0.40) (n = 6)	1.90 (0.23) (n = 10)	2.25 (0.25) (n = 8)
	Age at first childbirth (in years)	27.33 (1.02) (n = 6)	28.30 (1.97) (n = 10)	28.75 (0.94) (n = 8)
	Age at menopause (in years)	-	-	50.33 (0.69)
	Number of years since menopause (in years)	-	-	2.65 (0.47)
	Number of reproductive years (in years)	-	-	37.75 (0.78)

Note. *There were no ambidextrous participants in pre and postmenopausal groups and no left handed participants in the perimenopausal group. Values in parentheses for laterality quotient represent the range of scores **The upper row represents the mean for number of children including women with and without children, and the lower row represents the mean only for women with a child/children.

5.4.3. Comparison of demographic characteristics and reproductive markers between recent and longer-term postmenopausal women

Investigating the effects of Time since menopause on word-finding abilities was a post hoc research aim. The demographic and reproductive characteristics for these two groups of women are discussed below.

Postmenopausal women were sub-classified into recent (less than six years since menopause) and longer-term (greater than six years since menopause) groups according to the STRAW +10 classification (Harlow et al., 2012). Independent *t*-tests were conducted with the Demographic characteristics and Reproductive markers as the dependent variables and Time since menopause as the independent variable. The two groups differed significantly on age[11], $t(56) = -7.40$, $p < .001$, number of years of education, $t(56) = 3.89$, $p < .001$, and vocabulary T scores, $t(56) = 3.21$, $p = .002$. Longer-term menopausal women were older, had fewer years of education and lower vocabulary scores than recent postmenopausal women. Both the groups were matched on all the other variables (see Table 5.4). After excluding women without children, the two groups of postmenopausal women did not vary in the number of children. Recent and longer-term menopausal women were matched for age at menopause and reproductive years after excluding women with hysterectomies.

[11] The assumption of equal variances was violated and Levene's test was significant ($p < .001$). However, the statistical results with the assumption of unequal variances also showed significant differences between these two groups on age, $t(52.542) = -9.87$, $p < .001$.

Table 5.4

Means (± SEM) for demographic characteristics and reproductive markers across recent and longer-term postmenopausal women

		Recent (n = 16)	Longer-term (n = 42)
Demographic	Age (in years)	54.38 (0.86)	68.06 (1.09)
	Years of education (in years)	18.19 (0.49)	15.71 (0.34)
	Full Scale IQ	122.13 (1.87)	121.38 (1.14)
	Vocabulary T score	64.94 (0.91)	61.29 (0.61)
	Matrix reasoning T score	60.06 (1.31)	62.74 (0.95)
	Laterality quotient for right-handers	96.43 (+80 to +100) (n = 14)	91.58 (+50 to +100) (n = 38)
	Laterality quotient for left-handers	-90.00 (-100 to -80) (n = 2)	-60.00 (-60 to -60) (n = 1)
	Laterality quotient for ambidextrous participants	-	3.33 (-30 to +40) (n = 3)
Reproductive	Age at menarche (in years)	12.82 (0.33)	13.15 (0.21)
	Length of menstrual cycle (in days)	27.59 (0.77)	28.20 (0.18)
	Number of children**	1.88 (0.34) (n = 16)	2.17 (0.18) (n = 42)
		2.50 (0.26) (n = 12)	2.28 (0.17) (n = 40)
	Age at first childbirth (in years)	28.83 (1.01) (n = 12)	26.95 (0.90) (n = 40)
	Age at menopause (in years)***	51.81 (0.78) (n = 16)	51.15 (0.49) (n = 42)
		51.81 (0.78) (n = 16)	51.22 (0.55) (n = 37)
	Number of years since menopause (in years)***	2.57 (0.34) (n = 16)	16.85 (1.34) (n = 42)
		2.57 (0.34) (n = 16)	16.28 (1.46) (n = 37)
	Number of reproductive years (in years)***	38.94 (0.87) (n = 16)	37.94 (0.54) (n = 42)
		38.94 (0.87) (n = 16)	38.09 (0.60) (n = 37)

Note. *There were no ambidextrous participants in the recent menopausal group. Values in parentheses for laterality quotient represent the range of scores. **The upper row represents the mean for number of children including women with and without children and the lower row represents the mean for only women with a child/children. ***The upper rows represent the means for age at menopause, number of years since menopause and reproductive years when the data were analysed including women with and without hysterectomies. The lower row represents the means after women with hysterectomies were excluded.

The relationships between demographic and reproductive variables in this group of postmenopausal women were examined using Pearson correlations (see Table 5.5). This group of women was chosen in order to examine the associations between menopause-related markers and demographics. In line with previous correlations, age was positively associated with matrix reasoning T scores and negatively with education and age at first childbirth. There were no significant associations between FSIQ and reproductive markers. Higher vocabulary scores were associated with an early age at menarche and fewer years since menopause. Matrix reasoning scores increased with increase in the years since menopause. Among the reproductive markers, as age at menarche increased reproductive years decreased. Age at first childbirth was negatively associated with number of children and years since menopause. An increase in the age at menopause was correlated with an increase in the number of reproductive years.

Table 5.5

Relationship among the demographic and reproductive variables in postmenopausal women (n = 58, unless otherwise stated in parentheses)

	Age	Age at menarche	Menstrual cycle length	Age at first childbirth (*n* = 52)	Number of children	Age at menopause	Number of years since menopause	Number of reproductive years
Age	-	.21	.20	-.50**	.22	-.18	.95**	-.24
Full Scale IQ	.11	-.12	.20	-.00	.09	.05	.08	.09
Vocabulary T score	-.27	-.28*	.05	.03	-.06	.15	-.29*	.26
Matrix reasoning T score	.32*	.02	.23	-.01	.14	-.05	.30*	-.06
Number of years of education	-.49**	-.25	-.00	.12	.05	.15	-.49**	.24
Age at menarche			.16	.06	.14	-.02	.19	-.41**
Menstrual cycle length				-.11	.04	.06	.16	-.01
Age at first childbirth (*n* = 52)					-.34*	.25	-.53**	.19
Number of children						.02	.19	-.03
Age at menopause							-.48**	.92**
Number of years since menopause								-.51**

$^{*}p < .05$, $^{**}p < .01$

5.4.4. Self-reports of memory problems

This study did not include in-depth interviews to investigate self-reports of memory problems. However, as part of the background study participants were asked whether they experienced any problems with memory and if so, what kind of problems.

59.4% of the participants in Group I (46-55 years) reported having difficulties in remembering names of people and sometimes words. In this group, the percentage of women complaining of memory difficulties in the premenopause stage (55.5%) was lower than those in the perimenopause (63.6%) and the postmenopause (58.3%) stages. 58.3% of women in Group II (56-65 years) reported memory difficulties. Two of the participants in this group reported that these problems had begun at their menopause transition and had worsened over time. One of the participants remarked that it took her considerably more time to remember words at present than earlier. 54.5% of women in Group III (70-79 years) had experienced memory problems in their daily life. Most of them reported problems in remembering names and appointments and difficulties in retrieving words in conversations.

5.5. Discussion

The present chapter had two aims. First, it aimed to verify whether the current study sample was representative of the general population from which the sample was recruited. Second, to examine whether women across the Age groups (46-55, 56-65, 70-79 years) or Menopause stages (pre, peri, postmenopause) or Time since menopause groups (recent, longer-term menopausal) were matched in their demographic and reproductive characteristics.

Women in all the three age groups were representative of belonging to a group of highly educated individuals with high average to superior IQs ($M \pm SEM$: 120.78 ± 0.86) (WASI, Wechsler, 1999). Women across the three age groups were well matched for FSIQ, vocabulary T score, age at menarche and menstrual cycle length. They differed in the number of years of education, matrix reasoning T scores, age at first childbirth, number of children, age at menopause, number of years since menopause and reproductive years. Women across the menopause stages in Group I (46-55 years) were comparable on education, IQ, vocabulary T scores, matrix reasoning T scores and all the reproductive markers. However, postmenopausal women were significantly older than premenopausal women. Recent and longer-term postmenopausal women were matched on FSIQ, matrix-reasoning T scores, age at menarche, menstrual cycle length, age at first childbirth, age at menopause and reproductive years. They differed on age, vocabulary T scores and education. The following sections discuss in detail the differences in demographic and reproductive characteristics across age groups and menopause stages.

The average level of education for the current sample was 16.60 years with number of years of education ranging between 12 and 21 years. The oldest cohort (70-79 years) had significantly fewer years of education than the youngest cohort (46-55 years). Also, the percentage of women having 12 years of education decreased from the oldest to the youngest cohort, reflecting greater access to education in the younger cohorts. This could have been partly because of an increase in the school leaving age from 15 to 16 years in 1972 (Bolton, 2012), and therefore it is likely that the younger cohorts who were born between 1947 and 1967 would have had access to more years of education than the oldest cohort who were born between 1932 and 1942. Overall participation in higher education increased between 1950 and 1970 from 3.4% to 8.4% in the UK (Bolton, 2012), making it more likely that the younger age group spent more years in higher education. In the current study, approximately 56% of women aged 46-55 years had 17-18 years of education, whereas this percentage was 62.5% in 56-65 years old and 54.5% in 70-79 years old. Data from the England and Wales 2011 census showed that the percentage of individuals having qualifications of degree level or above in the older cohorts aged 50-65 years (27.7%) was lower than that for the younger cohorts aged 35-49 years (33.6%) (ONS, 2014 March 7). The current study only partly supported the national trend, with a lower percentage of women having 17 to 18 years of education in the oldest group. These results also suggest that the groups comprised of a higher percentage of women with more years of education than the general population across the age groups.

Previous studies have shown that vocabulary knowledge (crystallised intelligence) remains stable or increases with advancing age (Bowles & Salthouse, 2008; Kave & Halamish, 2015; Kave & Yafe, 2014; Kemper & Sumner, 2001; Verhaegen, 2003), whereas matrix reasoning (fluid intelligence) decreases with age (Gong et al., 2005). The current study was consistent with the literature with stable vocabulary scores across age groups. However, women in the oldest group (70-79 years) had significantly higher matrix reasoning scores than women in the youngest group (46-55 years). WASI-R is an age-scaled assessment tool and T scores were computed for each age group for the matrix reasoning subtask. Therefore, higher T scores in the older group possibly reflects cohort differences in this ability. The correlational analysis in postmenopausal women (48-79 years) showed that as number of years since menopause increased, matrix reasoning scores increased. Estrogen levels decline postmenopause but testosterone levels remain unchanged (Burger et al., 2007), and the total estradiol and free estradiol concentrations in longer-term postmenopausal women are lower than recent postmenopausal women (Chubak et al., 2004). Psychoendocrinological studies have shown that women having low estrogen levels and high testosterone to estrogen ratios perform better on tasks favouring males (Hampson, 1990b; Hampson & Kimura, 1988). Based on this evidence, it is plausible that change in estrogen levels postmenopause may likely have an effect for fluid rather than crystallised aspects of cognition. The findings of the current study were not in agreement with Gong et al.'s (2005) results, which may be due to differences in the test materials used. Gong et al. (2005) used the Culture Fair score and the Performance IQ subtask of WAIS-R (Wechsler, 1987) to measure fluid reasoning, whereas the current study used only the matrix reasoning subtask from WAIS (Wechsler, 1999).

As mentioned earlier, all the three age groups were matched on the age at menarche and the menstrual cycle length. The age at menarche decreased slightly from the older to the younger age groups. A similar trend had been observed in the Breakthrough Generations Study conducted in the UK (Morris et al., 2011), where age at menarche decreased from women born in the 1930's (women in oldest group of the current study sample were born between 1932 and 1942) to women born in the 1940s and thereafter (women in the two younger age groups were born between 1947 and 1967). This slight nonsignificant decrease in the menarcheal age in the younger cohorts could be related to improvements in nutrition levels (Parent et al., 2003). All women had regular menstrual cycles with a mean cycle length of 28.06 (*SEM*: ± 0.22) days (Oats et al., 2010). Women across the three age groups varied in the age at first childbirth and the number of children. The data showed trends for women in the oldest group (70-79 years) to have a lower age at first childbirth and higher number of children compared to the younger women. These results were in line with the national statistics which suggests an increase in average childbearing age since 1975 and a decrease in the number of children in the younger cohorts (Briggs, 2014; Charlton, 2007; ONS, 2014 December 4). An increase in maternal age has also been reported in other western countries which are mostly due to increasing levels of education, greater career involvement, effective contraception and economic uncertainties (Heck, Schoendork, Ventura, & Kiely, 1997; United Nations, 2013; Virtala, Kunttu, Huttunen, & Virjo, 2006).

The average age at menopause in the UK is 51 years (National Health Service, 2015, November 12); women aged 46-55 years and 70-79 years followed the national trends. The results were also in agreement with the international trends which show that the age at menopause for women in the industrialized countries ranges between 48 and 52 years (Gold, 2011; Gold et al., 2013; Luoto, Laprio, & Utela, 1994; McKinlay, Brambilla, & Posner, 2008; Shuster, Rhodes, Gostout, Grossardt, & Rocca, 2010; Sowers & Pietra, 1995). The current study sample found that women aged 56-65 years had a later age at menopause (53 years) than the women in the other two groups. Because of this, the number of reproductive years was also greater in this age group when compared with the other postmenopausal women. The age at menopause was higher than the average age at menopause in the UK and therefore, the data were checked for possible outlier values. Two women in this group had been prescribed hormone-based medication during their menopause transition and reported a later age at menopause. However, removing their data did not lower the age at menopause for the whole group. Therefore, the slightly higher age at menopause in this group possibly reflects a sample bias.

In summary, the results of the study showed that women across age groups varied on years of education, age at first childbirth, number of children, age at menopause and reproductive years. Women aged 56-65 years had a later age at menopause and greater number of reproductive years. Women in the oldest group aged 70-79 years had fewer years of education, younger age at first childbirth and more children. Individuals with more years of education produce a greater number of words on verbal fluency tasks and obtain a higher accuracy score on naming tasks than individuals with fewer years of education (Brickman et al., 2005; Connor et al., 2004; Elkadi et al., 2006; Gladsjo et al., 1999; Goral et al., 2007; Pena-Casanova et al., 2009a; Tsang & Lee, 2003; Van der Elst et al., 2006). Also, an earlier age-related decline in naming has been reported in individuals with fewer years of education (Welch et al., 1996). Similarly, a later age at first childbirth, later age at menopause and a longer reproductive period have been associated with higher word production on verbal fluency tasks (Ryan et al., 2009). Thus, based on the previous literature and results of the current chapter, it was predicted that the effects of age on word-finding in the current study sample may be shaped or influenced by interaction of age with demographic and reproductive variables.

The study design recruited women across the three menopause stages within a single age decade (46-55 years). In agreement with earlier cross-sectional studies, postmenopausal women in the current study were slightly older than premenopausal women (Berent-Spillson et al., 2012; Lokken & Ferraro, 2006). Women in the different menopause stages were well matched on all the demographic (education, IQ, vocabulary and matrix reasoning T scores) and reproductive markers (the age at menarche, the menstrual cycle length, the age at first childbirth, and the number of children).

Recent and longer-term menopausal women differed on age, vocabulary and education but they were matched on the remaining variables. As seen in Chapter 2, age has been associated with verbal fluency and verbal naming abilities. Education and vocabulary are also associated with word-finding abilities. Thus, it was predicted that the effects of time since menopause on word-finding abilities might result from an interaction between time since menopause, age, education and vocabulary.

Summary

In summary, the current study sample groups followed the national trends for reproductive characteristics. However, the results showed that the present sample comprised of women with more years of formal education than the expected national trends across age. Women across the age groups or time since menopause groups were not equally matched on all demographic and reproductive characteristics. Women in the different stages of menopause, in the youngest group aged 46-55 years, were comparable on the demographic and reproductive variables studied, except age.

The forthcoming chapters investigate the relationships between these variables and word-finding measures using correlations (see details in Chapters 6, 7 and 8). They also examine the effects of age, menopause stage and time since menopause on verbal fluency (Chapter 6) and verbal naming (Chapter 7) taking into consideration the role of the demographic and reproductive characteristics covered in the current chapter. The interactive effects of demographic (age, vocabulary, education) and reproductive characteristics (menopause stage, age at menarche, menstrual cycle length, age at first childbirth, number of children, age at menopause, number of years since menopause and reproductive years) on word-finding abilities are investigated in Chapter 8.

Chapter 6

The effects of age and menopause on verbal fluency

6.1. Introduction

Verbal fluency tasks are frequently used in neuropsychological studies to examine word-finding abilities. Common tests of verbal fluency require generation of words from a specific semantic set (category fluency) or beginning with a particular letter (letter fluency) within a stipulated time, usually one-minute (Benton, 1968; Borkowski et al., 1967; Newcombe, 1969).

The literature on cognitive ageing shows a consistent age-related decline in category fluency (Brickman et al., 2005; Kemper & Sumner, 2001; Parkin & Java, 1999; Troyer et al., 1997; Van der Elst et al., 2006). However, findings for letter fluency are mixed. Studies demonstrating a significant decline in letter fluency (Brickman et al., 2005; Gladsjo et al., 1999; Gordon & Kindred, 2011; Lanting et al., 2009; Pena-Casanova et al., 2009b; Ruff et al., 1996; Tombaugh et al., 1999; Van der Elst et al., 2006; Zimmermann et al., 2014) and no decline in letter fluency (Kemper & Sumner, 2001; Parkin & Java, 1999; Sauzeon et al., 2011; Schmitter-Edgecombe et al., 2000; Troyer et al., 1997) with advancing age have been published. Thus, it is often reported that age effects are more prominent for category than letter fluency tasks. A factor that has been associated with inconsistent findings for letter fluency is the sex of an individual. There is a strong consensus that girls outperform boys in verbal fluency (Maccoby & Jacklin, 1974; Halpern, 1992; Hyde & Linn, 1988). However, this female advantage has not always been found in older adults. Reports of greater word production by women compared to men (Bolla et al., 1990) or by men compared to women (Singh-Manoux et al., 2012) or no significant differences between sexes (Brickman et al., 2005; Lanting et al., 2009; Tombaugh et al., 1999; Troyer et al., 1997) in verbal fluency have been published. This variation in patterns of sex differences in verbal fluency across the life span suggests that the rate of age-related decline in verbal fluency may be either similar or greater in women than in men. A greater decline in this cognitive ability could be associated with the decrease in estrogen levels during menopause. Findings from the psychoendocrinological studies have shown a decline in verbal fluency postmenopause (Berent-Spillson et al., 2012), but the number of cross sectional studies remains limited and some others have also found no differences in verbal fluency between menopause stages (Fuh et al., 2003; Herlitz et al., 2007; Lokken & Ferraro, 2006; Weber et al., 2013). It is not clear whether both category and letter fluency, or only letter fluency are/is more sensitive to menopause effects. Another aspect that has received less attention is to what extent menopause effects on verbal fluency are interactive with advancing age in women.

As discussed in Chapter 5, along with age and menopause, formal education attained by adulthood and cumulative hormone exposure across the life span (as determined by reproductive markers) may also affect verbal fluency performance in midlife and late life. It has been shown in the literature that women having higher levels of education, later age at first childbirth, later age at menopause and greater number of reproductive years produce more words on these tasks than women with lower levels of education, younger age at first childbirth, early age at menopause and fewer reproductive years. The relationship between education and verbal fluency has received greater attention (Brickman et al., 2005; Elkadi et al., 2006; Gladsjo et al., 1999; Goral et al., 2007; Herlitz et al., 2007; Lokken & Ferraro, 2006; Tombaugh et al., 1999; Van der Elst et al., 2006) than the relationships among verbal fluency and IQ (Bolla et al., 1990; Steinberg et al., 2005) and reproductive characteristics (Ryan et al., 2009; Smith et al., 1999). The extent to which these characteristics that reflect early and midlife experiences influence verbal fluency in late life has not been established. Thus, inconsistencies remain with regard to (a) the effects of age on letter fluency, (b) the effects of menopause status on verbal fluency, (c) and the relationship between verbal fluency, education, verbal IQ and reproductive characteristics.

The effects of age and menopause on cognitive processes underlying verbal fluency performance have also been sparsely studied. As was mentioned in Chapters 2 and 3, verbal fluency is multifactorial in nature and performance on this task requires a number of cognitive processes such as lexical-semantic memory, attention and executive functions (Abwender et al., 2001; Azuma, 2004; Hirshorn & Thompson-Schill, 2006; Rende et al., 2002; Troyer et al., 1997). The total word count is the most frequently used dependent variable to quantify performance on this task. However, total words is a global measure of verbal ability and does not differentiate between the cognitive processes that support performance on this task. Researchers have used additional measures such as switching (a measure of executive function) and clustering (a measure of verbal semantic memory) to examine the effects of age on underlying cognitive processes (Lanting et al., 2009; Sauzeon et al., 2011; Troyer et al., 1997). Findings from these studies suggest that deficits in executive processes, as measured by switching, contribute to fewer word productions by older adults. Although this has been addressed to a certain extent in the literature on cognitive ageing, the number of studies is limited and results for the letter fluency task remain contradictory (Lanting et al., 2009; Troyer et al., 1997). No such investigations have been conducted in relation to menopause.

In the neuropsychological literature, cognitive processes underlying word production in verbal fluency have been measured using switch cost (Gurd & Cowell, 2015). Switch costs in verbal production is examined using tasks analogous to verbal fluency (category and letter fluency) such as the C-series task (Gurd, 1995). The basic difference between C-series tasks and traditional verbal fluency tasks is that on C-series tasks, participants are asked to alternately produce words from two or more overlearned categories such as months or days of the week instead of producing words from one category such as animals. C-series tasks are similar to verbal fluency tasks because they require sequential verbal output (Gurd, 1995). However, C-series tasks may depend on working memory to a greater extent than on semantic memory when compared with category fluency tasks. Therefore, studying this task across age groups and menopause stages may provide evidence of cognitive costs incurred as a result of increased demands that draw upon working memory and executive functions needed for task-switching during verbal production.

Based on the existing gaps and inconsistencies in the literature, the current study aimed to examine the effects of age and menopause on verbal fluency in women aged 46 to 79 years. It also investigated the effects of age and menopause on cognitive processing and strategy use during verbal production using tasks such as verbal fluency and C-series. A combination of data scoring approaches, adapted Troyer method (Troyer et al., 1997; Wadnerkar, 2008; Wadnerkar et al., 2008 June), time course and linguistic analyses, were used to investigate cognitive processing and strategy use (see section 6.3 for details). Detailed analyses were undertaken for the letter task because the effects of age on letter fluency are inconsistent. The coding of clusters on the semantic task is problematic and has a low inter-rater reliability (see Chapter 2 for details; Abwender et al., 2001). This makes Troyer et al.'s (1997) scoring rules unsuitable for analysing category fluency data. In contrast, the coding of clusters and switches on the letter fluency task has a high inter-rater reliability (Troyer et al., 1997; Wadnerkar, 2008). Additionally, these measures on the letter fluency task are sensitive to hormonal fluctuations (Wadnerkar et al., 2008 June; see Chapter 3 for details), thus, supporting detailed analyses of word-retrieval patterns in letter fluency. The relationships between verbal fluency performance, demographic variables (education and IQ) and reproductive markers (age at menarche, menstrual cycle length, age at first childbirth, number of children, age at menopause, number of years since menopause and number of reproductive years) were also explored.

6.2. Research hypotheses

6.2.1. Hypotheses for age group comparisons

It was hypothesized that the total number of words generated by younger women would be higher than that produced by older women on the category fluency task. A similar pattern of performance was expected for total number of words produced on the letter fluency task. Based on previous research, it was predicted that cognitive strategy use would differ by age (Lanting et al., 2009; Troyer et al., 1997). Older women would switch less and produce equal cluster sizes to younger women on the letter fluency task.

For the time course analysis, it was hypothesized that the total number of words, number of switches and mean cluster size would be time-dependent (Fernaeus et al., 2008; Zimmermann et al., 2014) and vary across age groups (Sauzeon et al., 2011). With the total time period divided into three 20 second parts, younger women were predicted to produce more words and switches than older adults in the initial time interval (0-20 seconds of the letter task). In contrast, older adults were predicted to produce more words and have a larger mean cluster size than younger adults in the later time intervals (20-40 and 40-60 seconds of the task). With respect to the linguistic feature analysis of produced words on the letter task, it was predicted that older women would produce words with higher frequency and shorter length compared to younger women.

For the C-series task, switch rates and switch costs were studied (see Chapter 4 or section 6.3.2 of current chapter for details). It was hypothesized that the switch rate would decrease from switching between two (letters of the alphabet and numbers) to switching between three (letters, numbers, months) to switching between four (letters, numbers, months, days of the week) categories and the switch rate decline would become steeper with increasing age. Switch cost was expected to rise with the increase in categories and switch costs would be greater in older women.

6.2.2. Hypotheses for menopause stage comparisons

It was predicted that there would be no effect of menopause stage on category fluency. For the letter fluency task, it was hypothesized that premenopausal women would produce more words than peri and postmenopausal women. These differences in word production ability could be attributed to declines in switching across menopause stages. Mean cluster size would remain unaffected by menopause stage.

As demonstrated in Chapter 3, young healthy women in the periovulatory phase of the menstrual cycle showed optimized word production in the letter fluency task by the heightened use of switching in the initial 20 seconds of the one-minute task. Based on this evidence, it was predicted that premenopausal women would produce more words and switch more and cluster the same as peri and postmenopausal women in the initial time interval. The frequency and word length of items produced was also expected to vary depending on the menopause stage. It was predicted that peri and postmenopausal women would produce words with higher frequency and shorter length compared to premenopausal women.

For the C-series task, it was hypothesized that women across the menopause stages would not differ in their switch rate. Switch cost was expected to rise with increase in the number of categories and switch costs would be greater in peri and postmenopausal women.

6.3. Methods

6.3.1. Sample

Speech samples for the verbal fluency and C-series tasks were collected from all 78 women. Due to technical recording errors, samples for the letter 'S' were missing from two participants in Group I (46-55 years).

6.3.2. Details of tasks, administration procedure and scoring

As explained in detail in Chapter 4, four tasks were completed. The first two were the traditional category and letter fluency tasks. For the category task, participants were asked to generate as many words as possible in one-minute from three categories of animals, fruits and vehicles. For the letter fluency task, participants were required to generate as many words as possible in one-minute beginning with the letters F, A, S. Total number of correct words produced (errors and repetitions were excluded) for each category or letter were counted for category and letter fluency tasks, respectively. The number of switches and mean cluster size were also calculated for the letter task (Troyer et al., 1997; Wadnerkar, 2008; Wadnerkar et al., 2008 June). In addition, the letter fluency data were analysed using the time course and linguistic methods as described in Chapter 3. The third task was the C-series task. Prior to administration of the C-series task, participants were asked to produce as many words as possible for one-minute from four overlearned categories numbers, letters of the alphabet, months and days of the week. They were asked to follow the canonical order in each category to make the task more automatic and reduce semantic load. This task served as a baseline for the C-series task, and was referred as OS fluency. The C-series task consisted of three conditions: switching between 2 (numbers, letters), 3 (numbers, letters, months) and 4 (number, letters, months, days) categories. Participants had to alternately produce words from the specified categories for each of the conditions for one-minute. For the OS task, switch rate was calculated at the syllable and word levels. For the C-series task, switch rates (words/second) and switch costs were measured. The switch cost was defined as the difference between the switch rate of the series and mean pre-task baseline rate (for those two categories), expressed as a percentage of the total mean switch rate per category (Gurd & Cowell, 2015).

For example, switch cost for the 2-series condition (letters, numbers) was calculated as follows

$$\text{Switch Cost} = \left(\frac{\text{Mean baseline rate of letters and numbers} - \text{2-series switch rate}}{\text{Mean switch rate for letters, numbers, months, days}} \right) \times 100$$

The number and type of errors (within-task, between-task and other errors) were also determined for the C-series task.

Letter fluency demands word-retrieval based on an orthographic criterion and requires the use of non-habitual search strategies (Perret, 1974), whereas in category fluency words are produced from natural subcategories using natural organized searches (Azuma, 2004). The letter fluency task is more demanding and therefore, the category task was administered first in the study followed by the letter task. C-series task rely on working memory and attention to a greater extent than category or letter fluency tasks, which makes C-series tasks more demanding than these tasks. Hence, the C-series task was administered after the category and the letter fluency tasks. All women completed the OS task prior to the C-Series task as it served as a baseline task. The same order of administration was followed for all participants. The responses were audio recorded for later scoring and analysis.

6.3.3. Statistical analysis

To investigate the relationships between the dependent measures (verbal fluency and C-series task performances), demographic and reproductive variables, Pearson correlations were conducted. The correlational analyses were performed separately for each Age group, Menopause stage and Time since menopause group in order to determine differences, if any, between cohorts.

A series of ANOVAs were conducted to examine differences in mean scores across Age groups (46-55, 56-65, 70-79 years), Menopause stages (pre, peri, postmenopause) and Time since menopause (recent: less than six years post menopause, longer-term: more than six years post menopause). The effects of Age group and Time since menopause on verbal fluency and C-series task performance were studied with and without women with hysterectomies. The effects of Menopause stage on verbal fluency and C-series task performance were examined in the younger group of women aged 46-55 years.

Women across Age groups, Menopause stages and Time since menopause groups were not equally matched on all demographic and reproductive variables (see Chapter 5 for details). Subsequent ANCOVAs were performed with covariates that could account for variation in the model linked to demographic and reproductive factors that were not well matched among the groups. The results from the correlational analyses were used to determine the potential covariates. A variable was used as a covariate if it was associated with the dependent measure, the direction and magnitude of the correlation did not vary across groups and did not have a strong association with any other potential covariate. The complete details of the statistical models used are presented in the results section.

6.4. Results

The results are discussed in three sections defined by each task: category fluency, letter fluency and C-series. For each section, the results from the correlational analyses are presented first followed by the ANOVAs and ANCOVAs.

6.4.1. Category fluency

6.4.1.1. Correlations between category fluency, demographic and reproductive variables

Correlation patterns across Age groups

Vocabulary and education were positively correlated with category fluency (see Table 6.1). Correlates between vocabulary and category fluency were particularly strong but varied with respect to age. The magnitude of association was lower in the oldest age group (Group III). Education was consistently moderately correlated with category fluency in all the three age groups. There was a weak relationship between age and performance across all the age groups.

Among the reproductive markers, a moderate negative association was found between age at first childbirth and category fluency in Group II (see Table 6.2). As the women's age at first childbirth increased, their total number of words produced decreased. This association was comparatively weak in Groups I and III. No additional significant correlations were seen between category fluency and the other reproductive markers in the three age groups.

Correlation patterns across Menopause stages

Positive associations between category fluency, vocabulary, education and age were seen in the youngest group of women (Group I) as per their classification into stages of menopause (see Table 6.1). With respect to vocabulary and education, the magnitude of association decreased from pre to peri to postmenopause groups; and for age, the magnitude of association was moderate in pre and perimenopausal women but near zero in postmenopausal women. Age at first childbirth had a strong negative association with category fluency only in the postmenopausal group (see Table 6.2). No other strong associations were seen.

Correlation patterns across Time since menopause groups

Moderate positive associations were observed between vocabulary and category fluency in both recent and longer-term menopausal groups, with a slightly lower magnitude in the latter group. Correlates with education and age differed in magnitude and direction across groups. No significant correlations with reproductive characteristics were found in both the groups.

In summary, the results suggested that vocabulary and education were the most consistent correlates with category fluency across age. Among the reproductive characteristics, age at first childbirth may have a role in determining category fluency. In relation to menopause, correlations between category fluency, vocabulary and education were graded, with strongest associations in pre than peri than postmenopause. Across time since menopause, vocabulary was the most consistent correlate with category fluency.

The following subsection (6.4.1.2) presents the results from the ANOVAs and ANCOVAs comparing women across Age groups, Menopause stages and Time since menopause for category fluency. Covariates for the ANCOVAs were chosen based on the criteria outlined in section 6.3.3 and correlational analyses. For Age group comparisons, number of years of education was included as a covariate. Vocabulary was significantly associated with performance, but women across the three age groups were matched on their vocabulary scores. Age at first childbirth was correlated with performance, but the direction of association differed across age groups. Therefore, these two variables were excluded as covariates in the ANCOVA models.

Women in the youngest group were matched on the number of years of education, vocabulary T scores and reproductive markers across the Menopause stages. A mixed set of associations was seen between age and category fluency across menopause stages (see Table 6.1). Therefore, no further ANCOVA was conducted. For Time since menopause comparisons, vocabulary was deemed suitable to be used as a covariate.

Table 6.1

Correlations between total number of words produced in category fluency and demographic variables as a function of menopause stage, age group and time since menopause. Category fluency measure is based on the average of scores in the animals, fruits and vehicles categories

Word-finding	Independent variable	Group	*n*	Demographic variable		
				Vocabulary T score	Education (in years)	Age (in years)
Category fluency total number of words	Menopause stage	Premenopause	9	.85**	.71*	.33
		Perimenopause	11	.60†	.23	.40
		Postmenopause	12	.33	-.07	.05
	Age group	Group I (46-55 years)	32	.61**	.32†	.19
		Group II (56-65 years)	24	.51*	.30	-.12
		Group III (70-79 years)	22	.36	.39	-.19
	Time since menopause	Recent menopausal	16	.56*	-.05	.45†
		Longer-term menopausal	42	.36*	.33	-.18

†$p < .10$, *$p < .05$, **$p < .01$

Table 6.2

Correlations between total number of words in category fluency and reproductive markers as a function of menopause stage, age group and time since menopause. Category fluency measure is based on the average of scores in the animals, fruits and vehicles categories

Word-finding	Independent variable	Group	*n*	Reproductive variable						
				Age at menarche	Menstrual cycle length	Age at first childbirth[+]	Number of children	Age at menopause	Number of years since menopause	Number of reproductive years
Category fluency total number of words	Menopause stage	Premenopause	9	.12	-.01	.24	-.03	-	-	-
		Perimenopause	11	.35	-.38	-.06	-.13	-	-	-
		Postmenopause	12	-.17	.16	-.53	-.49	.08	-.05	.14
	Age group	Group I (46-55 years)	32	.07	-.02	-.08	-.21	.08 (*n* = 12)	-.05 (*n* = 12)	.14 (*n* = 12)
		Group II (56-65 years)	24	-.32	-.24	-.50*	.36†	.02	-.12	.19
		Group III (70-79 years)	22	-.20	.07	.11	-.18	.21	-.24	.26
	Time since menopause	Recent menopausal	16	-.37	-.20	-.10	-.17	.37	.27	.45†
		Longer-term menopausal	42	-.24	-.00	-.05	-.04	.14	-.20	.23

Note. [+]*Sample size for age at first childbirth variable*, Premenopause: 6, Perimenopause: 10, Postmenopause: 8; Group I: 24, Group II: 23, Group III: 21; Recent menopausal: 12, Longer-term menopausal: 40. †$p < .10$. *$p < .05$. **$p < .01$.

6.4.1.2. ANOVAs and ANCOVAs comparing women across Age groups, Menopause stages and Time since menopause on category fluency performance

Age group comparisons

ANOVA with Category (animals, fruits, vehicles) as the repeated measure and Age group (46-55, 56-65, 70-79 years) as the between group factor was conducted to examine mean differences in the total number of words produced. Analyses were conducted without and then with covariates.

An analysis of the data without covariates showed no significant effects of Age group, but the mean scores indicated that women aged 70-79 years tended to produce fewer words than women aged 46-55 and 56-65 years (see Table 6.3). For the total number of words, a main effect of Category was significant, $F(2, 150) = 82.18$, $p < .001$. Post hoc *t*-tests with Bonferroni corrected comparisons ($\alpha = .05/3 = .017$) revealed that the number of words for the category of animals was significantly higher than that of fruits, $t(77) = 6.42$, $p < .001$, and vehicles, $t(77) = 12.89$, $p < .001$, and more words were produced in the category of fruits than that of vehicles, $t(77) = 7.06$, $p < .001$. The Category x Age group interaction was not significant.

The analysis was repeated with number of years of education as a covariate and no significant effects of Age group were found. However, in line with the correlational analysis, education was significantly associated with performance, $F(1, 74) = 8.67$, $p = .004$.

As was mentioned in section 6.3.3, an Age group analysis was also performed after excluding women with hysterectomies ($n = 73$). There were significant effects of Age group, $F(2, 70) = 4.79$, $p = .011$, and Category, $F(2, 140) = 68.53$, $p < .001$, on the total number of words produced. Post hoc independent *t*-tests with Bonferroni corrected comparisons ($\alpha = .05/3 = .017$) confirmed that women aged 70-79 years produced significantly fewer words than women aged 46-55 years, $t(48) = 2.97$, $p = .005$, and 56-65 years, $t(39) = 2.62$, $p = .012$. Women aged 46-55 years did not differ significantly from women in the 56-65 years group. The maximum number of words was produced in the category of animals followed by fruits and vehicles. No significant Category x Age group interaction was seen. There were no significant effects of Age and Category after controlling for education.

Table 6.3

Category fluency means (± SEM) for total number of words collapsed across categories (animals, fruits, vehicles) as a function of age group, menopause stage and time since menopause

Independent variable	Group	*n*	Total number of words
Menopause stage	Premenopause	9	18.85 (1.42)
	Perimenopause	11	18.94 (0.82)
	Postmenopause	12	19.17 (0.92)
Age group *(including women with and without hysterectomies)*	Group I (46-55 years)	32	19.00 (0.58)
	Group II (56-65 years)	24	19.68 (0.93)
	Group III (70-79 years)	22	17.35 (1.00)
Age group *(excluding women with hysterectomies)*	Group I (46-55 years)	32	19.00 (0.58)
	Group II (56-65 years)	23	19.48 (0.95)
	Group III (70-79 years)	18	16.06 (0.84)
Time since menopause *(including women with and without hysterectomies)*	Recent menopausal	16	20.25 (0.74)
	Longer-term menopausal	42	18.10 (0.74)
Time since menopause *(excluding women with hysterectomies)*	Recent menopausal	16	20.25 (0.74)
	Longer-term menopausal	37	17.38 (0.72)

Menopause stage comparisons

An ANOVA with Category (animals, fruits, vehicles) as the repeated measure and Menopause stage (pre, peri, postmenopause) as the between group factor was conducted. A main effect of Menopause stage was not significant (see Table 6.3), but there was a significant effect of Category on the total number of words, $F(2, 58) = 42.88$, $p < .001$. More words were produced in the animals category followed by fruits and vehicles. Category x Menopause stage interaction was nonsignificant.

Time since menopause comparisons

An ANOVA with Category (animals, fruits, vehicles) as the repeated measure and Time since menopause (recent, longer-term) as the between group factor was performed. There was a significant effect of Category, $F(2, 112) = 58.67$, $p < .001$, but not of Time since menopause (see Table 6.3) and Category x Time since menopause interaction. More words were produced in the animals category followed by fruits and vehicles.

After controlling for vocabulary, there were no effects of Category, Time since menopause and Category x Time since menopause interaction. Vocabulary was significantly associated with performance, $F(1, 55) = 9.78$, $p = .003$. When the data were examined excluding women with hysterectomies, there was a significant effect of Time since menopause for category fluency, $F(1, 51) = 5.72$, $p = .021$. Recent postmenopausal women produced more words than longer-term postmenopausal women. However, after controlling for vocabulary both the groups did not significantly vary in their performance.

6.4.2. Letter fluency

The letter fluency data were analysed using three approaches and the results are presented in subsections according to adapted Troyer method (Troyer et al., 1997; Wadnerkar, 2008; Wadnerkar et al., 2008 June), time course and linguistic features.

6.4.2.1. Adapted Troyer method (Troyer et al., 1997; Wadnerkar, 2008; Wadnerkar et al., 2008 June)

6.4.2.1.1. Correlations between letter fluency measures, demographic and reproductive variables

Pearson correlations were used to study the relationships between the letter fluency measures (total number of words, number of switches and mean cluster size), demographic variables (see Table 6.4) and reproductive markers (see Table 6.5) for each Age group, Menopause stage and Time since menopause group separately.

Correlation patterns across Age groups

Vocabulary and education were moderately correlated with letter fluency performance in Group III with mixed patterns in Groups I and II (see Table 6.4). In Group I, there was a strong positive association between the total number of words and vocabulary, but the association was weak with the number of years of education. In contrast, in Group II, the magnitude of association between the total number of words and education was greater than that between the total number of words and vocabulary. Correlations with age were weak across age groups.

Associations between the number of switches and vocabulary, education and age were near zero across all the age groups. The mean cluster size was moderately associated with the number of years of education in all the three age groups, and with vocabulary only in Group I. Correlations between mean cluster size and age were near zero to low across age groups. No significant associations were seen between the dependent measures and any of the other reproductive markers.

Correlation patterns across Menopause stages

In the youngest group of women (Group I), vocabulary and education were positively associated with the total number of words (see Table 6.4). Associations with vocabulary were strong in pre and postmenopausal women but not in perimenopausal women. With respect to education, the magnitude of correlation was strong in premenopausal women and low in the other two groups. Correlations with age were moderate across menopause stages with the strongest association in premenopausal women.

Sporadic correlations were found between switches, vocabulary, education and age across menopause stages. Correlations among mean cluster size, vocabulary and education were positive and strong in the premenopause group but weak to moderate in the other two groups. Associations between age and mean cluster size were weak across menopause stages. Moderate negative associations were seen between the total number of words and the number of children in peri and postmenopause groups but not in the premenopausal group (see table 6.5). A later age at menarche was associated with smaller mean cluster size in the postmenopause group (see Table 6.5).

Correlation patterns across Time since menopause groups

Associations between total words, vocabulary and education were moderate in both recent and longer-term menopausal women (see Table 6.4). Age was weakly associated with total words in both the groups.

Correlations among switches, vocabulary and education were near zero in the longer-term group, and moderate in the recent group. Mean cluster size was positively related to vocabulary and education in both the groups. These associations were weak to moderate across the two groups. The mean cluster size increased with increase in age and number of years since menopause only in the recent group (see Table 6.5). No other significant associations were found.

In summary, the correlational analyses suggested that vocabulary and education were most consistently correlated with letter fluency across age. The associations of vocabulary and education with mean cluster size, but not with the number of switches, supports previous research that these two dependent measures are dissociable (Troyer et al., 1997), with clustering strategy based in part on women's vocabulary knowledge. In relation to menopause, vocabulary and education were the most consistent correlates with letter fluency performance. Associations with education were graded according to menopause stage with the strongest association in the premenopause group. Across time since menopause, again vocabulary and education were the most consistent correlates with total words. The number of children may also have a role in letter fluency performance and use of switching strategy. Mean cluster size might be influenced by number of years since menopause.

The following subsection (section 6.4.2.1.2) reports the results from the ANOVAs and ANCOVAs comparing women across Age groups, Menopause stages and Time since menopause on letter fluency performance. For Age group comparisons, number of years of education was used as a covariate for total number of words and mean cluster size. No ANCOVAs were performed for the number of switches. For Menopause stage comparisons, age was included as covariate for total words and mean cluster size. For Time since menopause comparisons, education was deemed suitable to be employed as a covariate for total number of words.

Table 6.4

Correlations between the dependent measures for letter fluency (total number of words, number of switches, mean cluster size) and demographic variables as a function of menopause stage, age group and time since menopause. Letter fluency measures are based on average scores on the fluency tasks across the letters F, A, S

Independent variable	Group	Dependent variable	Demographic variable		
			Vocabulary T score	Education (in years)	Age (in years)
Menopause stage	Premenopause (n = 9)	Total words	.76*	.60†	.57
		Switches	.20	.51	.72*
		Mean cluster size	.69*	.73*	.31
	Perimenopause (n = 11)	Total words	.19	.17	.20
		Switches	.01	-.18	.05
		Mean cluster size	.07	.41	.26
	Postmenopause (n = 12)	Total words	.62*	.17	.36
		Switches	.48	.39	-.06
		Mean cluster size	.24	.11	.46
Age group	Group I (46-56 years) (n = 32)	Total words	.56**	.24	.35*
		Switches	.15	.16	-.07
		Mean cluster size	.35†	.42*	.23
	Group II (56-65 years) (n = 24)	Total words	.25	.42*	-.11
		Switches	.06	-.06	-.10
		Mean cluster size	.18	.37†	-.09
	Group III (70-79 years) (n = 22)	Total words	.43*	.54**	-.26
		Switches	.01	.01	.05
		Mean cluster size	.17	.35	-.05
Time since menopause	Recent menopausal (n = 16)	Total words	.51*	.34	.10
		Switches	.45†	.32	.07
		Mean cluster size	.35	.08	.56*
	Longer-term menopausal (n = 42)	Total words	.33*	.45**	-.18
		Switches	.02	-.04	-.02
		Mean cluster size	.10	.31*	.13

†p <.10, *p < .05, ** p < .01.

Table 6.5

Correlations between the dependent measures for letter fluency (total number of words, number of switches, mean cluster size) and reproductive markers as a function of menopause stage, age group and time since menopause. Letter fluency measure is based on the average of scores across F, A, S

Dependent variable	Group	*n*	Reproductive variable						
			Age at menarche	Menstrual cycle length	Age at first childbirth[+]	Number of children	Age at menopause	Number of years since menopause	Number of reproductive years
Total words	Premenopause	9	-.09	-.06	-.04	.11	-	-	-
	Perimenopause	11	.15	-.23	-.05	-.53	-	-	-
	Postmenopause	12	-.19	.31	-.01	-.45	.26 (*n* = 12)	.13 (*n* = 12)	.30 (*n* = 12)
	Group I 46-55 years	32	-.10	.07	-.02	-.27	.26	.13	.30
	Group II 56-65 years	24	.05	-.00	-.09	.34	-.15	.01	-.17
	Group III 70-79 years	22	-.14	-.07	.23	-.04	.32	-.36	.34
	Recent menopausal women	16	.01	.35	.36	-.28	.11	.01	.07
	Longer-term menopausal women	42	-.11	-.18	.05	.06	.13	-.20	.17
Switches	Premenopause	9	-.09	.23	-.25	.61	-	-	-
	Perimenopause	11	-.10	-.20	.27	-.28	-	-	-
	Postmenopause	12	.20	.32	-.39	.11	.22 (*n* = 12)	-.40 (*n* = 12)	.11 (*n* = 12)
	Group I 46-55 years	32	.06	.19	-.01	.18	.22	-.40	.11
	Group II 56-65 years	24	-.02	-.08	.23	.15	.17	-.20	.16
	Group III 70-79 years	22	-.05	-.07	.36	-.03	.38†	-.20	.37†
	Recent menopausal women	16	.14	.26	-.42	.25	.27	-.45†	.18
	Longer-term menopausal women	42	-.02	-.10	.29†	.00	.27†	-.11	.26†
Mean cluster size	Premenopause	9	.31	-.22	.10	-.37	-	-	-
	Perimenopause	11	.50	.28	-.01	-.04	-	-	-
	Postmenopause	12	-.58*	.26	.15	-.44	.07 (*n* = 12)	.54† (*n* = 12)	.29 (*n* = 12)
	Group I 46-55 years	32	.03	.13	.02	-.32†	.07	.54†	.29
	Group II 56-65 years	24	-.12	-.35†	-.17	.25	.01	-.11	.06
	Group III 70-79 years	22	.09	-.03	.11	-.13	-.08	-.00	-.11
	Recent menopausal women	16	-.49†	-.04	.30	-.28	.34	.63**	.48†
	Longer-term menopausal women	42	.05	.01	-.15	.04	-.21	.17	-.21

†p <.10, *p < .05, **p < .01. [+]*Sample size for age at first childbirth variable*, Premenopause: 6, Perimenopause: 10, Postmenopause: 8; 46-55 years: 24, 56-65 years: 23, 70-79 years: 21; Recent menopausal: 12, Longer-term menopausal: 40

6.4.2.1.2. ANOVAs and ANCOVAs comparing women across Age groups, Menopause stages and Time since menopause on letter fluency performance

Age group comparisons

The total number of words, the number of switches and the mean cluster size were analysed for the effects of Age group in three separate ANOVAs. For all three dependent variables, Letter (F, A, S) was the repeated measure and Age group (46-55, 56-65, 70-79 years) was the between group factor. The analyses were performed first without covariates and then with covariates.

Women across the three Age groups did not significantly differ on the total number of words, the number of switches or the mean cluster size (see Table 6.6). A significant effect of Letter was seen on the total number of words, $F(2, 146) = 27.02$, $p < .001$, and the mean cluster size, $F(2, 146) = 8.17$, $p < .001$, but not on the number of switches. Post hoc paired *t*-tests with Bonferroni corrections ($\alpha = .05/3 = .017$) showed that more words were produced with the letter S than with the letters F, $t(75) = -5.86$, $p < .001$, and A, $t(75) = -6.29$, $p < .001$. The mean cluster size for the letter A was significantly smaller than those of letters F, $t(77) = -2.67$, $p = .010$, and S, $t(75) = -3.67$, $p < .001$. The Letter x Age group interaction was not significant for total words, switches and mean cluster size.

No Letter or Age group effects were seen for the total number of words or the mean cluster size after controlling for education. The number of years of education covaried significantly with the total number of words produced, $F(1, 72) = 12.24$, $p = .001$, and the mean cluster size, $F(1, 72) = 11.66$, $p = .001$.

When women with hysterectomies were excluded, Age effects remained nonsignificant for total number of words, switches and mean cluster size. There was a significant effect of Letter for total words and mean cluster size, but not for switches.

More words were produced with letter S than with letters F and A. The mean cluster size for letter A was significantly smaller than those of letters F and S. Letter x Age group interaction was not significant. There were no significant effects of Letter, Age and Letter x Age group for any of the dependent measures after controlling for the number of years of education.

Table 6.6

Letter fluency means (± SEM) for total number of words, number of switches and mean cluster size collapsed across letters (F, A, S) as a function of menopause stage, age group and time since menopause

Independent variable	Group	*n*	Total number of words	Number of switches	Mean cluster size
Menopause stage	Premenopause	9	16.07 (1.35)	3.93 (0.48)	1.60 (0.17)
	Perimenopause	11	18.70 (0.85)	3.57 (0.58)	1.52 (0.08)
	Postmenopause	12	18.03 (1.50)	2.97 (0.67)	1.53 (0.12)
Age group	Group I (46-55 years)	32	17.71 (0.74)	3.45 (0.35)	1.55 (0.07)
	Group II (56-65 years)	24	17.19 (0.92)	3.61 (0.46)	1.49 (0.08)
	Group III (70-79 years)	22	15.97 (0.88)	3.41 (0.40)	1.62 (0.12)
Time since menopause	Recent menopausal	16	17.98 (1.22)	3.25 (0.53)	1.58 (0.10)
	Longer-term menopausal	42	16.49 (0.67)	3.46 (0.33)	1.54 (0.08)

Menopause stage comparisons

ANOVAs with Letter (F, A, S) as the repeated measure and Menopause stage (pre, peri, postmenopause) as the between group factor were conducted for the total number of words, number of switches and mean cluster size. Women across the three stages of menopause did not differ significantly on any of the dependent measures (see Table 6.6). There was a significant effect of Letter on the total number of words[12], $F(2, 54) = 11.57$, $p < .001$, but not on the number of switches or the mean cluster size. More words were produced with letter S followed by letters F and A. No significant Letter x Menopause stage interaction was seen for total words, switches and mean cluster size. There remained no significant effects of menopause stage on total words and mean cluster size after controlling for age.

Time since menopause comparisons

ANOVAs with Letter (F, A, S) as the repeated measure and Time since menopause (recent, longer-term) as the between group factor were performed for the total number of words, number of switches and mean cluster size. Women across the two groups did not differ significantly on any of the dependent measures (see Table 6.6). There were significant effects of Letter on the total number of words, $F(2, 110) = 17.76$, $p < .001$, and the mean cluster size, $F(2, 110) = 3.98$, $p = .021$, but not on the number of switches. More words were produced with letter S than with letters F and A. The mean cluster size for letter A was significantly smaller than that for letter S, but no other differences were noted. Letter x Time since menopause interactions were not significant for any of the measures.

After controlling for education, there were no effects of Time since menopause, Letter x Time since menopause for total number of words. There was a significant effect of Letter with maximum words being produced with letter S followed by letters F and A. Education covaried significantly with total words, $F(1, 54) = 11.65$, $p = .001$. The results remained the same after excluding women with hysterectomies (with or without covariates).

---

[12] The assumption of sphericity was violated. Results from Greenhouse-Geisser correction also showed significant differences across letters on the total number of words.

6.4.2.1.3. Correlations between the dependent measures

Based on Troyer et al.'s (1997) method, the data were further analysed to examine inter-correlations among the three dependent variables. Pearson correlations were computed separately for each Age group, Menopause stage and Time since menopause group in order to examine whether the associations between the total number of words produced and use of cognitive strategy differed between Age groups or Menopause stages or Time since menopause (see Table 6.7).

Across age groups

The total number of words produced was positively correlated with the number of switches and the mean cluster size in all the three age groups. The magnitude of association between the total number of words and the mean cluster size was stronger than the association between the total number of words and the number of switches in Groups I and II. In contrast, equivalent moderate associations were seen between the total number of words, the number of switches and the mean cluster size in Group III.

Across menopause stages

The correlation patterns for women in different stages of menopause in Group I were examined separately (Table 6.7). The total number of words produced was positively associated with the number of switches and the mean cluster size across all the three menopause stages. The magnitude of correlation between the total number of words and the number of switches was strongest for women in the premenopause stage. Fisher's z test was used to examine if the correlation between the total words and the number of switches differed across menopause stages, but did not reveal any significant effects.

Across time since menopause

In relation to time since menopause, the magnitude of association between the total number of words and the mean cluster size was stronger than between the total words and the number of switches in both recent and longer-term menopausal women (see Table 6.7).

Table 6.7

Correlations between the total number of words and the number of switches and the mean cluster size as a function of menopause stage, age group and time since menopause

Independent variable	Group	*n*	Total words/ Switches	Total words/ Mean cluster size
Menopause stage	Premenopause	9	.69*	.68*
	Perimenopause	11	.44	.31
	Postmenopause	12	.45	.68*
Age group	Group I (46-55 years)	32	.43*	.57**
	Group II (56-65 years)	24	.37†	.60**
	Group III (70-79 years)	22	.44*	.44*
Time since menopause	Recent menopausal	16	.35	.52
	Longer-term menopausal	42	.43**	.50**

†$p < .10$, *$p < .05$, **$p < .01$

6.4.2.2. Time course analysis for the letter fluency task

Age group comparisons

The time course analysis compared women across the three Age groups on the total number of words, number of switches and mean cluster size in three separate

ANOVAs. For all three measures, Letter (F, A, S) and Time (T1, T2, T3) were the repeated measures and Age group was the between group factor.

There were no effects of Age group for any of the dependent measures. The results showed a significant effect of Letter on the total number of words, $F(2, 146) = 27.20$, $p < .001$, and the mean cluster size, $F(2, 146) = 8.75$, $p < .001$, but not on the number of switches. As seen in the previous analyses, the maximum number of words was produced for the letter S followed by letters F and A; and the mean cluster size for letter A was smaller than those of letters F and S. A significant effect of Time was seen on the total number of words[13], $F(2, 146) = 165.16$, $p < .001$, the number of switches, $F(2, 146) = 40.26$, $p < .001$, and the mean cluster size, $F(2, 146) = 4.01$, $p = .020$. The total number of words produced in T1 was significantly higher than the number of words produced in T2, $t(75) = 13.37$, $p < .001$, and in T3, $t(75) = 15.58$, $p < .001$, and more words were produced in T2 than in T3, $t(75) = 5.39$, $p < .001$ (T1 > T2 > T3) (Bonferroni corrected comparisons, $\alpha = .05/3 = .017$). The number of switches produced in T1 and T2 were not significantly different, but the number of switches produced in T3 was lower than those produced in T1, $t(75) = 7.34$, $p < .001$, and T2, $t(75) = 8.90$, $p < .001$ (T1 = T2 > T3) (Bonferroni corrected comparisons, $\alpha = .05/3 = .017$). In contrast, post hoc analysis did not reveal significant differences in the mean cluster size between the time frames. A marginally significant difference was seen between mean cluster sizes in T1 and T3, $t(75) = -2.41$, $p = .018$, with a larger mean cluster size in T3 compared to T1 (T1 = T2 < T3). Letter x Time x Age group interactions were not significant for any of the measures. Thus, the time course analysis showed that women

[13] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction also showed a significant effect of Time on the total number of words.

in all the three Age groups produced more words and switched more in the initial two 20 second time periods and that the mean cluster size slightly increased over time.

ANCOVAs conducted for total number of words and mean cluster size with number of years of education as a covariate, showed no significant effects of Age, Letter, Time or any additional interactions for the dependent measures. Excluding women with hysterectomies yielded same results for all the variables, when the analyses were conducted with or without covariates.

A post hoc time course analysis that considered only postmenopausal women in the three age groups (n = 57) showed no effects of Age group for total number of words, number of switches or mean cluster size. Main effects of Letter were significant for total number of words (S > F = A) and mean cluster size (S > A), but not for number of switches. Time had a significant effect on all the three measures (Total words: T1 > T2 > T3; Switches: T1 = T2 > T3; Mean cluster size: T2 > T1). A significant effect of Time x Age group was observed for mean cluster size, $F(4, 108) = 3.26$, $p = .014$. Post hoc one way ANOVAs did not reveal a significant effect of Age group on mean cluster size for any of the time intervals. Further, post hoc ANOVAs for each age group with Time as the repeated measure and mean cluster size as the dependent measure were conducted (Bonferroni corrections, $\alpha = .05/3 = .017$). There was a significant effect of Time on mean cluster size in women aged 56-65 years, $F(2, 46) = 7.53$, $p = .001$, and a nonsignificant trend was seen for 46-65 year olds, $F(2, 20) = 4.12$, $p = .032$. Women aged 46-55 years had a larger mean cluster size in T2 and T3 than in T1, and women aged 56-65 years had a larger mean cluster size in T3 than in T1 (see Figure 6.1). No other interactions were significant. After controlling for education, Time x Age group effects remained significant for mean cluster size, but main effects of Age group, Letter and Time were not significant.

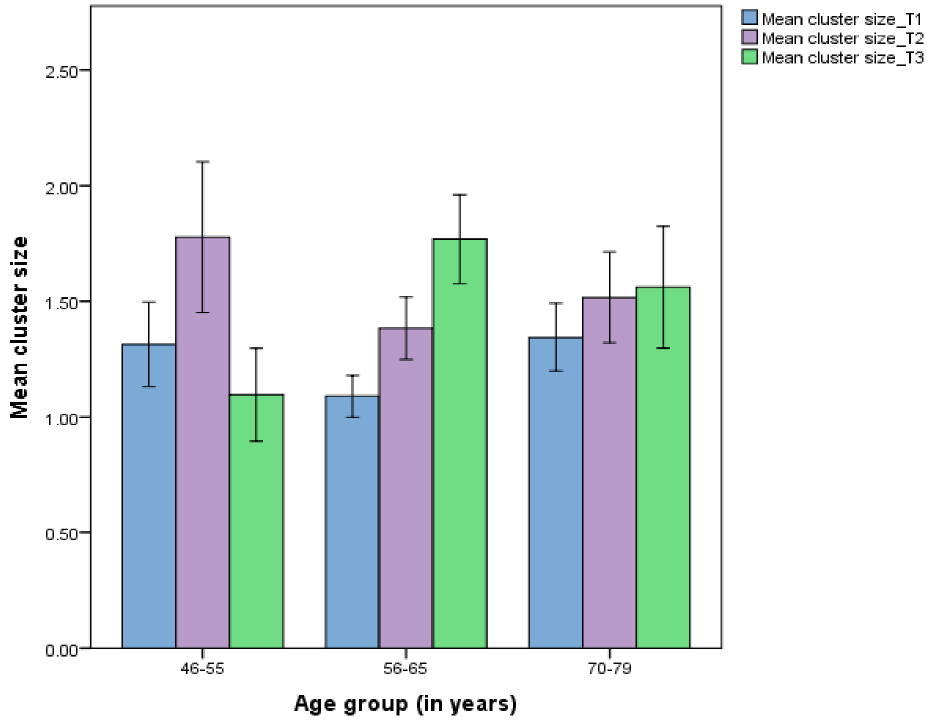

Figure 6.1. Letter fluency mean cluster size produced across time (T1, T2, T3) as function of age group (in postmenopausal women). Error bars represent ±1 standard error.

Menopause stage comparisons

Analyses were conducted to compare women across the three Menopause stages on the total number of words, number of switches and mean cluster size across the three time intervals. For the three dependent variables, separate ANOVAs with Letter (F, A, S) and Time (T1, T2, T3) as the repeated measures and Menopause stage as the between group factor were performed.

There were no effects of Menopause stage for any of the variables. A significant effect of Letter was seen for the total number of words, $F(2, 54) = 11.57$, $p < .001$, but not for number of switches or mean cluster size. The highest number of words was produced with letter S followed by letters F and A. Time had a significant effect on the total number of words, $F(2, 54) = 65.90$, $p < .001$, and the number of switches, $F(2, 54) = 11.72$, $p < .001$, but not on the mean cluster size. As seen in the age group comparisons, the total number of words decreased from T1 to T3 (T1 > T2 > T3) and the number of switches produced in T3 was lower than in T1 and T2 (T1 ≈ T2 > T3).

Time x Menopause stage had a significant effect for the number of switches, $F(4, 54) = 2.58$, $p = .047$, and mean cluster size, $F(4, 54) = 4.25$, $p = .005$. Post hoc one way ANOVAs did not reveal significant differences across menopause stages in the number of switches and the mean cluster size for any of the time intervals. Further, post hoc ANOVAs with Time as the repeated measure was conducted separately for each menopause group. Time had a significant effect on the number of switches in pre, $F(2, 14) = 6.47$, $p = .010$, and perimenopausal women[14], $F(2, 20) = 8.47$, $p = .002$, but not in postmenopausal women. Premenopausal women switched more in T2 followed by T1 and T3 (T2 > T1 = T3), whereas perimenopausal women switched significantly more in T1 and T2 than in T3 (T1 = T2 > T3) (see Figure 6.2). For mean cluster size, nonsignificant Time-related trend was observed in pre, $F(2, 14) = 3.99$, $p = .043$, and postmenopausal women, $F(2, 20) = 4.12$, $p = .032$, but not in perimenopausal women. Premenopausal women had a smaller mean cluster size in T2 compared to the mean cluster sizes in T1 and T3 (T2 < T1 = T3), but postmenopausal women had a larger mean cluster size in T2 than in T1 and in T3 (T2 > T1 = T3) (see Figure 6.3). No other interactions were significant.

After controlling for the effects of age, there was a significant effect of Letter but not Time for the total number of words. For mean cluster size, there were no effects of Letter or Time, but Time x Menopause stage continued to show a significant interaction.

---

[14] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction also showed significant differences.

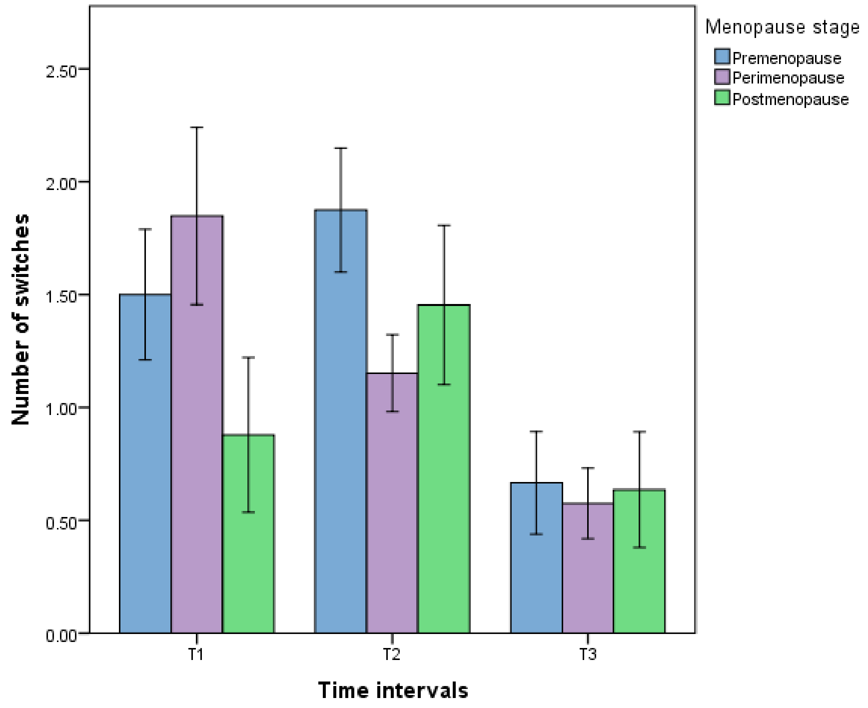

Figure 6.2. Number of switches produced across time (T1, T2, T3) as a function of menopause stage. Error bars represent ±1 standard error.

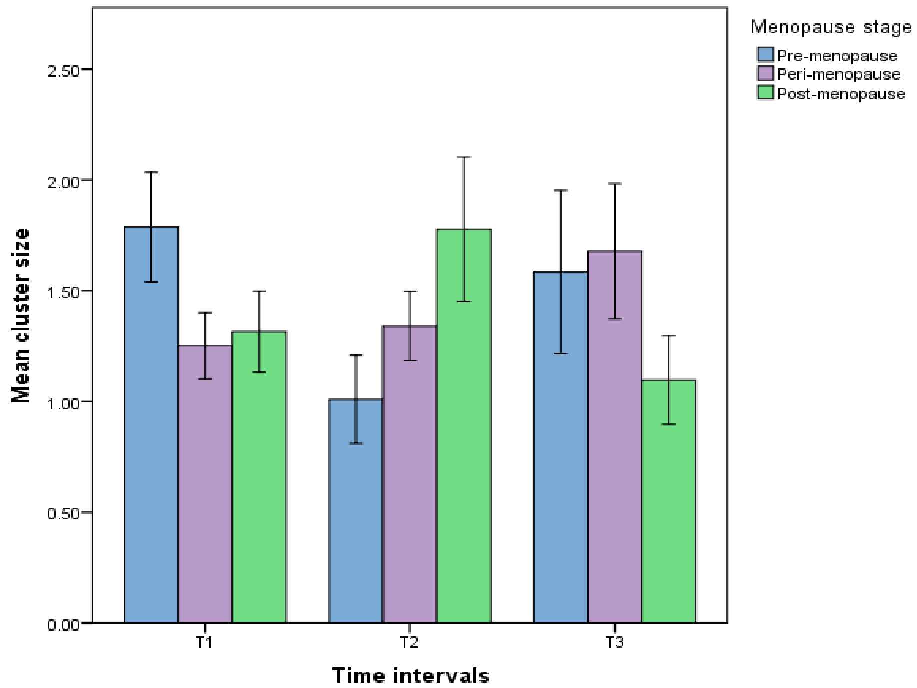

Figure 6.3. Letter fluency mean cluster size produced across time (T1, T2, T3) as a function of menopause stage. Error bars represent ±1 standard error.

Time since menopause comparisons

There was no significant effect of Time since menopause for any of the variables. The effects of Letter were significant on the total number of words, but not on the switches and the mean cluster size. More words were produced with letter S than with letters F and A. A main effect of Time was significant for total number of words[15], $F(2, 110) = 89.25$, $p < .001$, and switches, $F(2, 110) = 21.23$, $p < .001$, but not for mean cluster size. Maximum words were produced in T1 followed by T2 and T3 (T1 > T2 > T3). The number of switches in T1 and T2 were more than those produced in T3 (T1 = T2 > T3). Time x Time since menopause interaction was significant for switches, $F(2, 110) = 3.14$, $p = .047$. Post hoc analyses revealed significant effects of Time on the number of switches in recent, $F(2, 28) = 4.42$, $p = .021$, and longer-term, $F(2, 82) = 33.56$, $p < .001$ groups (Bonferroni corrected comparisons, $\alpha = .05/3 = .017$). Recent menopausal women switched more in T2 than in T3 and longer-term menopausal women had more switches in T1 and T2 than in T3.

After controlling for education, main effects of Letter and Time were significant for the total number of words. No other significant effects were observed. The same pattern of results was seen after excluding women with hysterectomies (with or without covariates).

[15] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction also showed a significant effect of Time on the total number of words.

6.4.2.3. Linguistic feature analysis for the letter fluency task

The data were analysed to examine the effects of Age group, Menopause stage and Time since menopause on word frequency and word length. Using separate ANOVAs for each measure, Letter (F, A, S) and Time (T1, T2, T3) were the repeated measures and Age group (46-55, 56-65, 70-79 years) or Menopause stage (pre, peri, postmenopause) or Time since menopause (recent, longer-term) was the between group factor.

Age group comparisons

Main effects of Age group for frequency and word length were not significant. There was a significant effect of Letter[16] on the word frequency, $F(2, 130) = 20.22$, $p < .001$, and the word length[17], $F(2, 130) = 20.22$, $p < .001$. Words produced with letter A had a higher mean frequency than those produced with letters F, $t(71) = 5.00$, $p < .001$, and S, $t(69) = 5.14$, $p < .001$. Similarly, length of words produced with letter A were longer than those produced with letters F, $t(74) = 14.61$, $p < .001$, and S, $t(74) = 15.51$, $p < .001$ (Bonferroni corrections applied, $\alpha = .05/3 = .017$). There were no significant effects of Time on either variable.

Time x Age group, $F(4, 130) = 3.11$, $p = .018$, and Letter x Time x Age group interactions, $F(8, 260) = 3.08$, $p = .002$, were significant for frequency (see Table 6.8). A nonsignificant age-related trend was observed for frequency of words[18] produced in T3 with letter A, $F(2, 2.97) = 45.09$, $p = .112$. Women aged 46-55 years produced words with higher mean frequency than women aged 56-65 and 70-79 years. When the

[16] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction also showed a significant effect of Letter on word frequency.

[17] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction also showed a significant effect of Letter on word length.

[18] The Levene's test was significant and therefore, the Welch's test results are reported.

data were re-examined excluding women with hysterectomies, the findings were the same as above for both the variables.

Menopause stage comparisons

Menopause stage had no effect on frequency or word length. There were significant effects of Letter on the word frequency[19], $F(2, 52) = 10.42$, $p < .001$, and the word length, $F(2, 52) = 116.38$, $p < .001$. Words produced with letter A had higher mean frequency and were longer compared to the frequency and length of the words produced with letters F and S. There were no significant effects of Time or any interactions.

Time since menopause comparisons

Recent and longer-term menopausal women did not differ in the frequency and length of the produced words. There was a significant effect of Letter on word frequency[20], $F(2, 94) = 14.15$, $p < .001$, and word length, $F(2, 52) = 116.38$, $p < .001$. Words produced with the letter A had higher mean frequency and word length than those with letters F and S. Main effects of Time[21], $F(2, 94) = 6.98$, $p = .001$, and Letter x Time interaction[22], $F(4, 188) = 5.75$, $p < .001$, were significant for frequency but not word length. Post hoc paired *t*-tests with Bonferroni corrections ($\alpha = .05/3 = .017$) revealed that the frequency of words produced in T1 was significantly higher than the frequency of words produced in T2, $t(52) = 2.77$, $p = .008$, and in T3, $t(52) = 4.12$, $p < .001$. No other significant interactions were found. Analyses conducted after excluding women with hysterectomies showed similar results as above.

---

[19] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction showed a significant effect of Letter on word frequency in the menopause stage comparison.
[20] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction showed significant effect of Letter on word frequency in the time since menopause comparison.
[21] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction showed significant effect of Time on word frequency in the time since menopause comparison.
[22] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction showed significant effect of Letter x Time on word frequency in the time since menopause comparison.

Table 6.8

Frequency of words produced (M ± SEM) across letters (F, A, S) and time (T1, T2, T3) as a function of age group

		Time		
	Letter	T1	T2	T3
Group I (46-55 years)	F	77.48 (17.89)	83.77 (26.23)	65.03 (20.89)
	A	948.32 (321.17)	311.46 (140.42)	1363.88 (591.85)
	S	88.68 (24.47)	110.69 (29.13)	99.88 (42.05)
	Mean (F,A,S)	321.81 (103.59)	173.10 (51.13)	540.62 (217.66)
Group II (56-65 years)	F	122.72 (33.11)	73.38 (28.29)	54.40 (29.25)
	A	1267.33 (394.08)	152.43 (78.49)	84.41 (36.01)
	S	69.85 (16.83)	118.09 (38.71)	82.44 (45.60)
	Mean (F,A,S)	486.63 (129.59)	116.44 (30.85)	74.45 (21.22)
Group III (70-79 years)	F	97.28 (38.58)	74.38 (32.72)	76.90 (16.53)
	A	812.11 (340.94)	207.88 (76.53)	93.91 (50.56)
	S	113.30 (31.57)	83.35 (37.43)	68.33 (13.89)
	Mean (F,A,S)	340.90 (128.53)	126.15 (28.66)	84.07 (18.15)

In summary, women across the three Age groups did not differ significantly in the total number of words, number of switches and mean cluster size in letter fluency. Total number of words had a stronger association with mean cluster size than with the number of switches in women aged 46-55 and 56-65 years, whereas the magnitude of associations between total words and switches or mean cluster size were equivalent in Group III. Time course analyses revealed that younger women (46-55 years) produced larger mean cluster sizes in the earlier time frame (T2) than in the later one (T3), whereas older women (56-65 years) produced larger mean cluster sizes in the later time period (T3) than the initial ones (when data from postmenopausal women were considered). Additionally, there was some evidence for younger women producing higher frequency words than the older women in T3 time interval, but there was no age effect on word length.

Women across the Menopause stages did not differ in total number of words, number of switches and mean cluster size. The correlation among total words and switches was strongest in premenopausal women compared to the other two groups. Time course analyses showed that premenopausal women produced more switches in T2 than in T1 and T3, whereas perimenopausal women switched more in T1 than in T2 and T3 and postmenopausal women did not differ in the number of switches across time periods. Premenopausal women had the largest mean cluster size in T1 compared to the other two menopause groups, whereas postmenopausal women had the largest mean cluster size in T2.

In relation to Time since menopause, recent and longer-term menopausal women did not vary in their letter fluency performance or cognitive strategy use. The time course analyses showed that recent menopausal women switched more in T2 than in T3 and longer-term menopausal women switched more in T1 and T2 than in T3. Linguistic feature analyses indicated that the frequency of words decreased from T1 to T3 in this group of women.

6.4.3. OS and C-Series tasks

6.4.3.1. Correlations between dependent measures, demographic and reproductive characteristics

The relationships between switch rate, switch cost, demographic (see Tables 6.9 and 6.11) and reproductive variables (see Table 6.10 and Table 6.12) were studied using Pearson correlations.

Switch rate

Correlation patterns across Age groups

Positive moderate associations were seen between vocabulary and switch rate across all the age groups, except for a low correlation between vocabulary and 3-series switch rate in Group III (see Table 6.9). Correlates with education were near zero to low in Group I, and low to moderate in Groups II and III; indicating an overall weak association with education. Age was moderately associated with switch rate in Group I, but these associations were weak in the older groups. With respect to reproductive characteristics, as the number of children increased, switch rate decreased only in Group I (see Table 6.10). These associations were near zero to low in Groups II and III. No other significant associations with other reproductive characteristics were found.

Correlation patterns across Menopause stages

In the youngest group (Group I), there were positive moderate associations between vocabulary and switch rate across menopause stages (see Table 6.9). Correlations among switch rate and education were near zero to moderate and sporadic across menopause stages. Similarly, associations with age were sporadic across menopause stages. Among the reproductive characteristics, as menstrual cycle duration decreased, 3-series switch rate increased. Fewer children were associated with higher switch rate on the 4-series condition in all menopause stages (see Table 6.10). However, these associations were strong in the premenopause group and moderate in peri and postmenopause groups. No other significant associations with reproductive markers were observed.

Correlation patterns across Time since menopause groups

Vocabulary was positively associated with switch rate (low to moderate associations) in both recent and longer-term menopausal women (see Table 6.9). Switch rates moderately increased with increase in years of education and with decrease in age in the longer-term group, but these associations were near zero to low for recent menopausal women. Increase in menstrual cycle duration, age at menarche and number of years since menopause moderately decreased the switch rate in the longer-term group (see Table 6.10). However, these associations were near zero to low in the recent group. No other significant associations were observed.

Thus, vocabulary was the most consistent correlate with switch rate across Age groups, Menopause stages and Time since menopause groups. The magnitude of these associations was low to moderate. Among the reproductive characteristics, number of children, menstrual cycle duration and number of years since menopause may have a role in switch rate on C-series tasks.

The following subsection (section 6.4.3.2) reports the results from the ANOVAs and ANCOVAs comparing women across Age groups, Menopause stages and Time since menopause for switch rate. For Age group and Menopause stage comparisons none of the variables were deemed to suitable to be used as covariates based on the selection criteria outlined in section 6.3.3; therefore, no ANCOVAs were conducted. For the Time since menopause comparison, vocabulary was used as a covariate in the analysis comparing recent and longer-term menopausal women for switch rate.

Table 6.9

Correlations between switch rate (SR) and demographic variables as a function of menopause stage, age group and time since menopause

Independent variable	Group	Dependent variable	Demographic variable		
			Vocabulary T score	Education (in years)	Age (in years)
Menopause stage	Premenopause (n = 9)	SR_2 series	.73*	.32	-.31
		SR_3 series	.52	-.02	.07
		SR_4 series	.43	.06	-.12
	Perimenopause (n = 11)	SR_2 series	.36	-.04	.46
		SR_3 series	.44	-.11	.38
		SR_4 series	.73*	-.24	-.01
	Postmenopause (n = 12)	SR_2 series	.36	.03	.56
		SR_3 series	.21	-.05	.29
		SR_4 series	.58*	-.03	.50
Age group	Group I (46-56 years) (n = 32)	SR_2 series	.42*	.10	.48**
		SR_3 series	.37*	-.07	.44*
		SR_4 series	.50**	-.03	.36*
	Group II (56-65 years) (n = 24)	SR_2 series	.38	.39	-.19
		SR_3 series	.40	.21	-.26
		SR_4 series	.35	.16	-.32
	Group III (70-79 years) (n = 22)	SR_2 series	.33	.40	-.24
		SR_3 series	.12	.18	-.24
		SR_4 series	.36	.41	-.18
Time since menopause	Recent menopausal (n = 16)	SR_2 series	.42	.24	.18
		SR_3 series	.16	.00	-.03
		SR_4 series	.38	.07	.06
	Longer-term menopausal (n = 42)	SR_2 series	.33*	.35*	-.15
		SR_3 series	.24	.20	-.39*
		SR_4 series	.40**	.31*	-.39*

*$p < .05$, ** $p < .01$

Table 6.10

Correlations between switch rate (SR) and reproductive variables as a function of menopause stage, age group and time since menopause

Dependent variable	Group	*n*	Reproductive variable						
			Age at menarche	Menstrual cycle length	Age at first childbirth+	Number of children	Age at menopause	Number of years since menopause	Number of reproductive years
SR_2-series	Premenopause	9	.22	-.11	.31	-.34	-	-	-
	Perimenopause	11	.17	-.57	-.27	.02	-	-	-
	Postmenopause	12	-.21	.07	.34	-.39	.24	.43	.30
	Group I 46-55 years	32	-.02	-.15	-.05	-.27	.24	.43	.30
	Group II 56-65 years	24	-.14	-.13	-.15	.29	.06	-.24	.12
	Group III 70-79 years	22	-.15	-.22	.15	-.25	-.03	-.12	.03
	Recent menopausal women	16	-.13	.21	.37	-.25	.20	-.01	.20
	Longer-term menopausal women	42	-.19	-.35*	-.02	-.06	-.04	-.12	.05
SR_3-series	Premenopause	9	-.22	-.39	.31	-.24	-	-	-
	Perimenopause	11	.23	-.63*	-.23	-.21	-	-	-
	Postmenopause	12	.07	-.01	.50	-.55	.20	.11	.15
	Group I 46-55 years	32	.02	-.28	-.03	-.36*	.20	.11	.15
	Group II 56-65 years	24	-.35	.01	-.35	.18	.16	-.36	.33
	Group III 70-79 years	22	.10	-.02	-.02	-.08	-.27	.02	-.27
	Recent menopausal women	16	.01	.14	.14	-.43†	.02	-.13	.01
	Longer-term menopausal women	42	-.24	-.23	.05	-.10	.05	-.34*	.14
SR_4-series	Premenopause	9	.59	-.36	.60	-.72*	-	-	-
	Perimenopause	11	.52	-.48	-.55	-.31	-	-	-
	Postmenopause	12	-.12	.16	.46	-.46	.39	.12	.40
	Group I 46-55 years	32	.14	-.06	.03	-.51**	.39	.12	.40
	Group II 56-65 years	24	-.17	.15	-.14	.15	-.16	-.17	-.04
	Group III 70-79 years	22	-.31	.13	.08	.16	.05	-.14	.16
	Recent menopausal women	16	.04	.36	.25	-.45†	.10	-.09	.08
	Longer-term menopausal women	42	-.36*	-.21	.15	.09	.09	-.36*	.23

Note. +*Sample size for age at first childbirth variable*, Premenopause: 6, Perimenopause: 10, Postmenopause: 8; 46-55 years: 24, 56-65 years: 23, 70-79 years: 21; Recent menopausal: 12, Longer-term menopausal: 40
†p <.10, *p < .05, **p < .01.

Switch cost

Correlation patterns across Age groups

Weak negative associations were seen between vocabulary scores and switch costs in all the age groups (see Table 6.11). Education was positively associated with switch costs in Group I and negatively in Groups II and III, and the magnitude of these correlations ranged between low to moderate. The relationship of switch cost with age was weak across all the three age groups. As the age at first childbirth increased, 3-series switch cost moderately increased in Group II, but this association was near zero in Group I and low in Group III (see Table 6.12). No other significant associations were observed with any other reproductive characteristics.

Correlation patterns across Menopause stages

In the younger group (Group I), correlations of switch cost with vocabulary were negative and weak across menopause stages (see Table 6.11). Associations between switch costs and number of years of education were strongest in postmenopausal women followed by pre and perimenopausal women. There were low to moderate correlations with age within each menopause stage. No significant associations were seen with any of the reproductive markers.

Correlation patterns across Time since menopause groups

In recent and longer-term menopausal women, correlations between switch costs and vocabulary were near zero to low (see Table 6.11). Education was positively associated with switch cost in recent menopausal women and negatively (low in magnitude) in longer-term menopausal women. Weak correlations were found between age and switch cost across time since menopause. No significant associations were found with reproductive markers in both groups of women.

Thus, the analyses showed that vocabulary may contribute to switch costs in C-series tasks. Among the reproductive characteristics, age at first childbirth may have a role to play. The covariates were chosen based on the criteria discussed in section 6.3.3. None of the variables were deemed suitable to be used as covariates in Age group or Menopause stage or Time since menopause analyses.

Table 6.11

Correlations between switch cost (SC) and demographic variables as a function of menopause stage, age group and time since menopause

Independent variable	Group	Dependent variable	Demographic variable		
			Vocabulary T score	Education (in years)	Age (in years)
Menopause stage	Premenopause (n = 9)	SC_2 series	-.28	.35	.00
		SC_3 series	-.20	.27	-.35
		SC_4 series	-.25	.39	-.25
	Perimenopause (n = 11)	SC_2 series	-.52	.15	.12
		SC_3 series	-.58	.18	.20
		SC_4 series	-.44	.13	.44
	Postmenopause (n = 12)	SC_2 series	.02	.50	-.37
		SC_3 series	.16	.57*	-.22
		SC_4 series	-.31	.49	-.44
Age group	Group I (46-56 years) (n = 32)	SC_2 series	-.27	.28	-.25
		SC_3 series	-.25	.33	-.17
		SC_4 series	-.36*	.30	-.08
	Group II (56-65 years) (n = 24)	SC_2 series	-.12	-.18	.25
		SC_3 series	-.10	-.04	.27
		SC_4 series	-.03	-.08	.30
	Group III (70-79 years) (n = 22)	SC_2 series	-.04	-.32	.16
		SC_3 series	.05	-.20	.25
		SC_4 series	-.20	-.40	.25
Time since menopause	Recent menopausal (n = 16)	SC_2 series	.05	.36	-.27
		SC_3 series	.18	.46†	-.16
		SC_4 series	-.06	.27	-.20
	Longer-term menopausal (n = 42)	SC_2 series	-.04	-.17	-.13
		SC_3 series	.03	-.08	.13
		SC_4 series	-.15	-.23	.17

*p < .05, ** p < .01

Table 6.12

Correlations between switch cost (SC) and reproductive variables as a function of menopause stage, age group and time since menopause

Dependent variable	Group	*n*	Reproductive variable						
			Age at menarche	Menstrual cycle length	Age at first childbirth[+]	Number of children	Age at menopause	Number of years since menopause	Number of reproductive years
SC_2-series	Premenopause	9	.00	-.27	-.04	-.12	-	-	-
	Perimenopause	11	.04	.00	.16	.11	-	-	-
	Postmenopause	12	-.09	.09	-.17	.15	-.40	.06	-.31
	Group I 46-55 years	32	.01	.04	.04	.09	-.40	.06	-.31
	Group II 56-65 years	24	-.06	.15	.37	-.32	-.03	.24	-.01
	Group III 70-79 years	22	-.15	.11	.11	.03	-.20	.22	-.13
	Recent menopausal women	16	-.24	-.02	.24	.04	-.31	.05	-.20
	Longer-term menopausal women	42	-.05	.20	.27†	-.12	-.01	-.10	.01
SC_3-series	Premenopause	9	.18	-.10	-.08	-.09	-	-	-
	Perimenopause	11	-.04	.07	.17	.24	-	-	-
	Postmenopause	12	-.26	.15	-.31	.33	-.26	.07	-.12
	Group I 46-55 years	32	-.05	.14	.06	.21	-.26	.07	-.12
	Group II 56-65 years	24	.13	.02	.50*	-.21	-.16	.35	-.23
	Group III 70-79 years	22	-.24	-.07	.24	-.10	.03	.13	.11
	Recent menopausal women	16	-.29	.04	.34	.17	-.17	-.02	-.06
	Longer-term menopausal women	42	.05	.08	.21	-.08	-.07	.13	-.08
SC_4-series	Premenopause	9	-.24	.17	-.33	.46	-	-	-
	Perimenopause	11	-.04	-.10	.21	.12	-	-	-
	Postmenopause	12	-.20	-.07	-.24	.42	-.53	.17	-.39
	Group I 46-55 years	32	-.11	.01	.08	.31	-.53	.17	-.39
	Group II 56-65 years	24	-.11	-.13	.25	-.23	.15	.14	.16
	Group III 70-79 years	22	.10	-.29	.09	-.28	-.22	.29	-.24
	Recent menopausal women	16	-.42	-.20	.07	.22	-.23	.01	-.06
	Longer-term menopausal women	42	.15	-.02	.05	-.26†	-.14	.19	-.19

Note. [+]*Sample size for age at first childbirth variable*, Premenopause: 6, Perimenopause: 10, Postmenopause: 8; 46-55 years: 24, 56-65 years: 23, 70-79 years: 21; Recent menopausal: 12, Longer-term menopausal: 40. †p <.10, *p < .05, **p < .01.

6.4.3.2. ANOVAs and ANCOVAs comparing women across Age groups, Menopause stages and Time since menopause on OS and C-series task performances

Separate ANOVAs were conducted in order to examine differences in baseline syllable and word rates between Age groups, Menopause stages and Time since menopause groups. Category (numbers, letters of the alphabet, months, days of the week) was the repeated measure and Age group (46-55, 56-65, 70-79 years) or Menopause stage (pre, peri, postmenopause) or Time since menopause (recent, longer-term) was the between group factor. Separate ANOVAs were also performed to compare mean differences in switch rate and switch cost across Age groups, Menopause stages and Time since menopause groups. Condition (2, 3, 4-series) was the repeated measure and Age group or Menopause stage or Time since menopause was the key between group factor.

Age group comparisons

<u>Baseline syllable rate and word rate</u>

Women across the three Age groups showed no significant differences in their baseline syllable and word rates. There was a significant effect of Category[23] on the syllable rate, $F(3, 225) = 159.36$, $p < .001$. The syllable rate was highest for numbers followed by the rates for days, months and letters. Post hoc comparisons using Bonferroni corrected paired *t*-tests ($\alpha = .05/6 = .008$) showed significant differences in syllable rate between numbers and letters, $t(77) = 20.52$, $p < .001$, numbers and months, $t(77) = 6.97$, $p < .001$, numbers and days, $t(77) = 3.79$, $p < .001$, letters and months, $t(77) = -14.60$, $p < .001$, letters and days, $t(77) = -18.02$, $p < .001$, and months and days, $t(77) = -5.94$, $p < .001$.

[23] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction also showed significant differences across Categories on syllable rate.

The effect of Category[24] on the word rate was also significant, $F(3, 225) = 131.35$, $p < .001$. Post hoc comparisons using Bonferroni corrected paired *t*-tests ($\alpha = .05/6 = .008$) showed significant differences in word rate between numbers and letters, $t(77) = -12.76$, $p < .001$, numbers and months, $t(77) = -2.82$, $p = .006$, numbers and days, $t(77) = -4.99$, $p < .001$, letters and months, $t(77) = 13.01$, $p < .001$, letters and days, $t(77) = 12.14$, $p < .001$, and months and days, $t(77) = -4.49$, $p < .001$. The word rate was highest for letters followed by the rates for days of the week, months and numbers. No Category x Age group interaction was seen for either variable.

Switch rate and Switch cost

A main effect of Age group for switch rate or switch cost was not significant. There were significant effects of Condition on switch rate[25], $F(2, 150) = 322.27$, $p < .001$, and switch cost[26], $F(2, 150) = 59.14$, $p < .001$. Post hoc paired *t*-tests with Bonferroni corrections ($\alpha = .05/3 =.017$) revealed significant differences in switch rates between the 2- and the 3-series, $t(77) = 16.79$, $p < .001$, between the 2 and the 4-series, $t(77) = 21.35$, $p < .001$, and between the 3 and the 4-series, $t(77) = 8.24$, $p < .001$. Similarly, there were significant differences in the switch costs between the 2- and the 3-series, $t(77) = -6.96$, $p < .001$, between the 2- and the 4-series, $t(77) = -4.03$, $p < .001$, and between the 3- and the 4-series, $t(77) = -8.25$, $p < .001$. The switch rate decreased and the switch cost increased from 2- to 3- to 4-series (see Figures 6.4 and 6.5).

[24] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction showed significant differences across Categories on word rate.

[25] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction showed significant differences across Conditions on switch rate.

[26] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction showed significant differences across Conditions on switch cost.

A nonsignificant Condition x Age group[27] trend for switch rate, $F(3.43, 128.62) = 2.52$, $p = .053$, and a significant Condition x Age group interaction, $F(4, 150) = 3.48$, $p = .010$, were observed. Post hoc ANOVAs showed differences between the three Age groups only for 3-series switch rate, $F(2, 75) = 6.79$, $p = .002$, where the switch rate decreased with age (see Figure 6.4). For switch cost, post hoc one-way ANOVA showed no differences between the Age groups in any of the conditions. Post hoc ANOVA with Condition as a repeated measure was conducted separately for each age group. Switch cost increased significantly from 2- to 3- to 4-series in women aged 46-55 years. However, in women aged 56-65 and 70-79 years, 2-series switch cost was significantly lower than 3 and 4-series switch costs, but there was no difference in switch cost between 3 and 4-series. The rise in switch cost from the 2-series to the 3-series condition (17%) was the highest in the oldest age group (Group III) when compared to the rise in the other two younger groups (approximately around 9% and 11% in Group I and Group II respectively) (see Figure 6.5).

There were no significant effects of Age group for switch rate and switch cost even when the data were re-analysed after excluding women with hysterectomies.

[27] The assumption of sphericity was violated for Condition for the switch rate measure. The results from sphericity assumed showed a significant effect, but the Greenhouse-Geisser correction showed a nonsignificant trend. Therefore, results from the Greenhouse-Geisser correction are reported.

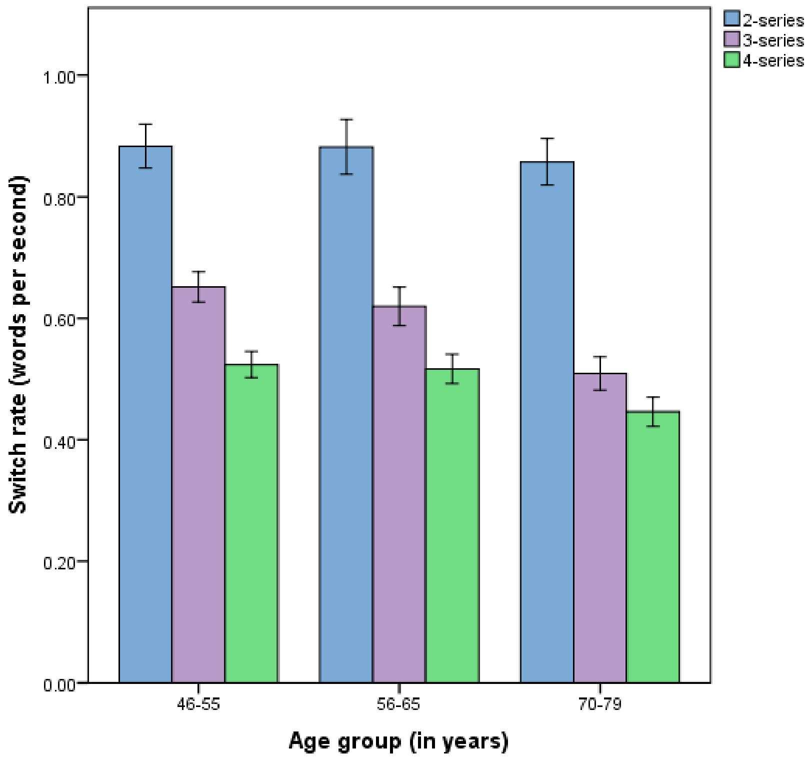

Figure 6.4. Switch rate (number of words per second) for each condition across age groups. Error bars represent ± 1 standard error.

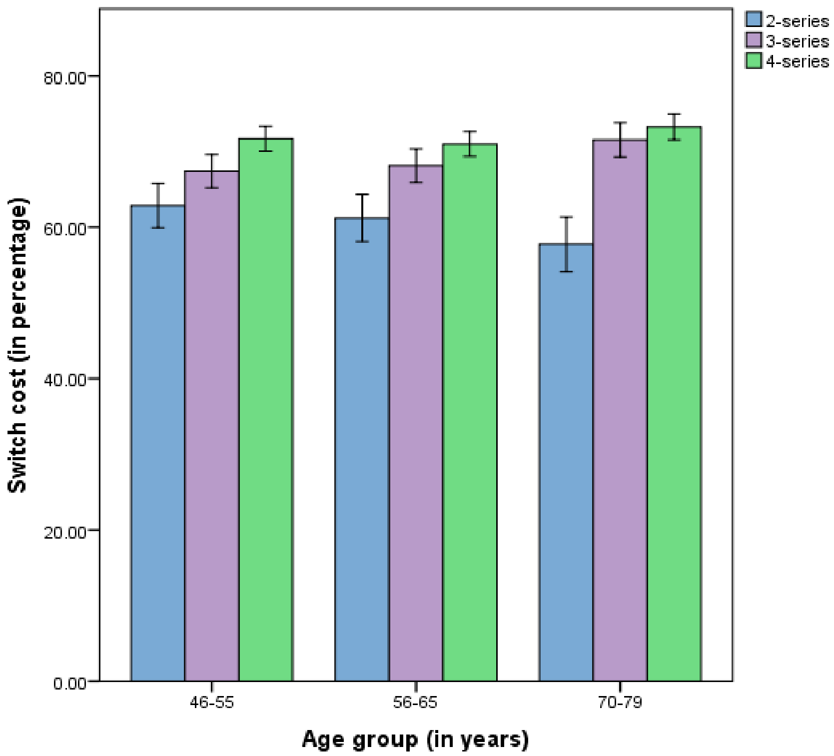

Figure 6.5. Switch cost (in percentage) for each condition across age groups. Error bars represent ± 1 standard error.

Errors

Three types of errors were analysed, within-task, between-task and other errors. The percentage of error type was calculated and served as the dependent variables. Three separate ANOVAs were conducted for each error type with Condition (2, 3, 4-series) as the repeated measure and Age group (46-55, 56-65, 70-79 years) as the between group factor. Women across Age groups did not differ significantly for any of the error types. There was a significant effect of Condition for within-task, $F(2, 150) = 4.04$, $p = .020$, and between-task error percentages[28], $F(2, 150) = 6.24$, $p = .002$, but not for other errors. The percentage of within task errors decreased and that of between-task errors increased as Condition increased from 2 to 4 categories. There were no significant interactions of Condition x Age group.

Correlations between dependent measures

The relationships within switch rates and switch costs across conditions were studied separately for each Age group (see Table 6.13). Pearson correlations showed that an increase in the 2-series switch rate was associated with increases in the 3 and 4-series switch rates across all the three age groups. Similar patterns of correlations were also obtained for the switch cost. The magnitudes of correlations were similar across all the groups, indicating that women in different age groups were utilizing similar strategies to perform the task.

[28] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction also showed significant differences.

Table 6.13

Correlations between switch rate (SR) or switch cost (SC) between conditions as a function of age group

		SR_3	SR_4		SC_3	SC_4
Group I (46-55 years) (*n* = 32)	SR_2	.75**	.72**	SC_2	.87**	.76**
	SR_3		.65**	SC_3		.85**
Group II (56-65 years) (*n* = 24)	SR_2	.74**	.61**	SC_2	.80**	.78**
	SR_3		.77**	SC_3		.80**
Group III (70-79 years) (*n* = 22)	SR_2	.69**	.55**	SC_2	.79**	.64**
	SR_3		.61**	SC_3		.72**

* $p < .05$, ** $p < .01$

In summary, the results showed that women across the three Age groups were matched on their baseline rates when they produced words from individual overlearned categories. Switch rate decreased with age especially when switching was performed between three categories (letters, numbers, months). In addition, women aged 70-79 years showed a greater increase in the switch cost percentage between the 2- and 3-series conditions than the other two younger groups (46-55; 56-65 years).

Menopause stage comparisons

<u>*Baseline syllable rate and word rate*</u>

Women across the menopause stages did not differ in their syllable and word rates. There was a significant effect of Category on the syllable rate[29], $F(3, 87) = 49.11$, $p < .001$. Similar to the age group comparisons, the maximum number of syllables was produced in the numbers category followed by days, months and letters of the alphabet. Similarly, Category effects were significant on the word rate, $F(3, 87) = 46.57$, $p < .001$.

[29] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction also showed a significant effect of Category on syllable rate.

More words were produced in the letter category followed by days, months and numbers' categories. There were no significant differences in word rates between months and days and between numbers and months. There was no significant Condition x Menopause stage effect for either syllable or word rate.

Switch rate and Switch cost

Women across the three stages of menopause did not differ significantly in their switch rate and switch cost (see Figures 6.6 and 6.7). Significant effects of Condition were seen on switch rate, $F(2, 58) = 131.86$, $p < .001$, and switch cost[30], $F(2, 58) = 15.85$, $p < .001$. Switch rate decreased and switch cost increased with increase in condition. No significant interactions were seen.

Errors

Error types did not vary across menopause stages and no significant interactions were seen. There were no significant effects of Condition on within-task and between-task errors. There were no other errors in the 2 and 3-series conditions, and only one participant made an other error in the 4-series condition, indicating a very low error rate across all the three groups.

[30] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction also showed a significant effect of Condition on switch cost.

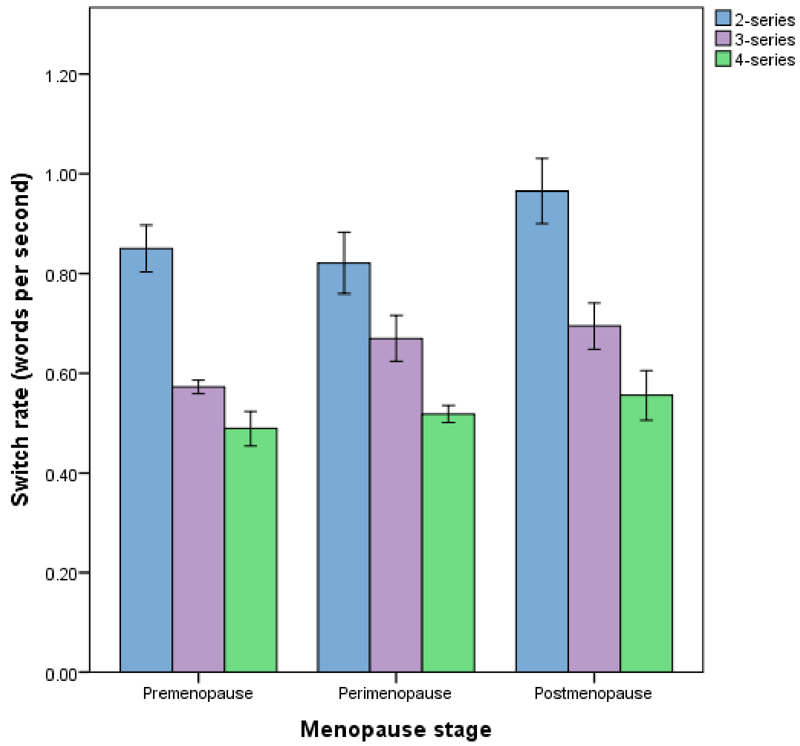

Figure 6.6. Switch rate (number of words per second) for each condition across menopause stages. Error bars represent ± 1 standard error.

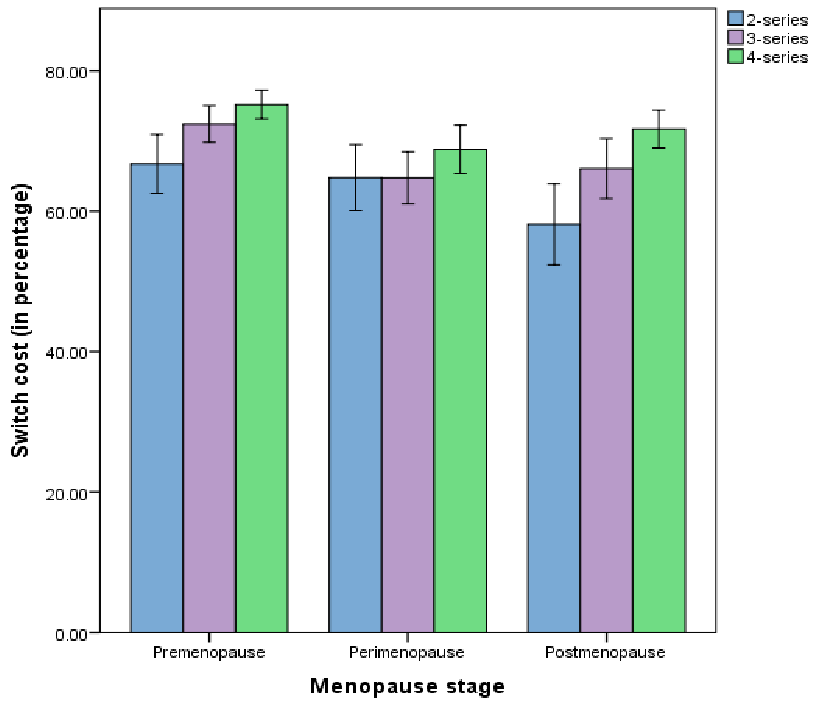

Figure 6.7. Switch cost (in percentage) for each condition across menopause stages. Error bars represent ± 1 standard error.

Correlations between dependent measures across menopause stages

The associations for switch rates and switch costs across conditions and menopause stages were examined using Pearson correlations. The results showed strong correlations among switch rate and among switch cost measures, except in the premenopause stage (see Table 6.14).

Table 6.14

Correlations between switch rate (SR) or switch cost (SC) between conditions as a function of menopause stage

		SR_3	SR_4		SC_3	SC_4
Premenopause (*n* = 9)	SR_2	.17	.48	SC_2	.75*	.52
	SR_3		.41	SC_3		.74*
Perimenopause (*n* =11)	SR_2	.92**	.61*	SC_2	.96**	.89**
	SR_3		.73*	SC_3		.93**
Postmenopause (*n* = 12)	SR_2	.79**	.89**	SC_2	.90**	.85**
	SR_3		.76**	SC_3		.82**

$*p < .05$, $**p < .01$

Time since menopause comparisons

Baseline syllable and word rate

Women across the two groups did not differ significantly in their syllable and word rates. There was a significant effect of Category on the syllable rate[31], $F(3, 168) = 112.72$, $p < .001$, and the word rate, $F(3, 168) = 71.67$, $p < .001$. The maximum number of syllables was produced in the numbers category followed by days, months and letters of the alphabet. The word rate was highest for letters followed by days, months and numbers. There were no significant interactions for either variable.

[31] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction showed a significant effect of Category on the syllable rate.

Switch rate and switch cost

Recent and longer-term menopausal women did not differ significantly in their switch rates and switch costs. There were significant effects of Condition on the switch rate[32], $F(2, 112) = 209.96$, $p < .001$, and the switch cost[33], $F(2, 112) = 42.32$, $p < .001$. Switch rate decreased and switch cost increased with increase in condition. No significant interactions were seen.

For switch rate, additional ANCOVA with vocabulary as a covariate was conducted. There were no significant effects of Condition, Time since menopause and Condition x Time since menopause for switch rate. Vocabulary was significantly associated to switch rate, $F(1, 55) = 8.18$, $p = .006$. After excluding women with hysterectomies, the results were the same as above for switch rate (with or without covariate) and switch cost.

Correlations between dependent measures

The associations for switch rates and switch costs across conditions and time since menopause were examined using Pearson correlations. The results showed strong correlations among switch rate and among switch cost measures in both the groups (see Table 6.15).

Table 6.15
Correlations between switch rate (SR) or switch cost (SC) between conditions as a function of time since menopause

		SR_3	SR_4	SC_3	SC_4
Recent menopausal	SR_2	.78**	.72**	.93**	.85**
(n = 16)	SR_3		.74**		.83**
Longer-term menopausal	SR_2	.70**	.65**	.72**	.64**
(n = 42)	SR_3		.75**		.74**

*$p < .05$, **$p < .01$

[32] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction also showed significant effects of Condition on switch rate.
[33] The assumption of sphericity was violated. The results from Greenhouse-Geisser correction also showed significant effects of Condition on switch cost.

6.4.4. Comparison of switching across tasks (letter fluency and C-series tasks)

The relationship between the number of switches in the letter fluency task and the switch rate in the C-series task was studied using Pearson correlations to examine whether both measures of switching represented the same construct of executive ability. The results showed weak correlations between the two variables across Menopause stages, Age groups and Time since menopause groups, indicating that the two outcome measures of switching were independent (see Table 6.16).

Table 6.16

Correlations between the number of switches produced on the letter fluency task and the switch rate in the three different conditions (2, 3, 4-series) on the C-series task as a function of menopause stage, age group and time since menopause

Independent variable	Group	*n*	Switch rate		
			2-series	3-series	4-series
Menopause stage	Premenopause	9	-.12	-.17	-.37
	Perimenopause	11	.22	.33	.09
	Postmenopause	12	.14	-.01	.19
Age group	Group I (46-55 years)	32	.06	.04	.02
	Group II (56-65 years)	24	.04	.01	.20
	Group III (70-79 years)	23	.17	-.18	.14
Time since menopause	Recent menopausal	16	.16	.03	.14
	Longer-term menopausal	42	.07	-.09	.18

A summary of all the findings are presented in Tables 6.17 (verbal fluency) and 6.18 (OS, C-series tasks).

Table 6.17

Summary of results for the verbal fluency tasks

			Effects of Age group		Effects of Menopause Stage (MS)	Effects of Time since menopause (TSM)		Correlational analyses
			Women with and without hysterectomies	Women without hysterectomies		Women with and without hysterectomies	Women without hysterectomies	
Verbal Fluency	Category fluency	Total number of words	NS	SF 70-79 years < 46-55 years ≈ 56-65 years NS (controlled for education)	NS	NS	SF Recent > Longer-term NS (controlled for education)	Vocabulary, education, age at first childbirth
	Letter fluency	Adapted Troyer's method						
		a. Total number of words	NS	NS	NS	NS	NS	Vocabulary, education, number of children
		b. Number of switches	NS	NS	NS	NS	NS	
		c. Mean cluster size	NS	NS	NS	NS	NS	
		Time course analysis						
		a. Total number of words	Age: NS Time: T1 > T2 > T3	Age: NS Time: T1 > T2 > T3	MS: NS Time: T1 > T2 > T3	TSM: NS Time: T1 > T2 > T3	TSM: NS Time: T1 > T2 > T3	- - -
		b. Number of switches	Age: NS Time: T1 ≈ T2 > T3	Age: NS Time: T1 ≈ T2 > T3	MS: NS Time: T1 ≈ T2 > T3 Time x MS: SF Pre: T2 > T1 = T3 Peri: T1 = T2 > T3	TSM: NS Time: T1 ≈ T2 > T3 Time x TSM: SF Recent: T2 > T3 Longer-term: T1 ≈ T2 > T3	TSM: NS Time: T1 ≈ T2 > T3 Time x TSM: SF Recent: T2 > T3 Longer-term: T1 ≈ T2 > T3	
		c. Mean cluster size	Age: NS Time: NS trend T1 < T2 < T3 Time x Age: NS *Postmenopausal women* Time x Age group: SF 46-55 years: T2 > T3 56-65 years: T3 > T1	Age: NS Time: NS trend T1 < T2 < T3 Time x Age: NS *Postmenopausal women* Time x Age: SF 46-55 years: T2 > T3 56-65 years: T3 > T1	MS: NS Time: NS Time x MS: SF T1: Pre > Peri, Post T2: Post > Pre, Peri	TSM:NS Time: NS Time x TSM: NS	TSM: NS Time: NS Time x TSM: NS	
		Linguistic feature analysis						
		a. Word frequency	Age, Time: NS Letter x Time x Age: SF For letter A in T3, 46-55 > 56-65 ≈ 70-79 years	Age, Time: NS Letter x Time x Age: SF For letter A in T3, 46-55 > 56-65 ≈ 70-79 years	MS, Time: NS	TSM: NS Time: T1 >T2 ≈ T3	TSM: NS Time: T1 >T2 ≈ T3	- -
		b. Word length	Age, Time: NS	Age, Time: NS	MS, Time: NS	TSM, Time: NS	TSM, Time: NS	

Note. SF: Significant findings, NS: Not significant

Table 6.18

Summary of results for the C-series task

			Effects of Age group		Effects of Menopause Stage (MS)	Effects of Time since menopause (TSM)		Correlational analyses
			Women with and without hysterectomies	Women without hysterectomies		Women with and without hysterectomies	Women without hysterectomies	
C-series task	OS task	Baseline syllable rate	Age: NS	Age: NS	MS: NS	TSM: NS	TSM: NS	-
		Baseline word rate	Age: NS	Age: NS	MS: NS	TSM: NS	TSM: NS	-
	C-series task	Switch rate	Age: NS Condition: SF 2-series > 3-series > 4-series Condition x Age: NS trend 3-series switch rate with increase in age	Age: NS Condition: SF 2-series > 3-series > 4-series Condition x Age: NS trend 3-series switch rate with increase in age	MS: NS Condition: SF 2-series > 3-series > 4-series Condition x MS: NS	TSM: NS Condition: SF 2-series > 3-series > 4-series Condition x TSM: NS	TSM: NS Condition: SF 2-series > 3-series > 4-series Condition x TSM: NS	Vocabulary (weak to moderate), Number of children
		Switch cost	Age: NS Condition: SF 2-series < 3-series < 4-series Condition x Age: SF Rise in switch cost percentage from 2 to 3 series 46-55 years: 9% 56-65 years: 11% 70-79 years: 17%	Age: NS Condition: SF 2-series < 3-series < 4-series Condition x Age: SF Rise in switch cost percentage from 2 to 3 series 46-55 years: 9% 56-65 years: 11% 70-79 years: 17%	MS: NS Condition: SF 2-series < 3-series < 4-series Condition x MS: NS	TSM: NS Condition: SF 2-series < 3-series < 4-series Condition x TSM: NS	TSM: NS Condition: SF 2-series < 3-series < 4-series Condition x TSM: NS	Vocabulary (weak to moderate), Age at first childbirth

Note. SF: Significant findings, NS: Not significant

6.5. Discussion

6.5.1. Effects of age on verbal fluency

The aim of the study was to investigate the effects of age and menopause on verbal fluency. The results indicated that category and letter fluency did not significantly decline with increasing age when all women in the sample were studied. However, when women with hysterectomies were excluded, the findings of the study replicated earlier reports of significant decline in category fluency with advancing age (Brickman et al., 2005; Kemper & Sumner, 2001; Parkin & Java, 1999; Troyer et al., 1997; Van der Elst et al., 2006), but there was no change in letter fluency (Kemper & Sumner, 2001; Parkin & Java, 1999; Sauzeon et al., 2011; Troyer et al., 1997). Women aged 70-79 years produced fewer words in category fluency than women aged 46-55 and 56-65 years (see Table 6.3). A declining trend was also seen for letter fluency (see Table 6.6).

The study sample included five women with hysterectomies in the two older age groups. Women who undergo hysterectomies with ovarian conservation experience an abrupt cessation of menses. The surgery causes disturbance in the ovarian function because of alterations in blood flow to the ovaries (Farquhar, Sadler, Harvey, & Stewart, 2005; Settnes et al., 2005). Findings from treatment studies suggest that when women with surgical menopause are supplemented with estrogen treatment, there is an improvement in their cognitive functions (Phillips & Sherwin, 1992; Sherwin & Phillips, 1990). The Religious Orders Study and the Memory and the Aging Project in the USA also found that when women with surgical menopause are supplemented with hormone therapy within 5 years of the surgery and are prescribed medications for at least 10 years, there is a slower decline in cognitive abilities (Bove et al., 2014). Of the five women who had had hysterectomies in the current study, three were past users of hormone replacement therapy for a span of three to six years and one of them had initiated hormone therapy right after the surgery for a period of five years (41-46 years of age). It is likely that this exogenous hormone supplementation may have had a neuroprotective effect in this group of women and masked the age-related decline in category fluency.

However, after controlling for education the effects of age on category fluency were not significant. In line with earlier reports, the present study also showed that as the number of years of education increased, the total number of words produced on the category fluency task increased (Brickman et al., 2005; Elkadi et al., 2006; Gladsjo et al., 1999; Van der Elst et al., 2006) (see Table 6.1) and education was contributing to performance similarly across age groups. Therefore, it is possible that higher levels of education in the older groups might have also contributed to the nonsignificant finding (see Chapter 8 for detailed discussion).

6.5.2. Effects of menopause on verbal fluency

With reference to the effects of menopause on verbal fluency, the current study showed that women across menopause stages remained stable in their performance on category (see Table 6.3) and letter fluency (see Table 6.6) tasks even after controlling for the effects of age. These results are consistent with findings from earlier cross-sectional studies, which reported no significant effect of menopause on verbal fluency (Fuh et al., 2003; Herlitz et al., 2007; Lokken & Ferraro, 2006; Weber et al., 2013). Berent-Spillson et al. (2012) showed that premenopasual women produced more words on the letter fluency task than peri and postmenopausal women. Cross study differences could have arisen due to discrepancies in research design. In the present study, none of the postmenopausal women in the younger 46-55 years age group had experienced surgical menopause (hysterectomy with or without oophorectomy), whereas Berent-

Spillson et al. (2012) included women who had experienced surgical menopause. Women with surgical menopause are at an increased risk for cognitive impairments and AD than naturally postmenopausal women (Rocca et al., 2012; Settnes et al., 2005). Therefore, inclusion of surgically menopausal women in Berent-Spillson et al.'s (2012) sample might have contributed to the lower mean score in postmenopausal women. In the current study, women across menopause stages were well matched on the number of years of education but that was not the case in Berent-Spillson et al.'s (2012) study. Berent-Spillson et al.'s (2012) premenopausal women had more years of education than women in their peri and postmenopausal groups. As shown in the current study, education is positively associated with verbal fluency performance. Therefore, greater word production in premenopausal women may have been confounded with education levels in Berent-Spillson et al.'s (2012) study.

6.5.3. Effects of age and menopause on cognitive strategy use in letter fluency

Adapted Troyer's method (Troyer et al., 1997; Wadnerkar, 2008; Wadnerkar et al., 2008 June) analysis

A secondary aim of the study was to investigate the effects of age and menopause on the underlying cognitive processes and cognitive strategy use in verbal fluency. The present study made use of additional measures such as switches and mean cluster size to examine cognitive strategy use (Troyer et al., 1997; Wadnerkar, 2008; Wadnerkar et al., 2008 June). The results showed that switches and mean cluster size were associated with total word production (see Table 6.7), indicating they were measuring a cognitive process involved in verbal fluency. Additionally, it was found that vocabulary and education were positively associated with mean cluster size but not with number of switches. These findings support earlier literature which suggests that these two cognitive strategies are separate (Troyer et al., 1997). Further, it supplements previous literature which suggest that clustering is a measure of semantic or vocabulary knowledge (Gomez & White, 2006; Troyer et al., 1997; Troyer et al., 1998a), by demonstrating a positive association with vocabulary and education.

It is not clearly established whether switching and clustering on the letter fluency task are affected by age (Lanting et al., 2009; Troyer et al., 1997). In agreement with previous studies, the findings of the present study showed that the use of switching (Sauzeon et al., 2011; Troyer et al., 1997) and clustering (Sauzeon et al., 2011) strategies during the complete one-minute duration of the task did not differ across age groups. Contradictory to our expectation, the association between the total number of words and switches also did not show a grading by age. A moderate association was found between the two measures across all the three groups. To explore this finding, the data for the youngest group of women, aged 46-55 years, were further probed to examine the correlation patterns separately for the three stages of menopause. These analyses revealed that the association between total words and switches was strongest for premenopausal women than for peri and postmenopausal women. In line with the findings of the pilot data-mining project (Chapter 3) and Wadnerkar et al.'s (2008 June) study, these results suggest that high levels of estrogen in midlife premenopausal women may facilitate executive processes such as switching. Differences in correlation patterns across menopause stages could also be explained based on evidence from neuropsychological and psychoendocrinological studies. Behavioural and neuroimaging studies have shown that switching is frontally-mediated (Hirshorn & Thompson-Schill, 2006; Troyer et al., 1997; Troyer et al., 1998a). It is also known that the prefrontal cortex is a major neurofunctional substrate for estrogen action in human females (Bixo et al., 1995; Keenan et al., 2001). Estrogen levels are high in the premenopause stage than in the peri and postmenopause stages (Burger et al., 2002; Burger et al., 2007).

These high estrogen levels might have facilitated cognitive functions dependent on the frontal cortex such as switching, thereby, resulting in a stronger association between total words and switches in premenopausal women. Considering the results from both the age groups and menopause stage analyses, it can be suggested that the relationship between total words and switches in younger age groups is dependent on menopause status. Total words were strongly associated with switches and mean cluster size in premenopausal women, whereas in postmenopausal women (who were significantly older than premenopausal women), a strong association was only seen between total words and mean cluster size. This is consistent with the predictions that switching changes with age in verbal fluency (Lanting et al., 2009). Although there were differences in the cognitive strategy use across women in the different stages of menopause, their overall word performance was not affected. These findings indicate that they probably employed a combination of strategy changes and other cognitive processes that were not measured in the present study, in order to maintain word production.

Time course analysis

The current study also examined total word production and cognitive strategy in letter fluency across three equal 20 second time intervals. The results replicated previous reports of greater word production in the initial stages of recall (Graesser & Mandler, 1978; Fernaeus et al., 2008; Zimmerman et al., 2014). It was also found that more switches were produced in the initial time intervals, 0-40 seconds (T1, T2) and a larger mean cluster size was seen in the last 20 seconds (T3) of the task. These findings support earlier evidence which suggests that word-retrieval in the first half of the task is less effortful and reflects automatic cognitive processes (more word production and switching), whereas the latter half of the task requires a more effortful search for items based on semantic organization of the words (as evidenced by increase in clustering) (Crowe, 1998; Fernaeus & Almkvist, 1998).

Sauzeon et al. (2011) reported that younger adults switch more than older adults do in the first half of the task, whereas older adults produce larger clusters than younger adults in the latter half of the task. However, age did not interact with time for the use of cognitive strategies, switching and clustering, in the present study. Differences in findings between both the studies were possibly due to methodological discrepancies. The present study recruited women aged 46-79 years, whereas Sauzeon et al. (2011) compared a younger age group (M_{age}: 21.40 years) with an older group of women (M_{age}: 69.75 years). Participants across age groups were well matched for vocabulary in the current study, but in Sauzeon et al.'s (2011) study, the older group had higher vocabulary scores compared to the younger group which might have boosted their clustering in the second half of the task. There were also differences in how the time intervals between the studies were divided. The present study divided the one-minute task into three equal 20-second time intervals but Sauzeon et al. (2011) spliced the total one-minute task into time intervals of 30 second each. This makes it difficult to compare the study findings of both studies in detail. When the data from postmenopausal women were considered, women aged 46-55 years produced larger mean cluster sizes in the earlier time period (T2) than the later one (T3), whereas women aged 56-65 years produced larger mean cluster sizes in the later time period (T3) than the initial ones (see Figure 6.1). These results indicate that differences in the use of cognitive strategies across time in the letter fluency task may mask the age-related decline on this cognitive ability.

The time course analysis was also applied to analyse letter fluency responses obtained from women aged between 46-55 years across stages of menopause. Word production in the three different time intervals was not affected by menopause stage. However, there were differences in cognitive strategy use between menopausal groups across time intervals. Premenopausal women switched more in T2 than in T1, whereas perimenopausal women switched more in T1 than in T2 and postmenopausal women did not differ in the number of switches across time intervals (see Figure 6.2). Premenopausal women had a larger mean cluster size compared to peri and postmenopausal women in T1, whereas postmenopausal women had a larger mean cluster size in T2 (see Figure 6.3); thus, supporting earlier evidence of heightened use of clustering in older women in later time intervals (Sauzeon et al., 2011). The results also suggest that women across menopause stages maintain their overall word production in letter fluency by differential use of the cognitive strategies, switching and clustering, across time.

Linguistic feature analysis

The present study also investigated the linguistic features, frequency and length, of the produced words on the letter fluency task. Overall, the results showed the word frequency and word length did not vary across time, age and menopause stage. However, an interactive effect of time and age was found. Women aged 46-55 years showed a trend to produce words with higher frequency than women aged 56-65 and 70-79 years in the later time interval (40-60 seconds). Word frequency is considered as measure of lexical access (Brysbaert, 1996; Oldfield & Wingfield, 1965). Therefore, findings of the current study suggest that there may be subtle effects of age on lexical access.

6.5.4. Effects of age and menopause on switch rate and switch costs in C-series tasks

The current study also employed a C-series task to investigate the effects of age and menopause on cognitive processes that support word production. Two measures, switch rate and switch cost were used to quantify performance. The C-series task requires the efficient use of both automatic (production of words from the overlearned sequence such as months) and effortful (switching between overlearned sequences such as months and days) cognitive processes. It relies heavily on working memory and requires the participant to effectively use a number of executive processes such as initiation, selection and strategic organisation of appropriate responses, set shifting and monitoring. This reliance on executive processes can be tested by externally controlling the number of categories to switch within. The current study employed three C-series conditions, switching between 2, 3 and 4 categories. The results showed that the switch rate decreased and switch cost increased with conditions, indicating the sensitivity of the task to the effects of increased between category switching. Correlations between switch rates or switch costs across conditions in all age groups or menopause stages were strong in magnitude, suggesting that women across age or menopause stage used similar strategies to complete the task.

Switch rate is a measure of speaking rate (words per second) for each condition and switch cost is a measure of the time during which lexical search, category switching and verbal working memory are active (Gurd & Cowell, 2015). The present study indicated that with increase in age, speaking rate as measured by switch rate decreases. There was an increase in switch cost change from 2- to 3-series in women aged 70-79 years compared to those in the younger groups. It has been reported that working memory is compromised with advancing age (Craik & Salthouse, 2008) and this might have contributed to such a finding. Performance on C-series tasks is dependent on frontal and parietal mediated cognitive processes (Gurd, Weiss, Amunts, & Fink, 2003). The neural literature suggests that with increase in age there is a reduction in volume of areas in the frontal cortex (lateral prefrontal cortex, orbitofrontal cortex, prefrontal white matter) and changes in brain activity in these areas (Raz & Rodrigue, 2006; Raz et al., 2005). Taken together, these findings explain why an age-related increase in switch cost was observed in the present study. Switch rates and switch costs did not differ across menopause stages, indicating that estrogen decline in menopause transition and postmenopause may not affect between-category switching.

6.5.5. Relationship between switching in letter fluency and switching on C-series task

Switching on the letter fluency was not associated with switch rate on the C-series tasks in any of the menopause stages or age groups (see Table 6.16). Neuroanatomical evidence suggests that switching on letter fluency is frontally-mediated (Troyer et al., 1997), whereas task-switching in C-series paradigms is governed by the superior parietal cortex (Gurd et al., 2003). The current findings support and provide behavioural evidence that switching within the same category and switching between categories may be two separate processes, that age in different ways.

6.5.6. Relationship between verbal fluency, C-series task performances, and demographic and reproductive variables

The study also aimed to explore the relationships between the dependent measures on the verbal fluency and C-series tasks, demographic and reproductive characteristics. The findings of the study supported earlier literature by demonstrating positive associations between verbal fluency and vocabulary (Bolla et al., 1990; Steinberg et al., 2005) and education (Brickman et al., 2005; Elkadi et al., 2006; Gladsjo et al., 1999; Van der Elst et al., 2006). Among all the demographic and reproductive characteristics, vocabulary and education were the most consistent correlates with verbal fluency performance. Regression analyses further confirmed that number of years of education was a significant predictor of word production on category and letter fluency tasks (see Appendix 3). For the C-series task, vocabulary was found to be associated with switch rate, but these associations were lower in magnitude compared to those on the traditional verbal fluency tasks. The vocabulary subtask of WASI (Wechsler, 1999) measures crystallised intelligence or vocabulary knowledge. Therefore, differences in magnitude of associations across tasks possibly suggest differences in contribution of vocabulary knowledge to task performance.

With respect to reproductive markers, there were no clear patterns of associations. The age at first childbirth was associated with category fluency performance and switch cost on C-series task. On the other hand, letter fluency and switch rate were found to be associated with the number of children. A more detailed examination of the combined role of demographic and reproductive characteristics in determining word-finding abilities is presented in Chapter 8.

The association between vocabulary and category fluency was graded by age with the strongest correlation seen in the youngest group aged 46-55 years, despite age groups being matched on vocabulary scores. These findings may have occurred because of bigger sample sizes in the younger groups. It is also plausible that the category task measures different cognitive processes based on the age of the individual. Kemper and Sumner (2001), who examined verbal fluency ability in younger and older adults, showed that in younger adults verbal fluency is associated with vocabulary measures, whereas in older adults task performance is related to processing efficiency such as reading rate. These results highlight the importance of examining underlying strategies in category fluency across age. The correlational analyses also found a consistent moderate relationship between education and verbal fluency (category and letter) within each age group, despite groups varying in the years of education. These results indicate that education may have a protective effect on verbal fluency and possibly delay age-related decline in these cognitive abilities (see Chapter 8 for further discussion).

In relation to menopause, correlation between vocabulary and category fluency were graded by menopause stage, with the strongest associations in pre followed by peri and postmenopausal women. Also, for the letter fluency task associations with vocabulary and education were strongest in perimenopausal women. Women across menopause stages were matched on vocabulary and education, and therefore such patterns of correlations possibly indicate an effect of menopause status.

6.5.7. Effects of Time since menopause on verbal fluency, switch rate and switch costs

A post hoc research aim of the study was to investigate the effects of time since menopause on verbal fluency and C-series tasks performance. In agreement with the literature, recent and longer-term menopausal women did not differ in verbal fluency performance (Elsabagh et al., 2007) (see Tables 6.3 and 6.6). However, there were some differences in cognitive strategy use in letter fluency between the two groups. Recent menopausal women produced more switches in T2 (20-40 seconds) than in T3 (40-60 seconds), whereas longer-term menopausal switched more both in T1 (0-20 seconds) and T2 than in T3. Recent and longer-term menopausal women did not differ in their switch rate and switch costs on the C-series tasks.

Summary

In summary, the results of the study showed that in a sample well controlled for vocabulary, the effects of age on verbal fluency were subtle in midlife and late-life women. The effects of age on higher-order cognitive processes such as task-switching in healthy older women were evident in more complex and demanding tasks such as the C-series task. Verbal fluency and C-series tasks performances were unaffected by menopause stage or time since menopause. There was an interaction between time interval and age or menopause status or time since menopause on cognitive strategy use in letter fluency. These results highlight the importance of using scoring procedures such as adapted Troyer method (Troyer et al., 1997; Wadnerkar, 2008; Wadnerkar et al., 2008 June), switching and clustering measures, and the time course analysis to examine the cognitive strategies used in verbal fluency.

Chapter 7

The effects of age and menopause on verbal naming

7.1. Introduction

Like verbal fluency tests, naming tasks have also been used as tests of word-finding abilities (Kave & Yafe, 2014). Naming ability can be assessed using picture naming and naming-to-auditory-definitions tasks. Picture naming requires the participant to identify a pictured object and retrieve the common name for it (Lezak et al., 2004), whereas naming-to-auditory-definitions involves listening to a definition and retrieving the target word that best describes it. Performance on these tests is measured by accuracy and/or latency.

Evidence from literature on cognitive ageing suggests that older adults are less accurate than younger adults in picture naming (Albert et al., 1988; Connor et al., 2004; Gordon & Kindred, 2011; Gordon & Kurczek, 2014; Kave et al., 2010; Kave & Yafe, 2014; LaBarge et al., 1986; Neils et al., 1995; Tsang & Lee, 2003; Van Gorp et al., 1986, Welch et al., 1996; Worrall et al., 1995). Response latency also increases with increase in age (Mortensen et al., 2006; Thomas et al., 1977; Tsang & Lee, 2003). Studies that have used the naming-to-definitions task have found that older adults experience the ‘tip-of-the-tongue’ phenomenon, that is, when the individual feels he knows the word but is unable to retrieve it, more frequently in comparison to younger adults (Burke et al., 1991; Farrell & Abrams, 2011; Mortensen et al., 2006), again indicating that naming difficulties increase with advancing age irrespective of difference in stimulus type. Although most researchers have provided evidence of a decline in naming ability with increasing age, not all experimental studies support this finding. Studies that demonstrate no significant decline in naming with age (Nicholas, Brookshire, MacLennan, Schumacher, & Porazzo, 1989; see Goulet et al., 1994) and better performance by older adults have also been published (Farmer, 1990; Schmitter-Edgecombe et al., 2000). Despite extensive research for more than three decades, findings relating to the effects of age on naming ability remain inconsistent.

There has also been a disagreement on sex differences in naming ability, with some studies reporting a male advantage in picture naming (Hall et al., 2012; Lansing et al., 1999; Randolph, Lansing, Ivnik, Cullum, & Hermann, 1999; Tombaugh & Hubley, 1997; Welch et al., 1996), whilst others show no significant differences between the sexes (Cruice et al., 2000; Henderson, Frank, Pigatt, Abramson, & Houston, 1998; Ivnik, Malec, Smith, Tangalos, & Peterson, 1996; Tsang & Lee, 2003). Of these above-mentioned studies, some indicated that naming ability was affected by age and sex (Hall et al., 2012; Lansing et al., 1999; Randolph et al., 1999; Tombaugh & Hubley, 1997; Welch et al., 1996), whereas others showed only a significant effect of age (Cruice et al., 2000; Tsang & Lee, 2003). Based on the existing evidence, it is not clear whether age and sex exert an interactive effect on naming ability in older adults. Therefore, cognitive ageing studies which investigate sex differences or examine naming performance separately for men and women are needed. The current study is focused only on women.

As highlighted in Chapter 2, an additional consideration with midlife and late-life women is that naming performance might be affected by decreasing levels of sex hormones. Ryan et al. (2012) studied picture naming ability in postmenopausal women aged 56-67 years and found that low levels of free and total estradiol and high levels of testosterone relative to estradiol postmenopause were associated with low scores. However, Drake et al. (2000) did not find an association between naming and sex hormone levels in an older group of women aged 60 to 90 years. Thus, the effects of declining endogenous hormone levels following menopause on naming ability remain uncertain due to mixed findings and limited number of studies. To the best of the author's knowledge, there are no studies comparing naming abilities in women across pre, peri and postmenopause stages.

As discussed in Chapter 5, other factors that could determine naming performance in late-life women along with age and menopause status are education, IQ and cumulative hormone exposure across the lifespan. It has been shown that as the number of years of education (Connor et al., 2004; Elkadi et al., 2006; Pena-Casanova et al., 2009a; Tsang & Lee, 2003; Welch et al., 1996) and IQ (Hawkins et al., 1993; Scott Killgore & Adams, 1999; Tombaugh & Hubley, 1997) increases, picture naming accuracy increases. On the other hand, the role of reproductive characteristics or cumulative hormone exposure across the lifespan in predicting naming performance has been less fully investigated. Smith et al. (1999), who used a cumulative index of hormone exposure across the lifespan, found that increased sex hormone exposure had a beneficial effect on picture naming performance.

Apart from the uncertainties regarding the possible effects of age, menopause status, education, IQ and cumulative hormone exposure on naming ability, research investigating these factors has largely focussed on accuracy scores, and comparatively little attention has been given to response latency measures. It is arguably useful to also measure latencies as these may capture subtle differences in naming abilities across age (Verhaegen & Poncelet, 2013). Healthy older adults may also have delayed access to the target word rather than no access, and response latencies would be sensitive to these differences in lexical access.

7.2. Research aims and hypotheses

Based on existing gaps in the literature, the current study investigated the effects of age and menopause on naming ability across two different modalities: visual (picture naming) and auditory (naming-to-auditory-definitions). Picture naming has frequently been studied in the cognitive literature and was therefore included in the present study as a baseline measure of word-finding ability. An auditory-based task was also incorporated because everyday discourse predominantly requires responses to spoken verbal communication. The effects of age and menopause were examined for both accuracy and latency of responses. As in Chapter 6, the relationships between naming accuracy, latency, demographic (number of years of education, vocabulary T scores) and reproductive characteristics (age at menarche, menstrual cycle length, age at first childbirth, number of children, age at menopause, number of years since menopause and number of reproductive years) were also investigated.

7.2.1. Hypotheses for age group and menopause stage comparisons

It was hypothesized that picture naming and naming-to-auditory-definitions accuracy would decrease with age and response latencies would increase with age. For the menopause stage comparisons in women aged 46-55 years, it was predicted that postmenopausal women would have lower accuracy scores and longer latencies than pre and perimenopausal women. Based on earlier findings, it was expected that the number of years of education and vocabulary scores would be associated positively with naming accuracy and negatively with naming latency. It was also hypothesized that reproductive markers related to lifelong estrogen exposure such as an early age at menarche, later age at menopause and greater number of reproductive years would be positively associated with accuracy and negatively with latency.

7.3. Methods

7.3.1. Sample

All 78 women were administered the picture naming test. Seventy-six participants completed the naming-to-auditory-definitions task with two (one each in the 56-65 years and 70-79 years age groups) excluded due to reported hearing loss.

7.3.2. Details of tasks, administration procedure and scoring

7.3.2.1. Tasks and administration procedure

Picture naming was examined using the BNT which consisted of 60 line drawings (Kaplan et al., 1983). Naming-to-auditory-definitions was assessed using a set of 60 target stimuli which were taken from the list developed by Harley and Bown (1998). The naming-to-auditory-definitions stimuli were divided into four lists (each with 15 items) based on frequency and neighbourhood density: high frequency, high neighbourhood density (HFHN), high frequency, low neighbourhood density (HFLN), low frequency, high neighbourhood density (LFHN), and low frequency, low neighbourhood density (LFLN). Participants were administered all four sets in the same order (HFHN, HFLN, LFHN, LFLN). The naming-to-auditory-definitions task was completed first followed by the picture naming task, and a break of 10-15 minutes was given between the tasks.

7.3.2.1. Scoring

Picture naming

Accuracy was calculated as the number of correct responses given spontaneously plus the number of correct responses produced after a semantic cue had been given following a visual misperception. For four items, alternative responses (*brush* for *broom*, *toadstool* for *mushroom*, *dromedary* for *camel* and *mouth organ* for *harmonica*) were accepted as correct responses as these were classified as synonyms in the Oxford thesaurus of English (Waite, 2009). The maximum accuracy score was 60. Latency times were manually marked (see Chapter 4 for details). The analysis required manual marking of latencies and therefore, 10% of the data were checked for inter-rater reliability. Pearson correlations were conducted and a correlation of 0.9 was found between the raters, indicating good inter-rater reliability in marking response latencies. Only latencies for correct responses were used for the final statistical analyses. In total, 6.15% of the responses were discarded (5.21% in the 46-55 years group, 5.14% in the 56-65 years group and 8.64% in the 70-79 years group). Mean (*M*) and standard deviation (*SD*) scores were computed for each participant in order to determine extreme values. Latencies greater or less than the $M \pm 2SD$ were replaced by the $M \pm 2SD$ (Obler et al., 2010). Mean latencies were obtained for each participant after data trimming and these were used for comparisons across age, menopause stage and time since menopause[34].

The total percentage of errors produced by each participant was also calculated. Errors were further classified as semantic errors (semantically related words, for example producing *set square* for *protractor* or producing a circumlocution such as *a hanging thing in the garden*, *have one in the house* for *hammock*), phonological error (*projector* for *protractor*), mixed error (*elevator* for *escalator*) and no responses.

Naming-to-auditory-definitions

Accuracy was calculated as the number of correct responses given. Synonyms produced instead of target words were also accepted as correct responses, provided that they were either listed as synonyms in the Oxford thesaurus of English (Waite, 2009) or there was agreement between two raters that the word was a synonym. The maximum accuracy

[34] Statistical analysis was also conducted for response latencies without data trimming. These findings are reported in Appendix 4.

score was 60 (HFHN- 15, HFLN- 15, LFHN-15, LFLN- 15). Response latencies were obtained from DMDX (Forster & Forster, 2003). Latencies were manually marked by the researcher if the voice trigger had been activated because of an extraneous noise such as cough, tongue-click and lip-smacking. Latencies for correct responses were used in the final statistical analysis, resulting in 15.48% of the data being excluded (13.75% in the 46-55 age group, 15.14% in the 56-65 age group, 18.49% in the 70-79 age group). The mean and standard deviation scores for each participant were computed. Latencies greater or less than the $M \pm 2SD$ were considered as extreme values, and were replaced by the $M \pm 2SD$. After the data were trimmed, mean latencies were obtained for each participant and used for comparisons across age, menopause stage and time since menopause[35].

7.3.3. Statistical analyses

Pearson correlations were conducted to investigate the associations between the dependent measures (naming accuracy and latency), demographic and reproductive variables. As the study was cross-sectional, the analyses were performed separately for each Age group, Menopause stage and Time since menopause group in order to determine patterns of similarity or difference between the cohorts.

A series of ANOVAs and ANCOVAs were performed to examine mean differences in naming accuracy and latency (picture naming or naming-to-auditory-definitions) across Age groups (46-55, 56-65, 70-79 years), Menopause stages (pre, peri, postmenopause) and Time since menopause (recent: less than six years postmenopause, longer-term: more than six years postmenopause). The effects of Age group and Time since menopause on naming accuracy and latency were studied with

[35] Statistical analysis was also conducted for response latency measures without data trimming. These findings are reported in Appendix 4.

and without women with hysterectomies. Menopause stage effects were studied in the youngest group of women aged 46-55 years.

Women in the different Age groups, Menopause stages and Time since menopause groups were not equally matched on all demographic and reproductive characteristics (see Chapter 5 for details). Therefore, subsequent ANCOVAs were conducted to control for the effects of demographic and reproductive factors. Of particular interest were potential covariates that could account for variation in the model linked to demographic and reproductive factors that were not well matched between groups. The results from the correlational analyses were used to determine covariates. A variable was used as a covariate if it was associated with the dependent measure, the direction and magnitude of the correlation did not vary across groups, and it did not have a strong association with any other possible covariate to be used in the model.

7.4. Results

The results are reported in two sections defined by task type: picture naming and naming-to-auditory-definitions.

7.4.1. Picture naming

7.4.1.1. Correlations between dependent measures, demographic variables and reproductive markers

Correlation patterns across Age groups

Correlations between accuracy and vocabulary were generally strong and positive but varied with respect to age group (see Table 7.1). The magnitude of the associations was lower in the older age groups. There was a consistent pattern of moderate positive relationships between accuracy and the number of years of education in all the age groups. The magnitude of the association between age and accuracy was weak within each age group.

Correlations of latency with vocabulary and education were less consistent than with accuracy (see Table 7.1). As vocabulary score increased, latencies decreased only in Group I. An increase in the years of education was associated with a decrease in latency in Groups I and III but only moderately so. The correlation between age and latency was significant and highest in the oldest age group (Group III) compared to the other two groups (Groups I and II).

With respect to reproductive characteristics, a later age at menopause, fewer years since menopause and more reproductive years were correlated with higher picture naming accuracy in the oldest group (Group III) (see Table 7.2). Also, in the oldest group, more reproductive years and fewer years since menopause were associated with shorter latencies (see Table 7.2). Early age at first childbirth and greater number of children were associated with shorter latencies in Group II.

Correlation patterns across Menopause stages

In the younger group of women (Group I), associations of vocabulary with accuracy and latency were strong in the pre and perimenopausal women but low to moderate in postmenopausal women (see Table 7.1). Education was positively associated with accuracy and negatively with latency in premenopausal and postmenopausal women. These associations were near zero to low in the perimenopausal group. Age had generally weak associations with the dependent measures.

No consistent pattern of associations between accuracy, latency and reproductive characteristics were observed across menopause stages. In the perimenopause group, a later age at menarche was associated with higher accuracy scores, but the direction and magnitude of this association in the pre and postmenopause groups were negative and low, respectively (see Table 7.2). A later age at first childbirth was associated with shorter latencies in premenopausal women (see Table 7.2).

Correlation patterns across Time since menopause groups

Accuracy was moderately correlated with vocabulary and education in recent and longer-term menopausal women (see Table 7.1). In the longer-term menopausal group, as age increased, accuracy decreased moderately. Correlations among latency and vocabulary were near zero in magnitude (see Table 7.1). Latency increased with increase in age and decrease in years of education in both the groups, but the magnitude of the associations varied between groups.

A later age at menopause, fewer years since menopause and longer reproductive years were associated with higher accuracy scores in both the groups (see Table 7.2). Latency significantly increased with an increase in menstrual cycle duration, early age at menopause and more years since menopause in the longer-term group.

The results showed that vocabulary and education were the most consistent correlates with accuracy across age. For latency, vocabulary and education correlations were age specific. Age was associated with latency in the oldest group. Reproductive characteristics showed the strongest pattern of correlations in the oldest group for accuracy, and to some degree also with latency. In relation to menopause, correlation with vocabulary for accuracy and latency were graded, with stronger associations in pre than in peri than in postmenopause groups. Vocabulary and education were again the most consistent correlates with accuracy in recent and longer-term menopausal women. Age was associated with latency in the longer-term group. Significant associations between accuracy, latency and reproductive characteristics were mostly seen in the longer-term menopausal women.

Table 7.1

Correlations between picture naming accuracy, latency and demographic variables as a function of menopause stage, age group and time since menopause

Dependent variable	Independent variable	Group	*n*	Demographic variable		
				Vocabulary T score	Education (in years)	Age (in years)
Picture naming accuracy	Menopause stage	Premenopause	9	.80**	.78*	.23
		Perimenopause	11	.66*	-.14	.01
		Postmenopause	12	.47	.38	.17
	Age group	Group I (46-55 years)	32	.68**	.33†	.22
		Group II (56-65 years)	24	.42*	.47*	-.24
		Group III (70-79 years)	22	.40†	.38†	-.26
	Time since menopause	Recent menopausal	16	.46†	.31	.16
		Longer-term menopausal	42	.36*	.43**	-.36*
Picture naming latency	Menopause stage	Premenopause	9	-.71*	-.46	.21
		Perimenopause	11	-.51	-.09	-.32
		Postmenopause	12	-.13	-.60*	.04
	Age group	Group I (46-55 years)	32	-.56**	-.34	-.23
		Group II (56-65 years)	24	-.10	.08	-.11
		Group III (70-79 years)	22	-.20	-.32	.45*
	Time since menopause	Recent menopausal	16	-.09	-.40	.21
		Longer-term menopausal	42	-.11	-.20	.46**

†$p < .10$. *$p < .05$. **$p < .01$.

Table 7.2

Correlations between picture naming accuracy, latency and reproductive markers as a function of menopause stage, age group and time since menopause

Dependent variable	Independent variable	Group	*n*	Reproductive marker						
				Age at menarche	Menstrual cycle length	Age at first childbirth[+]	Number of children	Age at menopause	Number of years since menopause	Number of reproductive years
Picture naming accuracy	Menopause stage	Premenopause	9	-.15	-.17	.30	.08	-	-	-
		Perimenopause	11	.73*	-.44	-.51	-.15	-	-	-
		Postmenopause	12	-.15	.28	-.28	.07	.20	-.06	.24
	Age group	Group I (46-55 years)	32	.01	-.05	-.24	-.01	.20	-.06	.24
		Group II (56-55 years)	24	-.16	.10	-.32	.28	-.15	-.11	-.05
		Group III (70-79 years)	22	-.12	-.12	.08	-.18	.41†	-.41†	.41†
	Time since menopause	Recent menopausal	16	-.15	.28	-.39	.10	.31	-.30	.33
		Longer-term menopausal	42	-.16	-.11	.14	-.16	.27†	-.40**	.31*
Picture naming latency	Menopause stage	Premenopause	9	-.48	-.18	-.81*	.22	-	-	-
		Perimenopause	11	-.00	.38	.10	.07	-	-	-
		Postmenopause	12	.23	-.22	.09	-.11	.18	-.20	.07
	Age group	Group I (46-55 years)	32	-.14	.02	-.15	.16	.18	-.20	.07
		Group II (56-55 years)	24	.21	.12	.37†	-.49*	-.20	.06	-.29
		Group III (70-79 years)	22	.33	.18	.35	-.09	-.30	.43*	-.39†
	Time since menopause	Recent menopausal	16	.29	-.25	.31	-.06	.15	.17	.04
		Longer-term menopausal	42	.30†	.31*	-.05	-.05	-.34*	.51**	-.44

Note. [+]*Sample size for age at first childbirth variable*, Premenopause: 6, Perimenopause: 10, Postmenopause: 8; Group I: 24, Group II: 23, Group III: 21; Recent menopausal: 12, Longer-term menopausal: 40. †p < .10. *p < .05. **p < .01.

The next section presents the ANOVA and ANCOVA models examining the effects of Age, Menopause stage and Time since menopause on picture naming accuracy and latency. Covariates were chosen based on theoretical and statistical considerations described in section 7.3.3. For age group comparisons, only number of years of education was deemed suitable to be used as a covariate for accuracy analyses. None of the variables were included as covariates in the latency analyses. For menopause stage comparisons, no further ANCOVAs were conducted. For time since menopause comparisons, number of years of education was employed as a covariate in the accuracy analyses and no ANCOVAs were conducted for the latency measure.

7.4.1.2. ANOVAs and ANCOVAs comparing women across Age groups, Menopause stages and Time since menopause for picture naming accuracy and latency

Separate ANOVAs were performed with picture naming accuracy or latency as the dependent measure and Age group (46-55, 56-65, 70-79 years) or Menopause stage (pre, peri, postmenopause) or Time since menopause (recent, longer-term) as the between group factor. Analyses were conducted without and then with covariates.

Age group comparisons

Accuracy

The analysis showed a violation of homogeneity of variances across groups, $F(2, 75) = 3.88$, $p = .025$. The variance ratio, that is, the ratio of the highest (70-79 years) and the lowest variance (56-65 years), 19.87/4.78 = 4.16, was high. Therefore, a one-way ANOVA was used and results from the Welch's test are reported. Women across the three Age groups did not differ statistically in picture naming accuracy, $F(2, 43.815) = 2.11$, $p = .134$. From the mean scores, it was evident that picture naming accuracy remained stable across the first two age groups (46-55 years & 56-65 years) and decreased in the oldest age group (70-79 years) (see Table 7.3). Adjusting for the effects of education did not reveal a significant effect of Age group on accuracy. Education was significantly associated with accuracy scores, $F(1, 74) = 10.93$, p = .001. There were no differences between the Age groups in picture naming accuracy after excluding women with hysterectomies (with or without the covariate).

Latency

A significant effect of Age was seen in picture naming latency, $F(2, 75) = 4.67$, $p = .012$. Post hoc comparisons with Bonferroni corrections ($\alpha = .05/3 = .017$) showed that women aged 70-79 years took significantly more time to give correct responses than women aged 56-65 years[36], $t(44) = -3.02$, $p = .004$. A near significant age-related trend was seen between the 70-79 and the 46-55 years age groups, $t(52) = -2.44$, $p = .018$, with women in the older group having longer latency. Women in the two younger groups had comparable mean latencies. The data continued to show an effect of Age group on latency after excluding women with hysterectomies, $F(2, 70) = 5.23$, $p = .008$. When the untrimmed data were analysed, there was a significant effect of Age on latency (see Appendix 4).

Shorter latency was associated with higher accuracy in all three age groups (46-55 years: $r = -.61$, $p < .001$; 56-65 years: $r = -.11$, $p = .614$; 70-79 years: $r = -.66$, $p = .001$).

Errors

The mean percentage of total errors produced for the three age groups was 6.1% (46-55: 5.16%, 56-65: 5.00% and 70-79 years: 8.71%). Women aged 46-55 years produced predominantly semantic errors (60.71%) followed by no responses (8.37%) and mixed errors (2.79%). Only one participant produced a single phonological error. Women aged 56-65 years had a similar profile of errors but they produced more mixed

[36] Levene's test was significant, but the analysis also showed a significant difference between the two groups when equal variances were not assumed.

errors than no responses (semantic: 83.42%, mixed: 7.86%, no responses: 4.55%). Only one woman in this group produced a single phonological error. The oldest age group, 70-79 years, had the same pattern of errors as 46-55 year olds (semantic: 85.34%, no responses: 8.13%, mixed: 6.53%). One way ANOVAs were conducted to examine the effects of Age on error percentages. The three Age groups differed significantly on the semantic error percentage[37], $F(2, 75) = 4.66$, $p = .012$ wherein the percentage of errors increased with advancing age. However, there were no differences between the groups on the total error, mixed error and no response error percentages. There was a significant effect of Age for semantic error percentage after excluding women with hysterectomies.

In sum, picture naming accuracy showed a nonsignificant age-related decline whereas naming latencies increased significantly after the age of 70 years. Errors in picture naming in healthy midlife and late-life women were predominantly semantic in nature.

Table 7.3

Picture naming means (± SEM) for accuracy and latency as a function of menopause stage, age group and time since menopause

Independent variable	Group	*n*	Accuracy	Latency (in msecs)
Menopause stage	Premenopause	9	56.00 (1.13)	1420.44 (172.55)
	Perimenopause	11	57.00 (0.67)	1348.09 (96.70)
	Postmenopause	12	57.42 (0.77)	1147.31 (63.50)
Age group	Group I (46-55 years)	32	56.88 (0.48)	1293.14 (64.59)
	Group II (56-65 years)	24	56.92 (0.45)	1277.33 (46.16)
	Group III (70-79 years)	22	54.82 (0.95)	1533.41 (72.97)
Time since menopause	Recent menopausal	16	57.38 (0.57)	1187.13 (51.49)
	Longer-term menopausal	42	55.79 (0.58)	1408.68 (50.11)

[37] Levene's test was significant, but the Welch's test also showed a significant difference between the Age groups on the semantic error percentage.

Menopause stage comparisons

Menopause stage had no effect on picture naming accuracy, $F(2, 29) = 0.70$, $p = .507$, or latency[38], $F(2, 29) = 1.70$, $p = .200$ (see Table 7.3). There was no effect of Menopause stage on the untrimmed latency data (see Appendix 4). The total error percentage was low across all three stages: 6.67% in premenopause, 4.85% in perimenopause and 4.31% in postmenopause. Of the total errors, premenopausal women produced predominantly semantic errors (68.65%) followed by no responses (7.54%) and mixed errors (1.59%). Perimenopausal women produced semantic errors (73.48%), mixed errors (5.30%) and no responses (3.03%). There was also a single phonological error by one participant in this group. In postmenopausal women, most errors were semantic (43.06%) followed by no responses (13.89%) and mixed errors (1.39%). The mean error percentage for all error types did not differ significantly across menopause stages.

Time since menopause comparisons

Time since menopause had a significant effect on latency[39], $F(1, 56) = 6.42$, $p = .014$, but not accuracy. Longer-term postmenopausal women took more time to produce accurate responses than recent postmenopausal women (see Table 7.3). When the untrimmed data were analysed, there was a significant effect of Time since menopause on latency (see Appendix 4).

There was no significant effect of Time since menopause on accuracy after controlling for number of years of education. Education was significantly associated with accuracy, $F(1, 55) = 10.95$, $p = .002$. The results remained the same (no effect of

[38] Levene's test was significant, but the Welch's test also showed no differences between Menopause stages on picture naming latency.

[39] Levene's test was significant, but the Welch's test also showed a significant effect of Time since menopause on response latency and semantic error percentage.

time since menopause for accuracy but a significant effect for latency) when the data were re-examined after excluding women with hysterectomies.

The total error percentage for both the groups was low (recent: 4.38%, longer-term: 6.98%). Recent menopausal women produced maximum number of semantic errors (61.98%) followed by no responses (11.98%) and mixed errors (1.04%). Longer-term menopausal women had maximum semantic errors (81.06%) followed by mixed error (7.91%) and no responses (6.27%). Time since menopause had a significant effect for mixed error percentage, $F(1, 56) = 4.44$, $p = .040$, but not for total error, semantic error and no response error percentages. Longer-term menopausal women had more mixed errors than recent menopausal women.

Thus, it can be summarised that menopause stage and time since menopause do not affect picture naming accuracy in healthy midlife and late-life women. Response latencies are also not affected by menopause stage, but as time since menopause increases, response latency increases.

7.4.2. Naming-to-auditory-definitions

7.4.2.1. Correlations between dependent measures, demographic and reproductive variables

Correlation patterns across Age groups

Accuracy was positively correlated with vocabulary and education (see Table 7.4). The association between accuracy and vocabulary was strong in Group I but low in Group II and moderate in Group III. The magnitude of correlation with education was low in Group I and moderate in Groups II and III. As age increased, accuracy decreased moderately in the two older groups.

A moderate negative association between latency and vocabulary was found in Group I only (see Table 7.4). Correlates with education were low to near zero in all the age groups. There was a weak negative correlation between latency and age in all the age groups.

With respect to reproductive characteristics, higher accuracy scores were associated with later age at menopause and greater number of reproductive years in Group I and with more children and fewer years since menopause in Group II (see Table 7.5). Correlations between latency and reproductive characteristics were either weak or negligible.

Correlation patterns across Menopause stages

In the younger group of women (Group I), there was a consistent strong positive association between accuracy and vocabulary in women across all the menopause stages. There were moderate to strong negative correlations between vocabulary and latency in pre and perimenopausal women but not in postmenopausal women (see Table 7.4). Correlates between accuracy, latency and education were strong in premenopausal but low to moderate in peri and postmenopausal women. Age was weak to moderately associated with accuracy across menopause stages, but associations with latency were near zero to low.

Correlations between accuracy, latency, and reproductive markers were sporadic across menopause stages. In postmenopausal women, accuracy increased significantly as menstrual cycle duration, age at menopause and number of reproductive years increased (see Table 7.5). Similarly, in this group, shorter latencies were associated with fewer children (see Table 7.5).

Correlation patterns across Time since menopause

Naming-to-auditory-definitions accuracy was positively correlated with vocabulary and education (see Table 7.4). The magnitude of association with vocabulary was strong in recent postmenopausal women and low in longer-term menopausal women (see Table 7.4). Education was moderately correlated with accuracy in both the groups. Correlations with age were weak in both the groups. Associations between latency, vocabulary and education were near zero to low in both the groups. Longer latencies were associated with increasing age only in the recent menopausal group.

With respect to reproductive characteristics, higher accuracy was associated with longer menstrual cycle duration, later age at menopause, fewer years since menopause and more reproductive years in the recent menopausal group, and with age at menarche in the longer-term group (see Table 7.5). Latency was significantly correlated with number of children only in the recent menopausal group.

Thus, vocabulary and education were the most consistent correlates with naming-to-auditory-definitions accuracy across age. In relation to menopause, vocabulary was the strongest correlate with accuracy across menopause stages. In relation to time since menopause, again vocabulary and education were the most consistent correlates with accuracy in recent and longer-term menopausal women. Reproductive characteristics that were found to be associated with higher accuracy were longer menstrual cycle duration, later age at menopause, fewer years since menopause and more reproductive years. Naming-to-auditory-definitions latency was less influenced by demographic and reproductive factors across Age groups, Menopause stages and Time since menopause groups.

The next section compares the groups on naming-to-auditory-definitions accuracy and latency using ANOVAs and ANCOVAs. For the ANCOVAs, covariates were chosen based on theoretical and statistical considerations outlined in section 7.3.3. In the age group comparisons, number of years of education was considered as a covariate in the accuracy analysis. None of the variables were deemed suitable to be used as covariates in the latency analysis. For menopause stage comparisons, age was considered as a suitable covariate only for the accuracy analysis. For time since menopause comparisons, number of years of education was used as a covariate for accuracy and no ANCOVAs were conducted for latency.

Table 7.4

Correlations between naming-to-auditory-definitions accuracy scores, latency times and demographic variables as a function of menopause stage, age group and time since menopause. Naming-to-auditory-definitions accuracy and latency means are based on the average of scores across the HFHN, HFLN, LFHN, LFLN categories

Dependent variable	Independent variable	Group	*n*	Demographic variable		
				Vocabulary T score	Education (in years)	Age (in years)
Naming-to-auditory-definitions accuracy	Menopause stage	Premenopause	9	.83**	.79*	.25
		Perimenopause	11	.65*	-.23	.19
		Postmenopause	12	.74**	.43	.41
	Age group	Group I (46-55 years)	32	.72**	. 27	.30
		Group II (56-65 years)	23	.29	.45*	-.36
		Group III (70-79 years)	21	.40†	.32	-.38†
	Time since menopause	Recent menopausal	16	.62*	.37	.27
		Longer-term menopausal	38	.29†	.35	-.25
Naming-to-auditory-definitions Latency	Menopause stage	Premenopause	9	-.41	-.51	.02
		Perimenopause	11	-.60†	.09	-.19
		Postmenopause	12	-.18	-.31	-.14
	Age group	Group I (46-55 years)	32	-.43*	-.14	-.20
		Group II (56-65 years)	23	.07	.07	-.15
		Group III (70-79 years)	21	.02	-.04	-.30
	Time since menopause	Recent menopausal	16	.05	-.14	.39
		Longer-term menopausal	38	-.02	-.05	.05

†*p* < .10. **p* < .05. ***p* < .01.

Table 7.5

Correlations between naming-to-auditory-definitions accuracy, latency and reproductive markers as a function of menopause stage, age group and time since menopause. Naming-to-auditory-definitions accuracy and latency means are based on the average of scores across the HFHN, HFLN, LFHN, LFLN categories

Dependent variable	Independent variable	Group	*n*	Reproductive marker						
				Age at menarche	Menstrual cycle length	Age at first childbirth[+]	Number of children	Age at menopause	Number of years since menopause	Number of reproductive years
Naming-to-auditory-definitions accuracy	Menopause stage	Premenopause	9	.08	-.11	.51	-.20	-	-	-
		Perimenopause	11	.39	-.17	-.24	-.17	-	-	-
		Postmenopause	12	-.21	.85**	.25	-.31	.72**	-.48	.72**
	Age group	Group I (46-55 years)	32	-.00	.34†	.05	-.26	.72**	-.48	.72**
		Group II (56-55 years)	23	-.28	.20	-.31	.54**	.16	-.44*	.27
		Group III (70-79 years)	21	-.27	.11	-.12	.29	.05	-.25	.14
	Time since menopause	Recent menopausal	16	-.11	.68**	.09	-.04	.48†	-.39	.45†
		Longer-term menopausal	40	-.32*	.19	-.02	.25	.13	-.26	.25
Naming-to-auditory-definitions latency	Menopause stage	Premenopause	9	-.04	-.06	.33	-.04	-	-	-
		Perimenopause	11	.02	.35	.24	-.19	-	-	-
		Postmenopause	12	.37	-.38	-.19	.75**	-.15	.02	-.28
	Age group	Group I (46-55 years)	32	.12	-.01	.16	.18	-.15	.02	-.28
		Group II (56-55 years)	23	.28	-.18	.28	-.07	-.08	-.06	-.21
		Group III (70-79 years)	21	.08	.32	.19	-.17	.19	-.27	.13
	Time since menopause	Recent menopausal	16	.36	-.38	-.25	.74**	.33	.24	.15
		Longer-term menopausal	40	.20	.17	.13	-.18	-.02	.05	-.10

Note. [+]*Sample size for age at first childbirth variable*, Premenopause: 6, Perimenopause: 10, Postmenopause: 8; Group I: 24, Group II: 22, Group III: 20; Recent-menopausal: 12, Longer-term menopausal: 38. †$p < .10$. *$p < .05$. **$p < .01$

7.4.2.2. ANOVAs and ANCOVAs comparing women across Age groups, Menopause stages and Time since menopause on naming-to-auditory-definitions accuracy and latency

ANOVAs with Frequency (High and Low) and Neighbourhood density (High and Low) as repeated measures and Age group (46-55, 56-65, 70-79 years) or Menopause stage (pre, peri, postmenopause) or Time since menopause (recent, longer-term) as the between group factor were conducted to examine mean differences in accuracy and latency. For both the dependent measures, separate ANOVAs were performed. Analyses were conducted first without and then with covariates.

Age group comparisons

<u>*Accuracy*</u>

Women across the three Age groups did not differ significantly in their accuracy scores (see Table 7.6). There were no significant effects of Frequency or Neighbourhood density on the accuracy of responses. However, a significant interaction of Frequency x Neighbourhood density was seen, $F(1, 73) = 60.12$, $p < .001$. Performance in the four different categories and the significant differences that were found between the categories are presented in Figure 7.1. From the figure, it is evident that accuracy scores were highest for LFHN and HFLN categories followed by HFHN and LFLN. After adjusting for the number of years of education, the effects of Age, Frequency, Neighbourhood density and Frequency x Neighbourhood density interaction on accuracy remained nonsignificant. The number of years of education was significantly associated with performance, $F(1, 72) = 8.62$, $p = .004$.

When the data were examined excluding women with hysterectomies, with or without covariates, the results did not reveal any differences between the Age groups for naming-to-auditory-definitions accuracy.

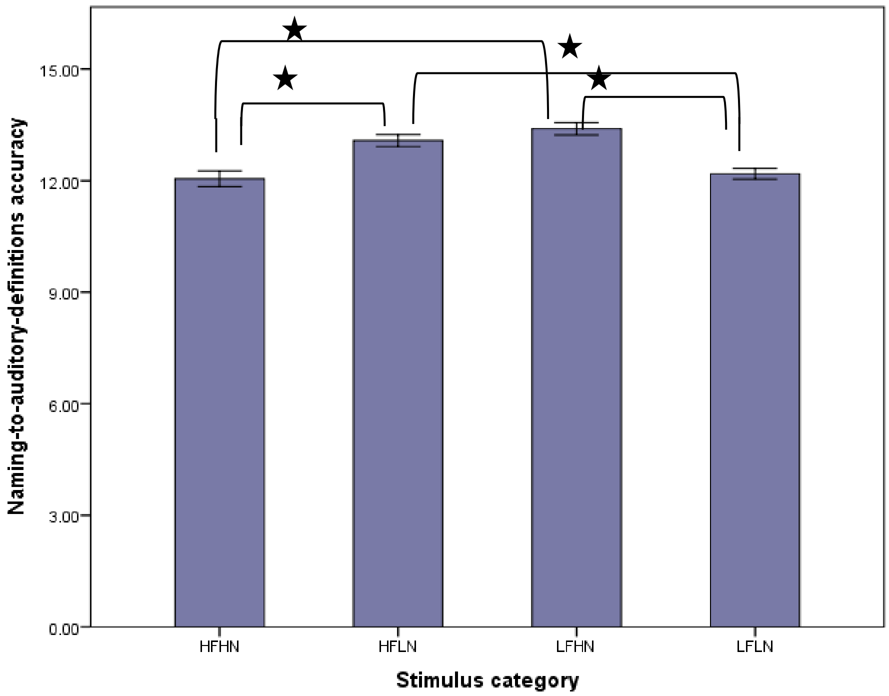

Figure 7.1. Naming-to-auditory-definitions accuracy as a function of stimulus category combined across age groups. Error bars represent ± 1 standard error.*$p < .01$.

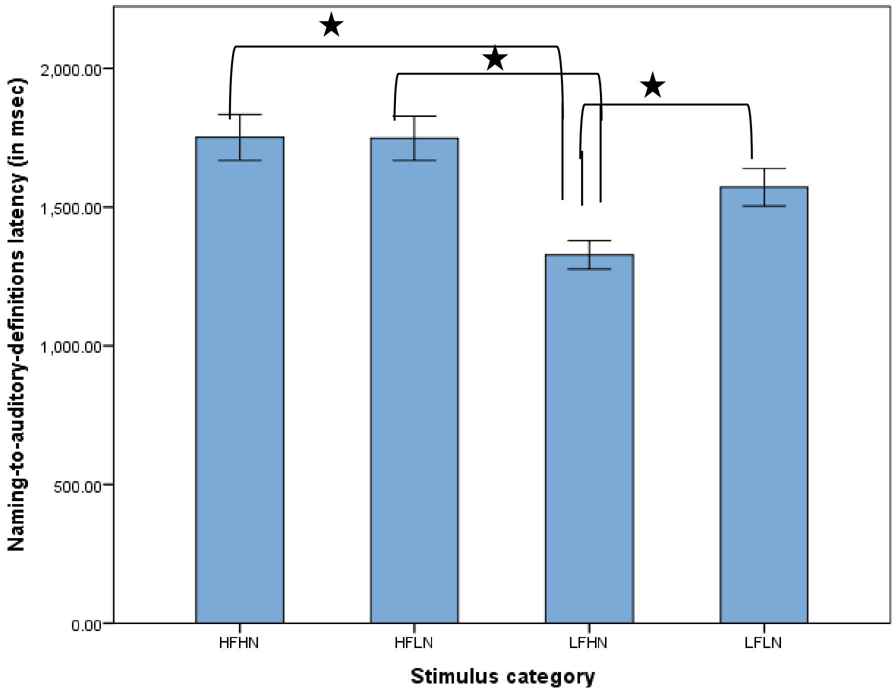

Figure 7.2. Naming-to-auditory-definitions latency as a function of stimulus category combined across age groups. Error bars represent ± 1 standard error. *$p < .01$.

Latency

The effect of Age group for latency was not significant. However, an age-related increase in the latency was evident (see Table 7.6). There were significant effects of Frequency, $F(1, 73) = 31.25$, $p < .001$ and Neighbourhood density, $F(1, 73) = 5.42$, $p = .023$, for response latencies. High frequency words took longer to be retrieved than low frequency words. Latencies for high neighbourhood density words were shorter than those for low neighbourhood density words. A significant interaction effect between Frequency x Neighbourhood density was also seen, $F(1, 73) = 6.52$, $p = .013$. The response latencies across the four stimulus categories are presented in Figure 7.2.

There was no significant effect of Age group on mean latencies when the data were analysed excluding women with hysterectomies. The results from the untrimmed data also showed no effect of Age group for naming-to-auditory-definitions latency (see Appendix 4).

Correlations showed that with an increase in accuracy, response time decreased in all three age groups, 46-55 years ($r = -.32$, $p = .077$), 56-65 years ($r = -.36$, $p = .095$), 70-79 years ($r = -.24$, $p = .301$).

In summary, naming-to-auditory-definitions accuracy does not significantly decline with increasing age and latency does not increase with age.

Table 7.6

Naming-to-auditory-definitions means (± SEM) for accuracy and latency as a function of age group

		HFHN	HFLN	LFHN	HFLN	HF	LF	HN	LN	Total
Naming-to-auditory-definitions accuracy	46-55 years	12.41	13.16	13.72	12.47	25.56	26.19	26.13	25.63	51.75
	(*n* = 32)	(0.34)	(0.25)	(0.25)	(0.22)	(0.46)	(0.38)	(0.48)	(0.38)	(0.72)
	56-65 years	12.09	13.39	13.57	11.87	25.48	25.43	25.65	25.26	50.91
	(*n* = 23)	(0.33)	(0.26)	(0.22)	(0.24)	(0.46)	(0.35)	(0.45)	(0.37)	(0.72)
	70-79 years	11.48	12.62	12.71	12.10	24.10	24.81	24.19	24.71	48.90
	(*n* = 21)	(0.42)	(0.33)	(0.35)	(0.30)	(0.67)	(0.57)	(0.62)	(0.54)	(1.05)
Naming-to-auditory-definitions latency (in msec)	46-55 years	1539.81	1648.80	1261.71	1513.76	1594.30	1387.73	1400.76	1581.28	1491.02
	(*n* = 32)	(91.54)	(142.37)	(70.86)	(83.98)	(105.79)	(69.30)	(64.57)	(96.27)	(76.18)
	56-65 years	1818.58	1841.96	1339.22	1619.21	1830.27	1479.21	1578.90	1730.59	1654.74
	(*n* = 23)	(142.12)	(142.63)	(90.32)	(142.40)	(124.57)	(104.92)	(106.44)	(121.72)	(103.51)
	70-79 years	1998.01	1795.16	1414.25	1605.47	1896.58	1509.86	1706.13	1700.31	1703.22
	(*n* = 21)	(204.88)	(113.58)	(117.53)	(142.36)	(139.86)	(117.05)	(144.55)	(112.01)	(121.44)

Menopause stage comparisons

<u>Accuracy</u>

Naming-to-auditory-definitions accuracy scores did not differ significantly between women in the different menopause stages (see Table 7.7). There were no main effects of Frequency and Neighbourhood density for the accuracy of responses, but the Frequency x Neighbourhood density interaction showed a significant effect, $F(1, 29) = 16.54$, $p < .001$. Accuracy scores in the four different categories and the significant differences that were seen between the categories are presented in Figure 7.3 (LFHN > HFHN ≈ LFLN). The Neighbourhood density x Menopause stage interaction was significant, $F(2, 29) = 3.62$, $p = .046$. Post hoc ANOVAs were conducted and women in the different menopause stages were compared on their accuracy scores for high and low neighbourhood density words. There was a nonsignificant trend of Menopause stage on naming-to-auditory-definitions accuracy for high neighbourhood density words, $F(2, 29) = 3.51$, $p = .043$ (Bonferroni corrections applied, $\alpha = .05/2 = .025$), but not for low neighbourhood density words. For high neighbourhood density words, perimenopausal women had higher scores than pre and postmenopausal women. After adjusting for age, effects of Menopause stage, Frequency, Neighbourhood density and other interactions were nonsignificant for accuracy.

<u>Latency</u>

A main effect of Menopause stage was not significant for latency (see Table 7.7). Frequency, $F(1, 29) = 4.95$, $p = .034$, and Neighbourhood density, $F(1, 29) = 8.73$, $p = .006$, effects were significant. High frequency words took longer to be retrieved than low frequency words. Latencies for high neighbourhood density words were shorter than those for low neighbourhood density words. No significant interactions were obtained. The response latencies across categories are presented in Figure 7.4. The untrimmed data also showed no significant effect of menopause stage (see Appendix 4).

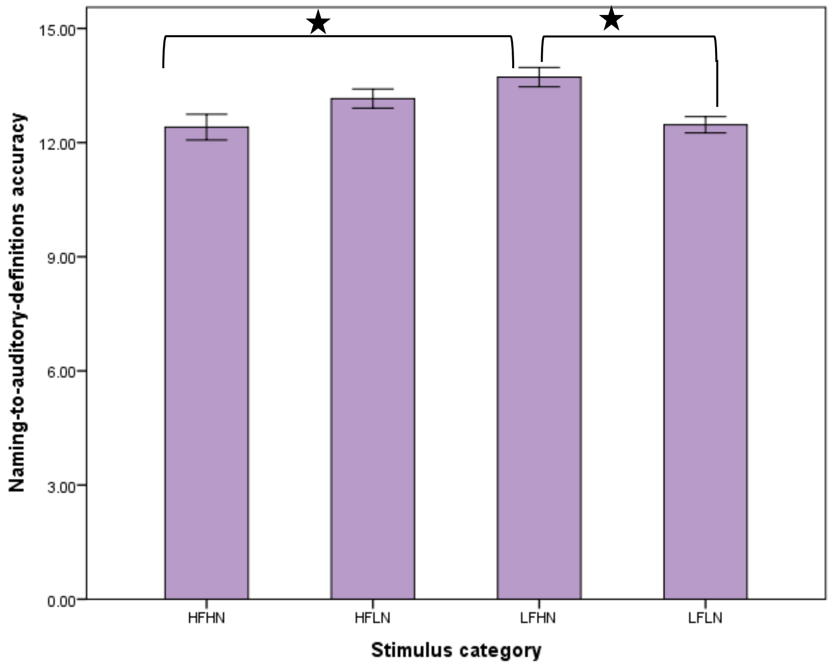

Figure 7.3. Naming-to-auditory-definitions accuracy as a function of stimulus category combined across menopause stages. Error bars represent ± 1 standard error.**p* < .01.

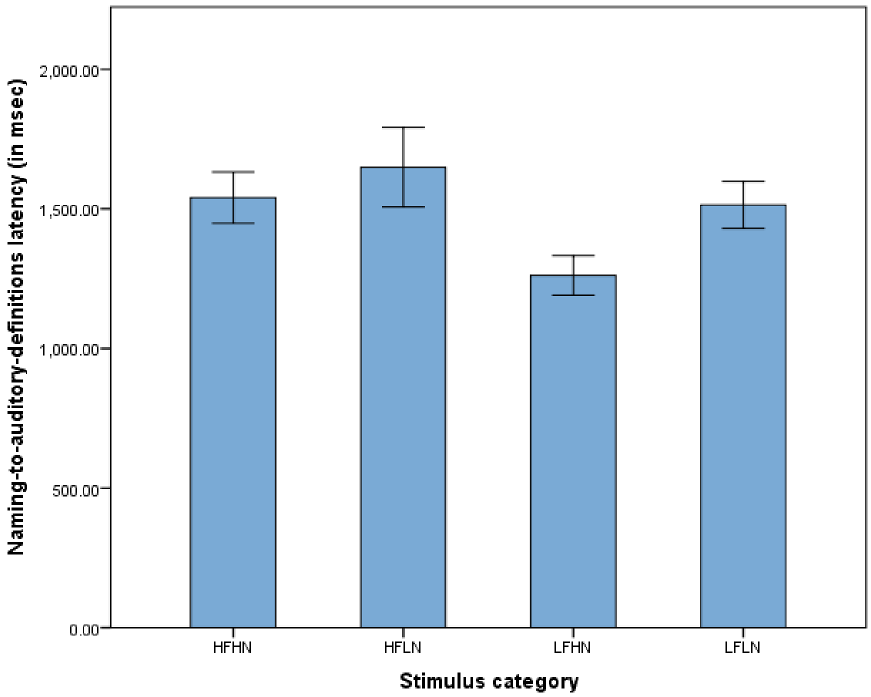

Figure 7.4. Naming-to-auditory-definitions latency as a function of stimulus category combined across menopause stages. Error bars represent ± 1 standard error.**p* < .01.

Table 7.7

Naming-to-auditory-definitions means (± SEM) for accuracy and latency as a function of menopause stage

		HFHN	HFLN	LFHN	LFLN	HF	LF	H N	LN	Total
Naming-to-auditory-definitions accuracy	Premenopause	12.11	12.56	12.89	12.33	24.67	25.22	25.00	24.89	49.89
	(*n* = 9)	(0.51)	(0.29)	(0.65)	(0.47)	(0.71)	(0.98)	(0.94)	(0.61)	(1.40)
	Perimenopause	13.36	13.27	14.36	12.36	26.64	26.73	27.73	25.64	53.36
	(*n* = 11)	(0.36)	(0.45)	(0.31)	(0.28)	(0.47)	(0.41)	(0.43)	(0.56)	(0.78)
	Postmenopause	11.75	13.50	13.75	12.67	25.25	26.42	25.50	26.17	51.67
	(*n* = 12)	(0.70)	(0.47)	(0.30)	(0.40)	(0.98)	(0.56)	(0.87)	(0.75)	(1.37)
Naming-to-auditory-definitions latency (in msec)	Premenopause	1701.82	1731.94	1292.41	1567.54	1716.88	1429.98	1497.12	1649.74	1573.43
	(*n* = 9)	(135.62)	(251.43)	(124.16)	(136.22)	(174.56)	(102.53)	(97.11)	(142.95)	(104.72)
	Perimenopause	1311.77	1678.13	1396.09	1600.33	1494.95	1498.21	1353.93	1639.23	1496.58
	(*n* = 11)	(162.71)	(299.97)	(152.00)	(189.84)	(225.48)	(159.06)	(137.04)	(218.20)	(175.49)
	Postmenopause	1627.34	1559.56	1115.49	1394.07	1593.45	1254.78	1371.41	1476.81	1424.11
	(*n* = 12)	(155.13)	(203.92)	(80.96)	(103.52)	(152.57)	(80.79)	(98.20)	(131.30)	(105.34)

Time since menopause comparisons

<u>Accuracy</u>

A main effect of Time since menopause on accuracy was significant, $F(1, 54) = 4.70$, $p = .035$, wherein recent postmenopausal women had higher accuracy scores than longer-term postmenopausal women (see Table 7.8). There were no effects of Frequency and Neighbourhood density on the accuracy scores. Frequency x Neighbourhood density had a significant effect on accuracy, $F(1, 54) = 54.45$, $p < .001$, and the same pattern of performance as in the age group analysis was seen. Higher accuracies were found for HFLN and LFHN words followed by LFLN and HFLN words. No other significant interactions were seen. After adjusting for the effects of number of years of education, effects of Time since menopause, Frequency, Neighbourhood density and other additional interactions were nonsignificant. Education significantly covaried with the naming-to-definitions accuracy, $F(1, 53) = 7.69$, $p = .008$. The analyses revealed the same results when the data were examined after excluding women with hysterectomies (with or without covariates).

<u>Latency</u>

Recent and longer-term postmenopausal women did not differ in their response latencies (see Table 7.8). Frequency had a significant effect on response latencies, $F(1, 54) = 36.57$, $p < .001$, but not Neighbourhood density. All women took longer to retrieve high frequency than low frequency words. There were no significant interactions. The results remained unchanged when the data were analysed excluding women with hysterectomies. The untrimmed data also showed no effect of Time since menopause (Appx. 4). In sum, naming-to-auditory-definitions accuracy and latency are unaffected by menopause stage and time since menopause particularly when years of education is taken into account. A summary of all the analyses is presented in Table 7.9.

Table 7.8

Naming-to-auditory-definitions means (± SEM) for accuracy and latency as a function of time since menopause

		HFHN	HFLN	LFHN	LFLN	HF	LF	H N	LN	Total
Naming-to-auditory-definitions accuracy	Recent menopausal	12.19	13.75	13.89	12.44	25.94	26.31	26.06	26.19	52.25
	(*n* = 16)	(0.54)	(0.34)	(0.24)	(0.34)	(0.72)	(0.45)	(0.69)	(0.56)	(1.03)
	Longer-term menopausal	11.63	12.88	13.05	12.00	24.50	25.05	24.68	24.88	49.55
	(*n* = 40)	(0.28)	(0.23)	(0.22)	(0.20)	(0.44)	(0.35)	(0.40)	(0.35)	(0.67)
Naming-to-auditory-definitions latency (in msec)	Recent menopausal	1758.02	1857.37	1246.14	1468.92	1807.69	1357.53	1502.08	1663.15	1582.61
	(*n* = 16)	(148.26)	(189.76)	(75.97)	(102.47)	(145.93)	(80.43)	(100.70)	(128.04)	(104.95)
	Longer-term menopausal	1879.63	1726.51	1348.72	1604.57	1803.07	1476.65	1614.17	1665.54	1639.86
	(*n* = 40)	(130.73)	(91.38)	(80.01)	(107.14)	(97.26)	(84.05)	(94.94)	(86.44)	(84.09)

Table 7.8

Summary of results for verbal naming tasks

		Effects of Age group		Effects of Menopause	Effects of Time since menopause		Correlational analysis
Verbal naming task	Dependent measure	Women with and without hysterectomies	Women without hysterectomies		Women with and without hysterectomies	Women without hysterectomies	
Picture naming	Accuracy	NS	NS	NS	NS	NS	Vocabulary, education, age at menopause, number of year since menopause and reproductive years
	Latency	SF 70-79 years > 56-55 years 56-65 years ≈ 46-65 years	SF 70-79 years > 56-55 years 56-65 years ≈ 46-65 years	NS	SF Recent < Longer-term	SF Recent < Longer-term	Age, age at menarche, menstrual cycle duration, age at first childbirth, number of children, number of years since menopause and reproductive years
Naming-to-auditory-definitions	Accuracy	NS	NS	NS	SF Recent > Longer-term Controlled for education, NS	SF Recent > Longer-term Controlled for education, NS	Vocabulary, education, menstrual cycle duration, number of children, age at menopause, number of years since menopause and reproductive years
	Latency	NS	NS	NS	NS	NS	Number of children

Note. SF: Significant findings, NS: Not significant.

7.5. Discussion

7.5.1. Effects of age on verbal naming

One of the aims of the study was to investigate the effects of age on verbal naming as examined by picture naming and naming-to-auditory-definitions. Results showed no significant decline in naming accuracy with increasing age as reported by previous researchers (Goulet et al., 1994; Nicholas et al., 1989). However, a nonsignificant age-related trend was seen after the age of 70 years. The findings for picture naming latency replicated previous research and showed an effect of age (Gordon & Kurczek, 2014; Mortensen et al., 2006; Thomas et al., 1977; Tsang & Lee, 2003). Women aged 70-79 years took longer to give correct responses than women aged 56-65 years. The lack of significant differences in accuracy combined with significant age-related increases in latency substantiates participants' subjective complaints of difficulty retrieving the word instantly but being able to remember it later. The error percentage was low and mostly consisted of semantically related words or circumlocutions, compared to other error types such as phonologically related words, mixed errors and no responses. Although the total number of errors produced was unaffected by age, the highest percentage of semantic errors was produced by women in the oldest age group. These results suggest that the vocabulary store and word meanings remain intact with age as shown by previous investigators (Bowles & Salthouse, 2008; Kave & Halamish, 2015; Kave & Yafe, 2014; Kemper & Sumner, 2001; Verhaegen, 2003), but are accompanied by an age-related decline in access, as indicated by the increase in response latencies.

Naming ability as assessed by the naming-to-auditory-definitions task was found to be unaffected by age. However, there were trends of decline in accuracy and increase in latency with advancing age. The words on the naming-to-auditory-definitions task were classified by frequency and neighbourhood density. The results revealed differences in word-retrieval based on these lexical characteristics of the words. All women were more accurate with high frequency, low neighbourhood density (HFLN) and low frequency, high neighbourhood density (LFHN) words compared to high frequency, high neighbourhood density (HFHN) and low frequency, low neighbourhood density (LFLN) words. These findings are in congruence with the results reported by Harley and Bown (1998), who showed a similar trend of accuracy scores across the different types of stimuli in young adults. For the latency measure, the results showed that high frequency words took longer to be retrieved than low frequency words. Inconsistencies in frequency effects from previous research, which suggests that high frequency words are more easily retrieved than low frequency words (Ellis & Morrison, 1998; Gerhand & Barry, 1999; Oldfield & Wingfield, 1965), could have occurred due to differences in stimulus type. These above-mentioned studies were conducted using picture naming stimuli, whereas the present study used the naming-to-auditory-definitions task. The effects of neighbourhood density in word production have not been consistently reported. Like previous researchers (Harley & Bown, 1998; Spieler & Balota, 2000; Vitevitch, 2002), the current study also found a facilitative effect of neighbourhood density. High neighbourhood density words were easily retrieved than low neighbourhood density words. Shorter latencies for high neighbourhood density words were mostly driven by LFHN words compared to HFHN words (see Figure 7.2) As discussed above, LFHN words were more accurately produced than HFHN words (see Figure 7.1). These results suggest that facilitative effects of neighbourhood density words may be more prominent for low than high frequency words. It is also possible that HFHN words may have more competitors than LFHN words and therefore, difficulty in inhibiting the associated responses would have contributed to such a finding in the current study. Frequency and neighbourhood density effects are potentially confounded by other lexical variables such as age of acquisition, word length and phonotactic probability, which were not investigated in the present study. Therefore, further examinations are required to confirm frequency and neighbourhood density effects in word production.

Thus, age-related decline in naming accuracy and latency may be subtle in healthy older women. It is of prime importance to understand why a significant decline is seen in some studies but not in all (as in the current one). A key demographic factor that might have contributed to the lack of strong age-related declines in verbal naming in the present study is education. In line with previous literature, education was positively associated with picture naming accuracy in the current study (Connor et al., 2004; Elkadi et al., 2006; Pena-Casanova et al., 2009a; Tsang & Lee, 2003; Welch et al., 1996). Welch et al. (1996) found that age-related decline in picture naming was evident only after the age of 80 in individuals with 12 or more years of education. In contrast, individuals with less than 12 years of education showed a decline in naming ability by the age of 70. Although women in the oldest group (70-79 years) had fewer years of education than the two younger groups (46-5, 56-65 years), the mean number of years of education for this group was still 15.36 (± 0.46) years. Education was moderately associated with performance in all the three age groups, suggesting that education contributed to task performance in a similar manner across cohorts. Therefore, high levels of education might have had a protective effect and delayed the age-related decline in naming ability as shown by Welch et al. (1996).

The results also showed some positive associations between naming accuracy and early age at menarche, longer menstrual cycle length, later age at menopause and greater reproductive years (although not consistently across all age groups). It has been suggested that these reproductive factors may signal greater hormone exposure across the lifespan (see Chapter 5 for details), which in turn may have a protective effect on naming ability in older adults (Smith et al., 1999). Moreover, the older group of women included participants with active lifestyles who attended social groups; and according to the cognitive reserve hypothesis (Stern, 2002), a healthy lifestyle, increased involvement in cognitive activities, higher education, and higher vocabulary levels are linked to better maintained cognitive functions in later life. A cumulative effect of education, above average IQ, active lifestyles and greater endogenous hormone exposure throughout the life period could be beneficial and delay age-related decline in naming ability. This is discussed in further detail in Chapter 8.

Alternatively, the lack of significant differences in naming across age may have resulted from other factors. Discrepancies between the current findings and those from previous research could have arisen because of variations in age groups compared, sex of the participants, sample size, and differences in administration and scoring of items on the BNT. A detailed critical analysis of the current study design and its effects on the findings is presented in Chapter 8.

7.5.2. Effects of menopause on verbal naming

The present study investigated the effects of menopause on verbal naming by comparing women aged 46-55 years across stages of menopause (pre: high hormone state, peri: variable hormone state, post: low hormone state). The study results did not support a direct facilitative effect of high hormone levels on verbal naming because women across the different stages of menopause remained stable in their performance. These results find support from Drake et al.'s (2000) study which reported no significant associations between sex hormone levels and picture naming performance in healthy older postmenopausal women aged 60 to 90 years. The findings of the current study are also in agreement with results from hormone therapy treatment trials which found no improvement in naming ability after treatment (Buckwalter et al., 2004; Grady et al., 2002; Pefanco et al., 2007; Shaywitz et al., 2003; Verghese et al., 2000; Yaffe et al., 2006). However, the current study does contrast with previous research conducted by Ryan et al. (2012), who found that high total and free estradiol levels were associated with higher picture naming accuracy in postmenopausal women aged 56-67 years. This inconsistency in relation to the findings of Ryan et al. (2012) might be due to several factors. Firstly, it is possible that menopause status does not affect verbal naming. However, this proposal requires testing with a larger sample size and correlation of actual blood serum levels. Secondly, difference in study designs may have contributed to discrepant results. Ryan et al. (2012) only included women in the postmenopausal group and measured blood serum levels of ovarian hormones. In contrast, in the present study, women across menopause stages were classified based on self-report and compared on their naming abilities. Therefore, these two studies may not be directly comparable which suggests that further research is needed to establish the effects of postmenopause endogenous hormone levels on naming ability.

7.5.3. Effects of time since menopause on verbal naming

A post hoc research aim was also to examine the effects of Time since menopause on verbal naming. The results showed that recent menopausal women had shorter picture naming latency and higher naming-to-auditory definitions accuracy than longer-term menopausal women. Recent and longer-term menopausal women did not differ in their picture naming accuracy and naming-to-auditory-definitions latency. These results find support from Henderson et al.'s (2013) study; thus, suggesting that there may not be a critical time window of negative effects from low endogenous hormone levels following menopause on naming abilities.

Summary

In conclusion, the effects of age on naming ability are subtle and therefore many studies may fail to find significant differences. Naming accuracy is also associated with other demographics such as vocabulary and education, and with reproductive factors such as menstrual cycle duration, number of children, age at menopause, number of years since menopause, and reproductive years. Response latency may be a more sensitive measure to detect the subtle age-related decline in naming. Verbal naming remains unaffected by menopause stage and time since menopause.

The final chapter discusses in detail the role of combined demographic and reproductive factors in determining word-finding ability as assessed by verbal fluency and verbal naming in healthy educated and midlife and late-life women.

Chapter 8

Discussion and conclusions

8.1. Introduction

This chapter brings together the findings presented in Chapters Five to Seven to illustrate the effects of age and menopause on word-finding abilities in midlife and late-life women. It also discusses limitations and future implications of the current research study.

Difficulty in retrieving words accurately during everyday conversation has been a primary concern in older adults and therefore, the effects of age on word-finding abilities is a central topic of research in the cognitive literature. Despite progress in this field, the impact of age on word-finding abilities in healthy adults remains uncertain. Moreover, it is also unclear whether lowered levels of sex hormones postmenopause additionally affect word-finding abilities in women.

Therefore, the current study was undertaken to supplement previous findings and resolve existing inconsistencies. The study had two primary aims. The first aim of the research was to examine the effects of age on word-finding abilities in women aged 46-79 years; and the second aim was to investigate the effects of menopause on this cognitive ability in a younger cohort of women aged 46-55 years. The study also aimed to examine the relationships between word-finding abilities, demographics such as vocabulary and education and reproductive characteristics such as age at menarche, menstrual cycle length, age at first childbirth, number of children, age at menopause, number of years since menopause and reproductive years. A test battery including screening and interview questionnaires, baseline IQ measures and word-finding tasks was administered. In order to obtain a comprehensive profile of word-finding performance, five different word-finding tasks were completed by the participants. The tasks included were category fluency, letter fluency, C-series, picture naming and naming-to-auditory-definitions. Information about demographic and reproductive characteristics was obtained using the questionnaires and baseline IQ tasks.

The present study had three important predictions. First, it was predicted that older women would obtain lower scores than younger women on all word-finding tasks. Second, it was hypothesized that women in fluctuating (perimenopause) and low estrogen states (postmenopause) would obtain lower scores than women in high estrogen states (premenopause) on the word-finding tasks. Third, it was hypothesized that reproductive characteristics that are associated with increased hormone exposure across the lifespan such as an early age at menarche, later age at menopause and greater number of reproductive years would be positively related to word-finding measures.

The data were analysed to examine differences across Age (46-55, 56-65, 70-79 years) or Menopause stage (pre, peri, postmenopause) on word-finding measures, demographic and reproductive characteristics using ANOVAs and ANCOVAs. The relationships between word-finding measures, demographic and reproductive characteristics were studied using Pearson correlations. The following section presents the key findings of the current study.

8.2. Summary of results

Women across the three age groups did not differ significantly on most of the word-finding measures. A significant effect of age was evident only for picture naming latency with women in the oldest group (70-79 years) having longer response latencies than women in the two younger groups. There was also some evidence that the rise in the switch cost from 2 to 3-series was highest in the oldest group compared to the two younger groups.

The results also showed that word-finding abilities were not affected by menopause stage. However, preliminary evidence indicated that the association between the total number of words produced and strategy use on the letter fluency task was dependent on the menopause stage of the individual. The total number of words was strongly correlated with the number of switches only in the premenopausal group. In the postmenopausal group, the correlation between total words and mean cluster size was stronger than the association between total words and switches. The magnitude of the correlations among total words, switches and mean cluster size was strong in premenopausal women and moderate in perimenopausal women. It was found that women across menopause stages used these cognitive strategies differently across time. Premenopausal women had larger mean cluster size in the initial time intervals (0-20 seconds) of the letter fluency task, whereas postmenopausal women had bigger mean cluster size in the latter half of the task (20-40 seconds).

The overall correlational analyses indicated that vocabulary and education were the most consistent correlates with performance on category fluency, letter fluency, picture naming and naming-to-auditory-definitions tasks. Correlations with vocabulary were graded by age and menopause status. The strongest association was seen in the youngest group of women aged 46-55 years. Similarly, the magnitude of correlation was strongest in premenopausal women followed by peri and postmenopausal women. Education was consistently moderately correlated with word-finding performance in all three age groups. Word-finding performance, as measured by the above-mentioned tasks, was weakly associated with age. For the C-series task, vocabulary was the most consistent correlate of switch rate. However, the magnitude of association was lower than that seen between vocabulary, verbal fluency and verbal naming measures. With respect to reproductive characteristics, no consistent pattern of associations was observed. The analyses indicated that markers related to fertility status such as age at first childbirth and number of children were associated with verbal fluency and C-series task performances. On the other hand, menopause-related markers such as age at menopause, number of years since menopause and reproductive years were associated with verbal naming.

8.3. Discussion

One of the primary aims of the research was to investigate the effects of age on word-finding abilities. The results showed that changes in word-finding abilities with increasing age are subtle and statistically nonsignificant for most of the dependent measures. These findings contrast to those reported in many of the early literature sources which suggest a decline in word-finding abilities with advancing age (Albert et al., 1988; Brickman et al., 2005; Connor et al., 2004; Gordon & Kindred, 2011; Gordon & Kurczek, 2014; Kave et al., 2010; Kave & Yafe, 2014; Kemper & Sumner, 2001; LaBarge et al., 1986; Neils et al., 1995; Troyer et al., 1997; Tsang & Lee, 2003; Van der Elst et al., 2006; Van Gorp et al., 1986, Welch et al., 1996; Worrall et al., 1995). However, discrepancies across studies are not uncommon. Some researchers have found no significant effects of age on word-finding abilities (Nicholas et al., 1989; Parkin and Java, 1999; Sauzeon et al., 2011; Troyer et al., 1997; Wierenga et al., 2008), and few others report that older adults perform better than younger adults (Farmer, 1990; Schmitter-Edgecombe et al., 2000). This disparity in results has further motivated researchers to study the reasons that underlie these inconsistencies. A key question that has been raised in recent years is why some individuals or groups of individuals experience an earlier age-related cognitive decline, whereas others do not. To unfold and better understand this phenomenon, age-related cognitive decline in healthy adults has been discussed in the context of reserve hypotheses (Opdebeeck, Nelis, Quinn, &

Clare, 2015; Singh-Manoux et al., 2011; Valenzuela & Sachdev, 2006). The remainder of this section outlines the reserve hypotheses and explains their relevance to the findings of the present study.

The reserve hypotheses were originally formulated to explain variations across individuals in the expression of Alzheimer's disease (Katzman, 1993; Satz, 1993; Stern, 2002). They have also been applied to describe individual differences in cognitive performance following brain injury or healthy brain ageing. The concept of reserve has been defined by using both passive and active models. According to the passive models, reserve refers to the construct of brain reserve (Katzman, 1993) or brain reserve capacity (Satz, 1993) and is associated with the structural organization of the brain (brain size, neuronal or synapse count). These models suggest that individuals differ in their brain reserve or brain reserve capacity. Every individual has a critical threshold of brain reserve and a lesion causes cognitive impairments if this threshold is exceeded. Thus, according to the passive models, an individual with a higher brain reserve and critical threshold has a greater resilience to neurodegeneration and shows cognitive decline at a later stage than an individual with a lower brain reserve.

The active models are based on a similar theoretical background but emphasise on the efficient use of strategies and networks to survive brain damage. These models put forward the concept of cognitive reserve and compensation mechanisms (Stern, 2002). Cognitive reserve is defined as "the ability to optimize or maximize performance through differential recruitment of brain networks, which perhaps reflect the use of alternative cognitive strategies" (Stern, 2002; pp. 451). Compensation refers to the use of alternative brain networks that are otherwise not recruited or used for the specific cognitive task by healthy controls. According to the active models, an individual with higher cognitive reserve and efficient compensatory mechanisms would show cognitive decline at a later stage than does an individual with lower cognitive reserve and inefficient compensatory mechanisms.

Cognitive reserve has been quantified using a number of proxy measures such as education, occupational attainment, height, physical activity, IQ, engagement in complex mental activities or social engagement (Satz, Cole, Hardy, & Rassovsky, 2011; Opdebeeck et al., 2015; Singh-Manoux et al., 2011; Valenzeula & Sachdev, 2006). Education has received maximum attention compared to other measures probably because of ease in collecting information about educational levels. The current study also gathered information about formal years of education of the participants. Women in the two younger groups aged 46-55 and 56-65 years had mean education of 17.41 and 16.67 years, respectively, and women in the oldest group aged 70-79 years had a mean education of 15.36 years. Correlational analyses showed a moderate association between number of years of education and word-finding measures in all age groups, indicating that education contributed equally to performance in all the groups. This was true despite fewer years of education in the oldest group of women. Education is a better predictor of verbal fluency performance in individuals with lower levels of education (0-8 years of education) than in individuals with higher levels of education (greater than 9 years of education) (Kempler et al., 1998) and this possibly explains the moderate association between education and word-finding abilities across all age groups in the current study. In addition, a greater difference in word finding performance has been reported between individuals with "fewer than 13 years" of education and those with "13 or more years" of education, but the difference in word-finding abilities between individuals with "13-16 years" of education and those with "17-21 years" of education is subtle (Tombaugh et al., 1999). Welch et al. (1996) also found that decline in word-finding abilities was seen at an earlier age in individuals with less than 12 years of education (decline was seen around 70 years of age) compared to those with more than 12 years of education (decline was seen around 80 years). In the current study sample, approximately 77% of the participants in the oldest group (70-79 years) had a minimum of A level or higher education and the remainder had 12 years of education. This greater percentage of women with higher levels of education might have contributed to the moderate association between education and word-finding measures in this group and contributed to a nonsignificant age-related declining trend on word-finding abilities.

The neural literature suggests that an increase in the number of years of education is associated with an increase in grey matter tissue volume of the temporal lobe (Ho et al., 2011), right superior temporal gyrus, left insula, bilateral anterior cingulate cortex (ACC) (Arenaza-Urquijo et al., 2013) and temporoparietal regions (Foubert-Samier et al., 2013; Liu et al., 2012). Studies have also shown that more years of education is associated with increased white matter in regions connecting the orbital and frontal areas (Foubert-Samier et al., 2013), increased cortical thickness in temporoparietal (Foubert-Samier et al., 2013; Liu, et al., 2012) and orbitofrontal areas (Liu et al., 2012), as well as decreased mean diffusivity in the hippocampus (Piras, Cherubini, Caltagirone, & Spalletta, 2011). Along with structural modifications, education has also been related to functional changes such as increased metabolic activity in the ACC and increased connectivity between ACC and right hippocampus, left inferior frontal lobe, right posterior cingulate cortex and left angular gyrus (Arenaza-Urquijo et al., 2013). Arenaza-Urquijo et al. (2013) also found that this increased connectivity between ACC and other regions was associated with greater word production on verbal fluency tasks, indicating that high levels of education might strengthen the connections between brain areas and thereby, improve behavioural performance on cognitive tasks. Many of the above-mentioned brain regions, such as the inferior frontal cortex, ACC and temporal cortex are recruited during word-finding tasks (see Chapter 2 for details). Taken together, the findings from the neural and neuropsychological studies suggest that additional structural and functional changes in the brain as a result of high levels of education may be neuroprotective and delay age-related cognitive decline. Older women in the current study had high levels of education which may have contributed to structural and functional modification in the brain areas supporting word-finding performance, and thereby masked the age-related declines in word-finding abilities.

At the outset, it was mentioned that active lifestyle, involvement in cognitively stimulating tasks, physical activity, high IQ levels, along with education increase reserve capacity in an individual. In the current study, the majority of the women in the two younger groups (46-55, 56-65 years) were recruited from the staff working in the university, and those in the older group (70-79 years) were recruited from the University Third Age (U3A). U3A is an organization where older people meet in social groups to pursue different physical activities (dancing, cycling, walks, yoga, etc), social activities (lunch and tea clubs, travel) and other interests such as learning a foreign language, taking up short history and memory courses. The IQ scores for all the age groups were in the high average to superior range according to WASI classification (Wechsler, 1999), suggesting that women in this study represented a 'supranormal' population and fell on the positive end of the normal distribution curve. Thus, it can be suggested that a combination of high levels of intelligence, education and engagement in cognitively stimulating activities may have increased the brain reserve or cognitive reserve or efficient compensatory mechanisms in the two older groups. This may have delayed the onset of cognitive decline (Opdebeeck et al., 2015; Valenzeula & Sachdev, 2006), thus failing to show significant age-related declines in word-finding abilities.

Apart from education, several other factors might have also contributed to nonsignificant findings. There is a considerable variation across studies in the age groups that have been considered in examining the effects of age on word-finding abilities. The current study only involved midlife, late-life women aged 46-79 years, and not including a younger age group (individuals in their 20s and 30s) may have limited finding significant effects of age on word-finding abilities. Nonsignificant effects of age can also be ascribed to differences in task administration, scoring, sample population (British population, only women were included) and sample size (sample size issues are discussed in section 8.5).

8.4. Exploratory analysis investigating the interactive effects of demographic and reproductive factors on word-finding performance in a subgroup of women from the study sample

In the previous section, it was discussed that the rate of age-related decline in word-finding abilities can differ among individuals based on their demographic characteristics such as education and IQ. Word-finding performance is also associated with reproductive characteristics as seen in the current study. Therefore, it is plausible that age or menopause-related effects on word-finding abilities may vary across women differing in their reproductive characteristics. The number of studies that have conducted research in this area are limited. A few studies have compared women differing in the type of menopause experienced (natural versus surgical menopause) on their cognitive abilities, and existing evidence suggests a greater risk of cognitive impairments and dementia in women with surgical menopause (Rocca et al., 2012; Settnes et al., 2005). As discussed in Chapter 5, the risk of AD also decreases in women with an early age at menarche (Paganini-Hill & Henderson, 1994), fewer children (Colucci et al., 2006), a later age at menopause (Sobow & Kloszewska, 2004), greater number of reproductive years (Fox et al., 2013) and increased cumulative hormone exposure across the lifespan (Fox et al., 2013). These findings suggest that the rate of age-related decline in word-finding abilities may be slower in women having greater hormone exposures than in women with low hormone exposures across the lifespan. Therefore, studies investigating the effects of age and menopause on word-finding abilities should classify women across these demographic and reproductive characteristics. The current study did not contain large samples to compare groups of women varying in their demographic and reproductive characteristics (for example, high versus low levels of education, parous versus nulliparous women). Hence, a preliminary analysis was conducted in a subgroup of women and the relationships between overall word-finding measures, demographic and reproductive characteristics were studied. The first aim of this preliminary analysis was to examine the association between age and word-finding abilities, and the second aim was to examine the relationship between menopause stage and word-finding performance. For the age analyses, data from postmenopausal women aged 48-79 years with no history of hysterectomy and who had had one or more child/children were analysed. For the menopause stage analyses, data from women aged 46-55 years across menopause stages, with no history of hysterectomy, and who had had one or more child/children were considered.

The first stage of data analyses reported in Chapters 6 & 7 employed a univariate approach to examine the effects of age and menopause on different word-finding measures. This approach was undertaken in order to compare the current study findings to existing literature because earlier studies have focused on either verbal fluency or naming tasks. The final stage of analyses in a subsample of women used a multivariate approach to examine age and menopause-related effects on word-finding abilities because of a number of reasons. Firstly, there is a risk of introducing Type I errors, that is, increasing the chance of reporting false positive results, when conducting a number of univariate ANOVAs, whereas Type I errors can be reduced in a multivariate approach. Secondly, the effects of age and menopause on word-finding abilities are subtle and therefore, a multivariate approach can reduce Type II errors and have greater power to detect these effects. Thirdly, a multivariate approach also considers the relationships between the dependent variables and can detect the effect of an independent variable based on a combination of dependent measures rather than a single measure alone.

Word-finding measures were used as dependent variables in the multivariate analyses. The demographic (age, vocabulary, education) and reproductive (menopause status, age at menarche, menstrual cycle length, age at first childbirth, number of children, age at menopause, number of years since menopause and number of reproductive years) factors were considered as covariates in order to examine the combined association between these variables and word-finding abilities. The dependent and covariate measures were selected based on previously conducted ANOVAs and ANCOVAs, correlations and earlier reports from the literature. For the age analyses, word-finding measures for which a significant effect of age (picture naming latency, category fluency total words) had been found in the univariate analyses were chosen as dependent variables. Additionally, the measures that were significantly associated with demographic or reproductive factors were considered as dependent variables. The demographic and reproductive characteristics that were significantly associated with word-finding performance as assessed by correlations or ANCOVAs were included as covariates in the multivariate models. Prior to finalizing dependent variables, Pearson correlations were conducted to study the inter-relationship between the five different word-finding measures after excluding women with hysterectomies (see Table 8.3). These analyses were performed to determine multicollinearity issues for the final multivariate models. If two variables were very strongly correlated (0.8-0.9), then only the one that made a greater contribution to word-finding performance was retained. A similar approach was used for selecting variables for the menopause stage analyses.

Table 8.1

Correlations between different word-finding measures (verbal fluency, naming and C-series measures) (n = 73, otherwise indicated)

		LF Total words	PN Accuracy	PN Latency	NAD Accuracy (*n* = 71)	NAD Latency (*n* = 71)	Switch Rate			Switch Cost		
							2-series	3-series	4-series	2-series	3-series	4-series
CF total words		.61**	.58**	-.58**	.53**	-.29*	.48**	.47**	.40**	-.06	-.13	-.05
LF total words			.44**	-.39**	.43**	-.21	.64**	.46**	.56**	-.01	.04	-.08
PN Accuracy				-.58**	.52**	-.12	.29*	.24*	.19	-.10	-.06	-.04
PN Latency					-.52**	.44**	-.47**	-.43**	-.33**	.09	.11	.03
NAD Accuracy (*n* = 71)						-.32**	.35**	.43**	.35**	.03	-.11	-.09
NAD Latency (*n* = 71)							-.24*	-.26*	-.28*	.05	.09	.13
Switch Rate	2-series							.70**	.64**	-.09	.01	.07
	3-series								.70**	-.06	-.38**	-.16
	4-series									-.09	-.21	-.42**
Switch Cost	2-series										.80**	.73**
	3-series											.81**

Note. CF: Category fluency, *LF:* Letter fluency, *PN:* Picture naming, *NAD:* Naming-to-auditory-definitions. **p* < .05. ***p* < .01.

8.4.1. Results from the multivariate analyses

8.4.1.1. Age analysis in women aged 48-79 years

Postmenopausal women with no hysterectomy and at least one child were included in this analysis (n = 45). Only the results of the final model are reported here (for details on preliminary MANOVAs that were conducted to retain the dependent variables and covariates, see Appendix 5). The dependent variables that were significantly or marginally associated with at least one or more covariates were retained in the final model. A similar approach was taken when selecting covariates. The model included Category fluency total number of words, Letter fluency total number of words, 3-series switch cost, Picture naming latency and Naming-to-auditory-definitions accuracy as dependent variables. Associations between these dependent variables were not greater than 0.8 (see Table 8.1). Age, number of years of education, menstrual cycle length, age at first childbirth and number of reproductive years were used as covariates. Results showed that all the covariates were significantly associated with overall word-finding performance, age, V = 0.52, F(5, 35) = 7.66, p < .001, number of years of education, V = 0.34, F(5, 35) = 3.67, p = .009, and menstrual cycle length, V = 0.34, F(5, 35) = 3.61, p = .010, age at first childbirth, V = 0.37, F(5, 35) = 4.05, p = .005, and number of reproductive years, V = 0.35, F(5, 35) = 3.70, p = .009. The outcomes from the post hoc univariate tests revealed that age was significantly associated with picture naming latency and 3-series switch cost. Number of years of education had a significant effect for letter fluency and naming-to-auditory-definitions accuracy. Menstrual cycle length had a significant effect for naming-to-auditory-definitions accuracy. The effect of age at first childbirth was significant for 3-series switch cost percentage and picture naming latency. The effect of number of reproductive years was significant for category fluency, picture-naming latency and naming-to-auditory-definitions accuracy.

8.4.1.2. Menopause stage analysis in women aged 46-55 years

Only women who had children (n = 24) were considered for the analysis. The dependent variables were Category fluency total number of words, Letter fluency total number of words, 4-series switch rate, Picture naming latency and Naming-to-auditory-definitions accuracy. Age, Menstrual cycle length and Menopause stage (Pre vs Peri, Pre vs Post) were entered as covariates in the model. For a variable to be included as a covariate in regression models, it has to be either continuous or categorical, with a maximum of two categories. Menopause stage was a categorical variable with three categories: pre, peri and postmenopause stages. Therefore, it was converted into two dummy variables (DVs 1 & 2) prior to including it as a covariate in the multivariate analyses. Premenopausal women are at high hormone states compared to women in peri and postmenopausal stages. Therefore, to study whether high hormone states facilitated overall word-finding performance premenopausal women were used as the reference group. DV1 compared women in the premenopausal group with the perimenopausal group, and DV2 compared the premenopausal group with the postmenopausal group. The results indicated a significant effect of DV1 (pre vs peri), $V = 0.52$, $F(5, 15) = 3.29$, $p = .033$ on overall word-finding ability. The univariate findings further showed a significant effect of this variable on naming-to-definition-accuracy. No other significant effects were noticed.

8.4.2. Discussion

The multivariate analyses were conducted to examine the relationships between overall word-finding performance, age or menopause status, education, IQ, and reproductive characteristics in a subsample of highly educated women who had had at least one child and had experienced natural menopause. The results showed that age was significantly associated with overall word-finding abilities. This effect was predominantly driven by the picture naming latency and 3-series switch cost measures, although the other variables (category fluency, letter fluency and naming-to-definitions accuracy) also showed a nonsignificant age-related trend. These findings are in line with the results of the univariate tests reported in Chapters 6 and 7. Longer response latencies with age may have resulted from an overall slowing of the cognitive processes ("General slowing hypothesis", Salthouse, 1996) or due to a weakening of connections between semantic knowledge and the lexical forms of the words ("Transmission deficit hypothesis", Burke et al., 1991). The study design does not allow detailed examination of this and therefore, requires future studies to investigate this aspect. As discussed in Chapter 6, performance on the C-series task relies on working memory to a great extent because it requires the individual to remember the target categories, the items that have been retrieved, the sequence of retrieval, and to avoid repetitions and errors. Gurd et al. (2002) found that activity in the frontal and parietal cortices are associated with task performance on C-series tasks. There is evidence of age-related changes in the structure and function of the frontal and parietal areas (Damoiseaux et al., 2008; Jerningan et al., 2001; Raz et al., 2005) and it is possible that these changes might have contributed to the association between age and 3-series switch cost.

Along with age, word-finding performance in midlife and late-life women (48-79 years) was also associated with years of formal education as shown by previous researchers (Brickman et al., 2005; Connor et al., 2004; Elkadi et al., 2006; Gladsjo et al., 1999; Goral et al., 2007; Hatch et al., 2007; Neils et al., 1995; Pena-Casanova et al., 2009a, 2009b; Tombaugh et al., 1999; Tsang & Lee, 2003; Van der Elst et al., 2006; Welch et al., 1996). Reproductive characteristics such as menstrual cycle length, age at first childbirth and reproductive years were also significantly covaried with overall word finding performance. These results find support from Ryan et al.'s (2009) study, which showed that later age at first childbirth, and greater number of reproductive years were associated with higher word production on verbal fluency tasks. The endocrinological changes that occur before, during and after pregnancy have not been clearly established. It is suggested that estrogen levels rise during pregnancy, decline to a very low level post childbirth (Oats et al., 2010), and remain in that low state until the end of lactation. Bernstein et al. (1985) found that plasma estrogen and free estradiol levels during regular menstrual cycles are at a lower level in parous women than in nulliparous women. Therefore, a later age at first childbirth may expose a woman to a high estrogen state (as in case of nulliparous women) for a longer duration and increase the cumulative hormone exposure. Similarly, greater reproductive years would also increase the cumulative hormone exposure across the lifespan and thereby facilitate word-finding abilities in later life.

The effects of menopause stage, demographic and reproductive variables on word-finding abilities were also examined using a multivariate approach. The results showed a significant difference between women in the pre and perimenopause stages on overall word-finding ability. Women in the perimenopause stage had a higher mean score than women in the premenopause stage. The range of scores for perimenopausal women was restricted and thus, it is difficult to determine if there was a true effect of menopause stage. It may be concluded that women across menopause stages, aged 46-55 years, do not significantly vary in their word-finding abilities as shown by previous researchers (Fuh et al., 2003; Herlitz et al., 2007; Lokken & Ferraro, 2006; Weber et al., 2013).

8.5. Limitations of the research

The present study examined the effects of age and menopause on word-finding abilities by using a comprehensive test battery. It also investigated the associations between vocabulary, education, reproductive characteristics and word-finding abilities. The data were analysed using standard scoring procedures and were tested statistically using a combination of correlations, univariate and multivariate ANOVAs. Despite a robust methodology and a strong data analysis procedure, there were some limitations in the research design.

The first limitation concerns the sample size and population from which the participants were recruited. Although 78 women participated in the current study, the sample size was modest when women were classified as a function of age or menopause status. Rodriguez-Aranda & Martinussen (2006) compared verbal fluency performance across successive age decades and reported that the effect size of comparisons was small. Similarly, Connor et al. (2004), who examined the effects of age on picture naming, also found a small decrement in percentage scores (2% per age decade), indicating that age effects on word-finding abilities in healthy adults may be small. Moreover, a small effect size has also been reported when comparing peri and postmenopausal women on letter fluency (Weber et al., 2013). Therefore, in order to detect a significant difference between groups with 80% power ($\alpha = .05$), data from a larger group of participants need to be analysed (Cohen, 1992). Restrictions of time and practical constraints limited the researcher from recruiting more participants. The small sample size across the groups may have limited the power of the current study to detect significant age or menopause stage effects on word-finding abilities.

Representative sampling has been a concern in most research studies on healthy adults. Individuals with higher education levels, good health and awareness are more likely to participate in research studies than those with fewer years of education, poor health and less awareness. As discussed previously, these individuals may have higher cognitive reserve and therefore show a slower age-related decline on individual word-finding measures. Participants in the present study were mainly recruited from among women who worked in the University or those who were active in social groups. This may have also contributed to nonsignificant findings and the results therefore cannot be generalized to the entire population.

There were also methodological limitations in the data collection procedure and the tasks used in the study. Self-reports were used to obtain information about reproductive variables such as age at menarche, menstrual cycle length, age at first childbirth and age at menopause. Subjective reports were also employed to classify women across menopause stages. Self-reporting is subject to recall bias and there may be inaccurate reporting of the exact year that an event happened. This method of obtaining information can only provide an estimate of hormone levels (high versus low). Previous work examining the effects of hormonal changes during menopause on cognition have examined the association between cognition and hormone levels as measured by immunoassays (Berent-Spillson et al., 2012; Herlitz et al., 2007; Weber et al., 2013). Therefore, the study findings provide only indirect evidence of effects of cumulative hormone exposure across the life span and sex hormonal changes during menopause on word-retrieval.

There were some limitations in the verbal naming tasks used. For picture naming, the standardised BNT (Kaplan et al., 1983) was administered and for naming-to-auditory-definitions, Harley and Bown's (1998) list of 60 words was used. The BNT requires the naming of common objects and is susceptible to ceiling effects. Accuracy scores for the BNT have also been shown to be affected by generational familiarity in cross-sectional research designs because individuals belonging to different birth cohorts may have different exposure to objects and items (Schmitter-Edgecombe et al., 2000). The lexical characteristics of a word determine the accuracy and the speed with which a word can be retrieved. The BNT items ranged in difficulty from low to high, but there were no separate lists of words that controlled for the effects of lexical characteristics such as frequency, age of acquisition, word length, imageability or neighbourhood density. Due to the unavailability of a computerised version of BNT, the paper form of the test was administered and response latencies were manually marked by the researcher using PRAAT (Boersma &Weenink, 2011), which may have resulted in some inaccuracies. Therefore, future studies investigating the effects of age on naming in healthy adults should test this cognitive ability employing a computerised test format and a controlled set of stimuli varying in lexical characteristics.

For the naming-to-auditory-definitions task, the words that were used varied only on two lexical characteristics, frequency and neighbourhood density. The present research aimed to obtain a global picture of the effects of age and menopause on word-finding abilities by using various test forms because existing literature has been inconsistent and scant, and studying the effects of lexical characteristics on word-finding was not a primary aim. The results showed an interactive effect of frequency and neighbourhood density on word-retrieval in the naming-to-auditory-definitions task. The effects of these variables needs further confirmation in future studies which use stimuli controlled on a number of lexical characteristics such as visual complexity, name agreement, age of acquisition, imageability and word length.

8.6. Implications and scope for future research

The results of the study have both clinical and research implications. The test battery was sensitive in measuring word-finding abilities in women aged 46-79 years. Therefore, it can be used in future cognitive assessments of women who report word-finding difficulties during menopause and with increasing age. Additionally, after development of standardized norms, the battery can also be used to assess word-finding abilities in clinical groups such as aphasia or dementia.

One of the key findings of the present study was that word-finding abilities did not significantly decline with advancing age and this was probably being moderated by the high levels of education, healthy lifestyle and active involvement in cognitive stimulating activities. All these factors are modifiable and hence can have major clinical implications in delaying age-related cognitive decline. Future detailed examination of the impact of these factors on cognitive abilities can help in formulating guidelines and policies related to healthy ageing. The results also suggest the need to examine whether age has a similar effect on word-finding abilities in a group of women with low levels of education (less than 12 years). It indicates the importance to develop normative data for word-finding measures based on levels of education.

The results also showed that age was significantly associated with overall word-finding performance rather than a single measure of word-finding ability. Thus, there is a need to develop a composite measure of word-finding abilities in order to examine the subtle effects of age and menopause on this particular cognitive ability in healthy adults.

Previous studies that examined the effects of brain or cognitive reserve on cognitive abilities considered education, physical activity, and social engagement as proxy measures but none of them included an index of hormonal exposure. Individual reproductive clinical markers such as an early age at menarche, later age at first childbirth, later age at menopause and greater reproductive years have been shown to be associated with better cognitive performance in later life (Lebrun et al., 2005; McLay et al., 2003; Ryan et al., 2009; Smith et al., 1999). The current study also found that some of these markers were correlated with performance on different word-finding measures. The results of the present study did not show a significant beneficial effect of high hormone state (premenopause) compared to a low hormone state of menopause (peri, postmenopause) on word-finding measures but there was some evidence that cognitive strategy use on verbal fluency tasks was dependent on menopause stage. Premenopausal women who have high levels of estrogen made a balanced use of switching and clustering to enhance word production (a frontally mediated cognitive function, Troyer et al., 1997), whereas post-menopausal women mostly relied on clustering (a measure of semantic memory, Troyer et al., 1997). Taken together, these findings suggest that high levels of sex hormones across the life span can facilitate cognitive functions in later life. Therefore, including a measure of reproductive history or cumulative hormone exposure across the lifespan as a behavioural measure of cognitive reserve may further help to explain differences in age-related declines across groups of women. Hormone assays should be included in order to establish a confirmed relationship between hormone levels and cognitive decline and to delineate independent and inter-related effects of age and menopause.

References

Abrahams, S., Goldstein, L. H., Simmons, A., Brammer, M. J., Williams, S. C. R., Giampietro, V. P., … Leigh, P. N. (2003). Functional magnetic resonance imaging of verbal fluency and confrontation naming using compressed image acquisition to permit overt responses. *Human Brain Mapping*, *20*, 29–40.

Abwender, D. A., Swan, J. G., Bowerman, J. T., & Connolly, S. W. (2001). Qualitative analysis of verbal fluency output: Review and comparison of several scoring methods. *Assessment*, *8*(3), 323–338.

Adams, M. M., Shah, R. A., Janssen, W. G. M., & Morrison, J. H. (2001). Different modes of hippocampal plasticity in response to estrogen in young and aged female rats. *Proceedings of the National Academy of Science of the United States of America, 98*(14), 8071–8076.

Albert, M. S., Heller, H. S., & Milberg, W. (1988). Changes in naming ability with age. *Psychology of Aging, 3*, 173–178.

Albert, M. L., Spiro III, A., Sayers, K. J., Cohen, J. A., Brady, C. B., Goral, M., & Obler, L. K. (2009). Effects of health status on word finding in aging. *Journal of the American Geriatrics Society*, *57*(12), 2300–2305.

Almeida, O. P., Lautenschlager, N. T., Vasikaran, S., Leedman, P., Gelavis, A., & Flicker, L. (2006). A 20-week randomized controlled trial of estradiol replacement therapy for women aged 70 years and older: Effect on mood, cognition and quality of life. *Neurobiology of Aging, 27*(1), 141–149.

American Society for Reproductive Medicine (n.d.). Premature ovarian failure. Retrieved from https://www.asrm.org/topics/detail.aspx?id=280

Amunts, K., Weiss, P. H., Mohlberg, H., Pieperhoff, P., Eickhoff, S., Gurd, J. M., … Zilles, K. (2004). Analysis of neural mechanisms underlying verbal fluency in cytoarchitectonically defined stereotaxic space: The roles of Brodmann areas 44 and 45. *NeuroImage*, *22*(1), 42–56.

Apter, D., Reinila, M., & Vihko, R. (1989). Some endocrine characteristics of early menarche, a risk factor for breast cancer, are preserved into adulthood. *International Journal of Cancer, 44*(5), 783–787.

Arenaza-Urquijo, E. M., Landeau, B., La Joie, R., Mevel, K., Mézenge, F., Perrotin, A., … Chételat, G. (2013). Relationships between years of education and gray matter volume, metabolism and functional connectivity in healthy elders. *NeuroImage*, *83*, 450–457.

Arevalo, M.-A., Azcoitia, I., & Garcia-Segura, L. M. (2015). The neuroprotective actions of oestradiol and oestrogen receptors. *Nature Reviews Neuroscience*, *16*, 17–29.

Arnsten, A. F. T. (1997). Catecholamine regulation of the prefrontal cortex. *Journal of Psychopharmacology, 11*(2), 151–162.

Auyeung, B., Lombardo, M. V, & Baron-Cohen, S. (2013). Prenatal and postnatal hormone effects on the human brain and cognition. *Pflügers Archives : European Journal of Physiology*, *465*(5), 557–571.

Azuma, T. (2004). Working memory and perseveration in verbal fluency. *Neuropsychology, 18*(1), 69–77.

Baldo, J. V, Arévalo, A., Patterson, J. P., & Dronkers, N. F. (2013). Grey and white matter correlates of picture naming: Evidence from a voxel-based lesion analysis of the Boston naming test. *Cortex*, *49*(3), 658–667.

Baldo, J. V., Schwartz, S., Wilkins, D., & Dronkers, N. F. (2006). Role of frontal versus temporal cortex in verbal fluency as revealed by voxel-based lesion symptom mapping. *Journal of the International Neuropsychological Society*, *12*(6), 896–900.

Baldo, J. V., & Shimamura, A. P. (1998). Letter and category fluency in patients with frontal lobe lesions. *Neuropsychology, 12*(2), 259–267.

Barrett-Connor, E., & Goodman-Gruen, D. (1999). Cognitive function and endogenous sex hormones in older women. *Journal of the American Geriatrics Society, 47*, 1289–1293.

Barrett-Connor, E. & Kritz-Silverstein, D. (1993). Estrogen replacement therapy and cognitive function in older women. *The Journal of the American Medical Association, 269*(20)*,* 2637–2641.

Barry, J. A., Parekh, H. S., & Hardiman, P. J. (2013). Visual-spatial cognition in women with polycystic ovarian syndrome: The role of androgens. *Human Reproduction, 28*(10), 2832-2837.

Bates, E., D'Amico, S., Jacobsen, T., Székely, A., Andonova, E., Devescovi, A., Herron, D., … Tzeng, O. (2003). Timed picture naming in seven languages. *Psychonomic Bulletin and Review, 10*(2), 344–380.

Bayles, K. A., & Tomoeda, C. K. (2007). *Cognitive-communication disorders of dementia*. San Diego, CA: Plural.

Bean, J. A., Leeper, J. D., Wallace, R. B., Sherman, B. M., & Jagger, H. (1979). Variations in the reporting of menstrual histories. *American Journal of Epidemiology, 109*(2), 181–185.

Bell, B. D., Seidenberg, M., Hermann, B. P., & Douville, K. (2003). Visual and auditory naming in patients with left or bilateral temporal lobe epilepsy. *Epilepsy Research*, *55*(1-2), 29–37.

Benton, A. L. (1965). *Manuel pour l'application du Test Rêtention Visuelle*. Paris, France: Les Editions du Centre de Psychologie Appliquée.

Benton, A. L. (1968). Differential behavioral effects in frontal lobe disease. *Neuropsychologia*, *6*(1), 53–60.

Benton, A. L., Hamsher, K., & Sivan, A. B. (1994). *Multilingual Aphasia Examination* (3rd ed.). Iowa City, IA: AJA Associates.

Berenbaum, S. A. (1998). How hormones affect behavioural and neural development: Introduction to the special issue on "gonadal hormones and sex differences in behaviour." *Developmental Neuropsychology*, *14*(2-3), 175–196.

Berenbaum, S. A, & Beltz, A. M. (2011). Sexual differentiation of human behavior: Effects of prenatal and pubertal organizational hormones. *Frontiers in Neuroendocrinology*, *32*(2), 183–200.

Berenbaum, S. A., Blakemore, J. E. O., & Beltz, A. M. (2011). A role for biology in gender-related behavior. *Sex Roles*, *64*(11-12), 804–825.

Berent-Spillson, A., Persad, C. C., Love, T., Sowers, M., Randolph, J. F., Zubieta, J.-K., & Smith, Y. R. (2012). Hormonal environment affects cognition independent of age during the menopause transition. *The Journal of Clinical Endocrinology and Metabolism*, *97*(9), 1686–1694.

Bernstein, L., Pike, M. C., Ross, R. K., & Henderson, B. E. (1991). Age at menarche and estrogen concentrations of adult women. *Cancer Causes & Control*, *2*(4), 221–225.

Bernstein, L., Pike, M. C., Ross, R. K., Judd, H. L., Brown, J. B., & Henderson, B. E. (1985). Estrogen and sex hormone-binding globulin levels in nulliparous and parous women. *Journal of the National Cancer Institute, 74*(4), 741–745.

Birn, R. M., Kenworthy, L., Case, L., Caravella, R., Jones, T. B., Bandettini, P. A, & Martin, A. (2010). Neural systems supporting lexical search guided by letter and semantic category cues: A self-paced overt response fMRI study of verbal fluency. *NeuroImage*, *49*(1), 1099–1107.

Bixo, M., Backstrom, T., Winbald, B., & Anderson, A. (1995). Estradiol and testosterone in specific regions of the human female brain in different endocrine states. *Journal of Steroid Biochemistry and Molecular Biology, 55*(3-4), 297–303.

Boersma, P., & Weenink, D. (2011). Praat: Doing phonetics by computer [Version 5.3.01] [Computer program]. Retrieved from http://www.fon.hum.uva.nl/praat/

Bokat, C. E., & Goldberg, T. E. (2003). Letter and category fluency in schizophrenic patients: A meta-analysis. *Schizophrenia Research, 64*, 73-78.

Bolla, K. I., Lindgren, K. N., Bonaccorsy, C., & Bleecker, M. L. (1990). Predictors of verbal fluency (FAS) in the healthy elderly. *Journal of Clinical Psychology, 46*(5), 623–628.

Bolton, P. (2012). Education: Historical statistics. Retrieved from http://www.parliament.uk/briefing-papers/SN04252.pdf

Bonin, P., Peereman, R., Malardier, N., Méot, A., & Chalard, M. (2003). A new set of 299 pictures for psycholinguistic studies: French norms for name agreement, image agreement, conceptual familiarity, visual complexity, image variability, age of acquisition, and naming latencies. *Behavior Research Methods, Instruments, and Computers, 35*(1), 158–167.

Borkowski, J. G., Benton, A. L., & Spreen, O. (1967). Word fluency and brain damage. *Neuropsychologia, 5*, 135–140.

Boss, L., Kang, D.-H., Marcus, M., & Bergstrom, N. (2014). Endogenous sex hormones and cognitive function in older adults: A systematic review. *Western Journal of Nursing Research*, *36*, 388–426.

Bousfield, W. A., & Sedgewick, H. W. (1944). An analysis of sequences of restricted associative responses. *Journal of General Psychology, 30*, 149–165.

Bove, R., Secor, E., Chibnik, L. B., Barnes, L. L., Schneider, J. A, Bennett, D. A, & De Jager, P. L. (2014). Age at surgical menopause influences cognitive decline and Alzheimer pathology in older women. *Neurology*, *82*(3), 222–229.

Bowles, N. L., Obler, L. K., & Albert, M. L. (1987). Naming errors in healthy aging and dementia of the Alzheimer type. *Cortex, 23*, 519–524.

Bowles, R. P., & Salthouse, T. A. (2008). Vocabulary test format and differential relations to age. *Psychology and Aging*, *23*(2), 366-376.

Brady, C. B., Spiro, A., III, & Gaziano, J. M. (2005). Effects of age and hypertension status on cognition: The veterans affairs normative aging study. *Neuropsychology*, *19*(6), 770–777.

Brayne, C., Gill, C., Huppert, F. A., Barkley, C., Gehlhaar, E., Girling, D. M., … Paykel, E. S. (1995). Incidence of clinically diagnosed subtypes of dementia in an elderly population. Cambridge Project for Later Life. *The British Journal of Psychiatry*, *167*(2), 255–262.

Brickman, A. M., Paul, R. H., Cohen, R. A, Williams, L. M., MacGregor, K. L., Jefferson, A. L., Tate, D. F., Gunstad, J., & Gordon, E. (2005). Category and letter verbal fluency across the adult lifespan: Relationship to EEG theta power. *Archives of Clinical Neuropsychology*, *20*(5), 561–573.

Briggs, H. (2014, July 16). ONS: Mothers' average age hits 30. British Broadcasting Corporation. Retrieved from http://www.bbc.co.uk/news/health-28329737

Brown, R., & McNeill, D. (1966). The "tip of the tongue" phenomenon. *Journal of Verbal Learning and Verbal Behavior, 5*, 325-337.

Brown, A. S., & Nix, L. A. (1996). Age-related changes in the tip-of-the-tongue experience. *The American Journal of Psychology, 109*(1), 79–91.

Brysbaert, M. (1996).Word frequency affects naming latency in Dutch when age of acquisition is controlled. *European Journal of Cognitive Psychology, 8*(2), 185–193.

Buckwalter, J. G., Crooks, V. C., Robins, S. B., & Petitti, D. B. (2004). Hormone use and cognitive performance in women of advanced age. *Journal of the American Geriatrics Society*, *52*(2)*,* 182–186.

Burger, H. G., Dudley, E. C., Robertson, D. M., & Dennerstein, L. (2002). Hormonal changes in the menopause transition. *Recent Progress in Hormone Research*, *57*, 257–275.

Burger, H. G., Hale, G. E., Robertson, D. M., & Dennerstein, L. (2007). A review of hormonal changes during the menopausal transition: focus on findings from the Melbourne Women's Midlife Health Project. *Human Reproduction Update*, *13*(6), 559–565.

Burke, D. M., & Graham, E. R. (2012). The neural basis for aging effects on language. In M. Guha (Eds.), *The handbook of the neuropsychology of language* (pp. 778–800). Malden, MA and Oxford: Wiley-Blackwell.

Burke, D. M., & Mackay, D. G. (1997). Memory, language and ageing. *Philosophical Transactions of the Royal Society: Biological Sciences*, *352*(1363), 1845–1856.

Burke, D. M., MacKay, D. G., Worthley, J. S., & Wade, E. (1991). On the tip of the tongue: What causes word finding failures in young and older adults? *Journal of Memory and Language, 30*, 542–579.

Cambridge Centre for Ageing and Neuroscience (2010, June). Language. Retrieved from http://www.cam-can.org/language/index.html

Capitani, E., Laiacona, M., & Basso, A. (1998). Phonetically cued word-fluency, gender differences and aging: A reappraisal. *Cortex*, *34*, 779–783.

Capitani, E., Laiacona, M., & Barbarotto, R. (1999). Gender affects word retrieval of certain categories in semantic fluency tasks. *Neuropsychology*, *3*, 273–278.

Castelo-Branco, C., Blümel, J. E., Chedraui P, Bocanera, R., Depiano, E., Fiqueroa-Casas, P. … Fiqueroa-Casas, P. (2006). Age at menopause in Latin America. *Menopause, 13*(4), 70-712.

Cattell, R. B. (1971). Abilities: Their structure, growth and action. Boston: Houghton-Mifflin.

Cattell, R. B. (1987). *Intelligence: Its structure, growth, and action*. New York: Elsevier.

Charlton, B. G. (2007). Psychological neoteny and higher education: Associations with delayed parenthood. *Medical hypotheses, 69*, 237–240.

Chubak., J., Tworoger, S. S., Yasui, Y., Ulrich, C. M., Stanczyk, F. Z., & Mctiernan, A. (2004). Associations between reproductive and menstrual factors and postmenopausal sex hormone concentrations. *Cancer Epidemiology, Biomarkers and Prevention, 13,* 1296–1301.

Cohen, J. (1992). A power primer. *Psychological Bulletin, 112*(1), 155-159.

Colombo, L., & Burani, C. (2002). The influence of age of acquisition, root frequency, and context availability in processing nouns and verbs. *Brain and Language*, *81*(1-3), 398–411.

Coltheart, M. (1981). The MRC Psycholinguistic Database. *The Quarterly Journal of Experimental Psychology Section A, 33*(4), 497-505.

Coltheart, M., Davelaar, E., Jonasson, J. T., & Besner, D. (1977). Access to the internal lexicon. In S. Dornic (Ed.), *Attention and Performance VI*, pp. 535-555. London: Academic Press.

Colucci, M., Cammarata, S., Assini, A., Croce, R., Clerici, F., Novello, C., … Tanganelli, P. (2006). The number of pregnancies is a risk factor for Alzheimer's disease. *European Journal of Neurology*, *13*(12), 1374–1377.

Comas-Herrera, A., Wittenberg, R., Pickard, L., & Knapp, M. (2007). Cognitive impairment in older people: Future demand for long-term care services and the associated costs. *International Journal of Geriatric Psychiatry, 22*, 1037-1045.

Connelly, M. T., Richardson, M., & Platt, R. (2000). Prevalence and duration of postmenopausal hormone replacement therapy use in a managed care organization, 1990–1995. *Journal of General Internal Medicine, 15*(8), 542–550.

Connor, L. T., Spiro, A., III, Obler, L. K., & Albert, M. L. (2004). Change in object naming ability during adulthood. *The Journals of Gerontology: Psychological Sciences*, *59*(5), 203–209.

Costafreda, S. G., Fu, C. H. Y., Lee, L., Everitt, B., Brammer, M. J., & David, A. S. (2006). A systematic review and quantitative appraisal of fMRI studies of verbal fluency: Role of the left inferior frontal gyrus. *Human Brain Mapping*, *27*(10), 799–810.

Cowell, P. E., Ledger, W. L., Wadnerkar, M. B., Skilling, F. M., & Whiteside, S. P. (2011). Hormones and dichotic listening: Evidence from the study of menstrual cycle effects. *Brain and Cognition*, *76*(2), 256–262.

Craig, M. C., Fletcher, P. C., Daly, E. M., Rymer, J., Cutter, W. J., Brammer, M., … Murphy, D. G. (2007). Gonadotropin hormone releasing hormone agonists alter prefrontal function during verbal encoding in young women. *Psychoneuroendocrinology, 32*(8-10), 1116–1127.

Craik, E I. M., & Byrd, M. (1982). Aging and cognitive deficits: The role of attentional resources. In E. I. M. Craik & S. Trehub (Eds,), *Aging and cognitive processes* (pp. 191-211). New York: Plenum.

Craik , F. I. M., & Salthouse, T. A. (Eds.). (2008). *Handbook of cognitive aging*. New York: Psychology Press.

Crowe, S. F. (1998). Decrease in performance on the verbal fluency test as a function of time: Evaluation in a young healthy sample. *Journal of Clinical and Experimental Neuropsychology, 20*(3), 391–401.

Cruice, M. N., Worrall, L. E., & Hickson, L. M. H. (2000). Boston naming test results for healthy older Australians: A longitudinal and cross-sectional study. *Aphasiology*, *14*(2), 143–155.

Damoiseaux, J. S., Beckmann, C. F., Arigita, E. J. S., Barkhof, F., Scheltens, P., Stam, C. J., … Rombouts, S. A. R. B. (2007). Reduced resting-state brain activity in the "default network" in normal aging. *Cerebral Cortex*, *18*(8), 1856–1864.

Daniel, J. M., Hulst, J. M., & Berbling, J. L. (2006). Estradiol replacement enhances working memory in middle-age rats when initiated immediately after ovariectomy but not after a long-term period of ovarian hormone deprivation. *Endocrinology, 147*(1), 607–614.

Darcy, I. (2010). DMDX Introductory Tutorial. Retrieved from http://www.iub.edu/~psyling/resources/dmdx-tutorial_id_2010.pdf

De Deyn, P. P., Goeman, J., Vervaet, A., Dourcy-Belle-Rose, B., Van Dam, D., & Geerts, E. (2011). Prevalence and incidence of dementia among 75-80-year-old community-dwelling elderly in different districts of Antwerp, Belgium: The Antwerp cognition (ANCOG) study. *Clinical Neurology and Neurosurgery*, *113*(9), 736–745.

Dell, G. S., Schwartz, M. F., Martin, N., Saffran, E. M., & Gagnon, D. A. (1997). Lexical access in aphasic and nonaphasic speakers. *Psychological Review*, *104*(4), 801–838.

den Heijer, T., Geerlings, M. I., Hofman, A., de Jong, F. H., Launer, L. J., Pols, H. A. P., & Breteler, M. M. B. (2003). Higher estrogen levels are not associated with larger hippocampi and better memory performance. *Archives of Neurology, 60*(2), 213–220.

Dietrich, T., Krings, T., Neulen, J., Willmes, K., Erberich, S., Thron, A., & Sturm, W. (2001): Effects of blood estrogen level on cortical activation patterns during cognitive activation as measured by functional MRI. *NeuroImage, 13*, 425–432.

Dowrick, A., & Southern, A. (2014). Dementia 2014: Opportunity for change. *Alzheimer's society*. Retrieved from https://www.alzheimers.org.uk/site/scripts/download_info.php?fileID=2317

Drake, E. B., Henderson, V. W., Stanczyk, F. Z., McCleary, C. A., Brown, W. S., Smith, C. A., Rizzo, A. A., Murdock, G. A., & Buckwalter, J. G. (2000). Associations between circulating sex steroid hormones and cognition in normal elderly women. *Neurology, 54*(3), 599–603.

Druks, J., & Shallice, T. (2000). Selective preservation of naming from description and the "restricted preverbal message". *Brain and Language, 72*, 100–128.

Dumas, J. A., Kutz, A. M., Naylor, M. R., Johnson, J. V., & Paul, A. N. (2010). Increased memory load-related frontal activation after estradiol treatment in postmenopausal women. *Hormones and Behavior*, *58*(5), 929–935.

Dunkin, J., Rasgon, N., Wagner-Steh, K., David, S., Altshuler, L., & Rapkin, A. (2005). Reproductive events modify the effects of estrogen replacement therapy on cognition in healthy postmenopausal women. *Psychoneuroendocrinology*, *30*(3), 284–296.

Edmonds, D. K. (2012). Puberty and its disorders. In Edmonds, D. K. (Ed.), *Dewhurst's Textbook of Obstetrics and Gynaecology* (8th Edition), Wiley-Blackwell, UK.

Elkadi, S., Clark, M. S., Dennerstein, L., Guthrie, J. R., Bowden, S. C., & Henderson, V. W. (2006). Normative data for Australian midlife women on category fluency and a short form of the Boston naming test. *Australian Psychologist, 41*(1), 37-42.

Ellis, A.W., & Morrison, C. M. (1998). Real age-of-acquisition effects in lexical retrieval. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 24*(2), 515–523.

Elsabagh, S., Hartley, D. E., & File, S. E. (2007). Cognitive function in late versus early postmenopausal stage. *Maturitas*, *56*(1), 84–93.

Erlanger, D. M., Kutner, K. C., & Jacobs, A. R. (1999). Hormones and cognition: Current concepts and issues in neuropsychology. *Neuropsychology Review, 9*(4), 175-207.

Farmer, A. (1990). Performance of normal males on the Boston naming test and the word test. *Aphasiology, 4*(3), 293–296.

Farrell, M. T., & Abrams, L. (2011). Tip-of-the-tongue states reveal age differences in the syllable frequency effect. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *37*(1), 277–285.

Farquhar, C. M., Sadler, L., Harvey, S. A., & Stewart, A. W. (2005). The association of hysterectomy and menopause: A prospective cohort study. *BJOG, 112*(7), 956–962.

Fernaeus, S. E., & Almkvist, O. (1998). Word production: Dissociation of two retrieval modes of semantic memory across time. *Journal of Clinical and Experimental Neuropsychology, 20*(2), 137–143.

Fernaeus, S.-E., Ostberg, P., Hellström, A., & Wahlund, L.-O. (2008). Cut the coda: Early fluency intervals predict diagnoses. *Cortex*, *44*(2), 161–169.

Feyereisen, P. (1997). A meta-analytic procedure shows an age-related decline in picture naming: Comments on Goulet, Ska, and Kahn. *Journal of Speech, Language, and Hearing Research*, *40*, 1328–1333.

Fitzpatrick S., Gilbert S. J., & Serpell L. (2013). Systematic review: Are overweight and obese individuals impaired on behavioural tasks of executive functioning? Neuropsychology Rev*iew, 23*(2), 138–156.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatry Research, 12*, 189–198.

Forbes-McKay, K. E., Ellis, A. W., Shanks, M. F., & Venneri, A. (2005). The age of acquisition of words produced in a semantic fluency task can reliably differentiate normal from pathological age related cognitive decline. *Neuropsychologia*, *43*(11), 1625–1632.

Ford, C. E., Jones, K. W., Polini, P. E., de Almeida, J. C., & Briggs, J. H. (1959). A sex chromosomal anomaly in a case of gonadal dysgenesis (Turner's syndrome). *Lancet, 1*(7075), 711–713.

Forster, K. I., & Forster, J. C. (2003). DMDX: A windows display program with millisecond accuracy. *Behavior Research Methods, Instruments, & Computers*, *35*(1), 116–124.

Foster, P. S., Drago, V., FitzGerald, D. B., Skoblar, B. M., Crucian, G. P., & Heilman, K. M. (2008). Spreading activation of lexical–semantic networks in Parkinson's disease. *Neuropsychologia*, *46*(7), 1908–1914.

Foubert-Samier, A., Catheline, G., Amieva, H., Dilharreguy, B., Helmer, C., Allard, M., Dartigues, J.-F. (2013). Education, occupation, leisure activities, and brain reserve: A population-based study. *Neurobiology of Aging, 33*(423), e15–e25.

Fox, M., Berzuini, C., & Knapp, L. A. (2013). Cumulative estrogen exposure, number of menstrual cycles, and Alzheimer's risk in a cohort of British women. *Psychoneuroendocrinology*, *38*(12), 2973–2982.

Fozard, J. L., & Gordon-Salant, S. (2001). Changes in vision and hearing with aging. In J. E. Birren & K.W. Schaie (Eds.), *Handbook of the psychology of aging*, (pp. 241–266). San Diego, CA: Academic Press.

Fu, C. H. Y., Morgan, K., Suckling, J., Williams, S. C. R., Andrew, C., Vythelingum, G. N., & McGuire, P. K. (2002). A functional magnetic resonance imaging study of overt letter verbal fluency using a clustered acquisition sequence: Greater anterior cingulate activation with increased task demand. *NeuroImage*, *17*(2), 871–879.

Fuh, J.-L.,Wang, S.-J., Lee, S.-J., Lu, S.-R., & Juang, K.-D. (2003) Alterations in cognitive function during the menopausal transition. *Journal of the American Geriatrics Society, 51*, 431–432.

Fuh, J.-L., Wang, S.-J., Lee, S.-J., Lu, S.-R., & Juang, K.-D. (2006). A longitudinal study of cognition change during early menopausal transition in a rural community. *Maturitas*, *53*(4), 447–453.

Geerlings, M. I., Ruitenberg, A.,Witteman, J. C. M., van Swieten, J. C., Hofman, A., van Duijn, C. M., … Launer, L. J. (2001). Reproductive period and risk of dementia in postmenopausal women. *The Journal of the American Medical Association, 285*(11), 1475–1481.

Gerhand, S., & Barry, C. (1999). Age-of-acquisition and frequency effects in speeded word naming. *Cognition*, *73*, B27–B36.

Gibbs, R. B. (2000). Effects of gonadal hormone replacement on measures of basal forebrain cholinergic function. *Neuroscience, 101*(4), 931– 938.

Gibbs, R. B. (2010). Estrogen therapy and cognition: A review of the cholinergic hypothesis. *Endocrine Reviews*, *31*(2), 224–253.

Gilhooly, K. J., & Logie, R. H. (1980). Age-of-acquisition, imagery, concreteness, familiarity, and ambiguity measures for 1,944 words. *Behavior Research Methods and Instrumentation, 12*, 395–427.

Gladsjo, J. A., Schuman, C. C., Evans, J. D., Peavy, G. M., Miller, S. W., & Heaton, R. K. (1999). Norms for letter and category fluency: Demographic corrections for age, education, and ethnicity. *Assessment*, *6*(2), 147–178.

Gold, E. B. (2011). The timing of the age at which natural menopause occurs. *Obstetrics and Gynecology Clinics of North America. 38*(3), 425–440.

Gold, E. B., Crawford, S. L., Avis, N. E., Crandall, C. J., Matthews, K. A., Waetjen, L. E., … Harlow, S. D. (2013). Factors related to age at natural menopause: Longitudinal analyses from SWAN. *American Journal of Epidemiology*, *178*(1), 865–874.

Gomez, R. G., & White, D. A. (2006). Using verbal fluency to detect very mild dementia of the Alzheimer type. *Archives of Clinical Neuropsychology*, *21*(8), 771–775.

Gong, Q.-Y., Sluming, V., Mayes, A., Keller, S., Barrick, T., Cezayirli, E., & Roberts, N. (2005). Voxel-based morphometry and stereology provide convergent evidence of the importance of medial prefrontal cortex for fluid intelligence in healthy adults. *NeuroImage*, *25*(4), 1175–1186.

Goral, M., Spiro, A., III, Albert, M. L., Obler, L. K., & Connor, L. T. (2007). Change in lexical retrieval skills in adulthood. *The Mental Lexicon*, *2*(2), 215–238.

Gordon, J. K., & Kurczek, J. C. (2014). The aging neighbourhood: Phonological density in naming. *Language, Cognition and Neuroscience*, *29*(3), 326–344.

Gordon, J. K., & Kindred, N. K. (2011). Word retrieval in ageing: An exploration of the task constraint hypothesis. *Aphasiology*, *25*(6-7), 774–788.

Gordon, H. W., & Lee, P. A. (1993). No difference in cognitive performance between phases of the menstrual cycle. *Psychoneuroendocrinology*, *18*(7), 521–531.

Goulet, P., Ska, B., & Kahn, H. J. (1994). Is there a decline in picture naming with advancing age? *Journal of Speech and Hearing Research, 37*, 629–644.

Gourovitch, M. L., Kirkby, B. S., Goldberg, T. E., Daniel, R., Gold, J. M., Esposito, G., Van Horn, J. D., & Berman, K. F. (2000). A comparison of rCBF patterns during letter and semantic fluency. *Neuropsychology, 14*, 353–360.

Grady, D., Yaffe, K., Kristof, M., Lin, F., Richards, C., & Barrett-Connor, E. (2002). Effect of postmenopausal hormone therapy on cognitive function: The heart and estrogen/progestin replacement study. *The American Journal of Medicine, 113*(7), 543–548.

Graesser, A., II, & Mandler, G. (1978). Limited processing capacity constrains the storage of unrelated sets of words and retrieval from natural categories. *Journal of Experimental Psychology: Human Learning and Memory*, *4*(1), 86–100.

Gruenwald, P. J., & Lockhead, G. R. (1980). The free recall of category examples. *Journal of Experimental Psychology: Human Learning and Memory*, 6, 225–240.

Gurd, J. M. (1995) Frontal dissociations: Evidence from Parkinson’s disease. *Journal of Neurolinguistics, 9*(1), 55–68.

Gurd, J. M., Amunts, K., Weiss, P. H., Zafiris, O., Zilles, K., Marshall, J. C., & Fink, G. R. (2002). Posterior parietal cortex is implicated in continuous switching between verbal fluency tasks: An fMRI study with clinical implications. *Brain*, *125*(5), 1024–1038.

Gurd, J. M., & Cowell, P. E. (2015). Discordant cerebral lateralisation for verbal fluency is not an artefact of attention: Evidence from MzHd twins. *Brain Structure & Function, 220*, 59-69.

Gurd, J. M., Weiss, P. H., Amunts, K., & Fink, G. R. (2003). Within-task switching in the verbal domain. *NeuroImage, 20*(1), S50–S57.

Guyton, A. C., & Hall, J. E. (2011). *Textbook of medical physiology*. Philadelphia, PA: Saunders.

Halari, R., Hines, M., Kumari, V., Mehrotra, R., Wheeler, M., Ng, V., & Sharma, T. (2005). Sex differences and individual differences in cognitive performance and their relationship to endogenous gonadal hormones and gonadotropins. *Behavioral Neuroscience*, *119*(1), 104–117.

Hall, J. R., Vo, H. T., Johnson, L. A., Wiechmann, A., & Bryant, S. E. O. (2012). Boston naming test: Gender differences in older adults with and without Alzheimer's dementia. *Psychology*, *3*(6), 485–488.

Halpern, D. F. (1992). Sex differences in cognitive abilities. Hillsdale, NJ: Erlbaum.

Hamberger, M. J., Goodman, R. R., Perrine, K., & Tamny, T. (2001). Anatomic dissociation of auditory and visual naming in the lateral temporal cortex. *Neurology, 56*(1), 56–61.

Hamberger, M. J., & Seidel, W. T. (2003). Auditory and visual naming tests: Normative and patient data for accuracy, response time, and tip-of-the-tongue. *Journal of the International Neuropsychological Society*, *9*(3), 479–489.

Hamberger, M. J., Seidel, W. T., Goodman, R. R., Perrine, K., & McKhann, G. M. (2003). Temporal lobe stimulation reveals anatomic distinction between auditory naming processes. *Neurology, 60*(9), 1478–1483.

Hamberger, M. J., & Tamny, T. R. (1999). Auditory naming and temporal lobe epilepsy, *Epilepsy Research*, *35*, 229–243.

Hampson, E. (1990a). Estrogen-related variations in human spatial and articulatory-motor skills. *Psychoneuroendocrinology*, *15*(2), 97–111.

Hampson, E. (1990b). Variations in sex-related cognitive abilities across the menstrual cycle. *Brain and Cognition, 14*, 26-43.

Hampson, E., & Kimura, D. (1988). Reciprocal effects of hormonal fluctuations on human motor and perceptual-spatial skills. *Behavioral Neuroscience*, *102*(3), 456–459.

Hampson, E., & Rovet, J. F. (2015). Spatial function in adolescents and young adults with congenital adrenal hyperplasia: Clinical phenotype and implications for the androgen hypothesis. *Psychoneuroendocrinology*, *54*, 60–70.

Hampson, E., Rovet, J. F., & Altmann, D. (1998). Spatial reasoning in children with congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *Developmental Neuropsychology*, *14*(2-3), 299-320.

Hao, J., Rapp., P. R., Leffler, A. E., Leffler, S. R., Janssen, W. G. M., Lou, W., … Morrison, J. H. (2006). Estrogen alters spine number and morphology in prefrontal cortex of aged female rhesus monkeys. *The Journal of Neuroscience*, *26*(9), 2571–2578.

Harley, T. A., & Bown, H. E. (1998). What causes a tip-of-the-tongue state ? Evidence for lexical neighbourhood effects in speech production. *British Journal of Psychology, 89,* 151–174.

Harlow, S. D., Gass, M., Hall, J. E., Lobo, R., Maki, P., Rebar, R. W., … de Villiers, T. J. (2012). Executive summary of the stages of reproductive aging workshop + 10: Addressing the unfinished agenda of staging reproductive aging. *Fertility and Sterility*, *97*(4), 843–851.

Hatch, S. L., Feinstein, L., Link, B. G., Wadsworth, M. E. J., & Richards, M. (2007). The continuing benefits of education: Adult education and midlife cognitive ability in the British 1946 birth cohort. *Journal of Gerentology: Social Sciences, 62B*(6), S404- S414.

Haugrud, N., Crossley, M., & Vrbancic, M. (2011). Clustering and switching strategies during verbal fluency performance differentiate Alzheimer's disease and healthy aging. *Journal of the International Neuropsychological Society*, *17*(6), 1153–1157.

Hawkins, K. A., Sledge, W. H., Orleans, J. F., Quinlan, D. M., Rakfeldt, J., & Huffman, R. E. (1993). Normative implications of the relationship between reading vocabulary and Boston naming test performance. *Archives of Clinical Neuropsychology*, *8*(6), 525–537.

Heck, K. E., Schoendorf, K. C., Ventura, S. J., & Kiely, J. L. (1997). Delayed childbearing by education level in the United States, 1969-1994. *Maternal and Child Health Journal*, *1*(2), 81–88.

Henderson, L.W., Frank, E.W., Pigatt, T., Abramson, R. K., & Houston, M. (1998). Race, gender, and educational level effects on Boston naming test scores. *Aphasiology, 12*(10), 901–911.

Henderson, V. W., Guthrie, J. R., Dudley, E. C., Burger, H. G., & Dennerstein, L. (2003). Estrogen exposures and memory at midlife: A population-based study of women. *Neurology, 60*(8)*,* 1369–1371.

Henderson, V. W., John, J. A. St.., Hodis, H. N., McCleary, C. A., Stanczyk, F. Z., Karim, R., … Mack, W. J. (2013). Cognition, mood, and physiological concentrations of sex hormones in the early and late postmenopause. *Proceedings of the National Academy of Sciences*, *110*(50), 20290–20295.

Henderson, V. W., Paganini-Hill, A., Emanuel, C. K., Dunn, M. E., & Buckwalter, J. G. (1994). Estrogen replacement therapy in older women: Comparisons between Alzheimer's disease cases and nondemented control subjects. *Archives of Neurology, 51*(9), 896–900.

Henderson, V. W., Paganini-Hill, A., Miller, B. L., Elble, R. J., Reyes, P. F., Shoupe D., … Farlow, M. R. (2000). Estrogen for Alzheimer's disease in women: Randomized, double-blind, placebo-controlled trial. *Neurology 54*(2), 295-301.

Henderson, V. W., & Popat, R. A. (2011). Effects of endogenous and exogenous estrogen exposures in midlife and late-life women on episodic memory and executive functions. *Neuroscience*, *191*, 129–138.

Henry, J. D., & Crawford, J. R. (2004). A meta-analytic review of verbal fluency performance following focal cortical lesions. *Neuropsychology*, *18*(2), 284–295.

Herlitz, A., Thilers, P., & Habib, R. (2007). Endogenous estrogen is not associated with cognitive performance before, during, or after menopause. *Menopause, 14*, 425–431.

Hernández-muñoz, N., Izura, C., & Ellis, A. W. (2006). Cognitive aspects of lexical availability. *European Journal of Cognitive Psychology, 18*(5), 730-755.

Hesson, J. (2012). Cumulative estrogen exposure and prospective memory in older women. *Brain and Cognition*, *80*(1), 89–95.

Hines, M. (2003). Sex steroids and human behavior: Prenatal androgen exposure and sex-typical play behavior in children. *Annals of the New York Academy of Sciences, 1007*, 272-282.

Hirshorn, E. A., & Thompson-Schill, S. L. (2006). Role of the left inferior frontal gyrus in covert word retrieval : Neural correlates of switching during verbal fluency, *44*, 2547–2557.

Ho, A. J., Raji, C. A., Becker, J. T., Lopez, O. L., Kuller, L. H., Hua, X., … Thompson, P. M. (2011). The effects of physical activity, education, and body mass index on the aging brain. *Human Brain Mapping*, *32*(9), 1371–82.

Hogervorst, E. (2013). Effects of gonadal hormones on cognitive behaviour in elderly men and women. *Journal of Neuroendocrinology*, *25*, 1182-1195.

Horn, J. L., & Cattell, R. B. (1967). Age differences in fluid and crystallized intelligence. *Acta Psychologica, 26*(2), 107-129.

Hyde, J. S. (2014). Gender similarities and differences. *Annual Review of Psychology*, *65*(1), 373–398.

Hyde, J. S., & Linn, M. C. (1988). Gender differences in verbal ability: A meta-analysis. *Psychological Bulletin, 104*, 53–69.

Impey, L. & Child, T. (Ed.) (2012). *Obstetrics and gynaecology*. Chichester: Wiley-Blackwell.

Indefrey, P. (2011). The spatial and temporal signatures of word production components: A critical update. *Frontiers in Psychology*, *2*(Article 255).

Indefrey, P., & Levelt, W. J. M. (2000). The neural correlates of language production. In M. S. Gazzaniga (Eds.), *The new cognitive neurosciences* (pp. 845–865). Cambridge, MA: MIT Press.

Indefrey, P., & Levelt, W. J. M. (2004). The spatial and temporal signatures of word production components. *Cognition*, *92*(1-2), 101–144.

Ivnik, R. J., Malec, J. F., Smith, G. E., Tangalos, E. G., & Petersen, R. C. (1996). Neuropsychological tests' norms above age 55: COWAT, BNT, MAE Token, WRAT-R, Reading, AMNART, Stroop, TMT, and JLO. *The Clinical Neuropsychologist, 10*, 262–278.

Jacobs, D. M., Tang, M. X, Stern, Y., Sano, M., Marder, K., Bell, K. L., … Mayeux, R. (1998). Cognitive function in nondemented older women who took estrogen after menopause. *Neurology, 50*(2), 368–373.

Jernigan, T. L., Archibal, S. L., Fennema-Notestine, C., Garnst, A. C., Stout, J. C., Bonner, J., & Hesselink, J. R. (2001). Effects of age on tissues and regions of the cerebrum and cerebellum. *Neurobiology of Aging, 22*(4), 581-594.

Jescheniak, J. D., & Levelt, W. J. M. (1994). Word frequency effects in speech production: Retrieval of syntactic information and of phonological form. *Journal of Experimental Psychology: Language, Memory, and Cognition, 20*(4), 824–843.

Joffe, H., Hall, J. E., Gruber, S., Sarmiento, I. A., Cohen, L. S., Yurgelun-Todd, D., & Martin, K. A. (2006). Estrogen therapy selectively enhances prefrontal cognitive processes: A randomized, double-blind, placebo-controlled study with functional magnetic resonance imaging in perimenopausal and recently postmenopausal women. *Menopause, 13*(3), 411-422.

Kaplan, E., Goodglass, H., & Weintraub, S. (1983). The Boston naming test. Philadelphia: Lea & Febiger.

Katzman, R. (1993). Education and the prevalence of dementia and Alzheimer's disease. *Neurology, 43*, 13–20.

Kavé, G., & Halamish, V. (2015). Doubly blessed: Older adults know more vocabulary and know better what they know. *Psychology and Aging, 30*(1), 68–73.

Kavé, G., Knafo, A., & Gilboa, A. (2010). The rise and fall of word retrieval across the lifespan. *Psychology and Ageing, 25,* 719–724.

Kave, G., & Yafe, R. (2014). Performance of younger and older adults on tests of word knowledge and word retrieval: Independence or interdependence of skills? *American Journal of Speech-Language Pathology, 23*, 36-45.

Kawas, C., Resnick, S., Morrison, A., Brookmeyer, R., Corrada, M., Zonderman, A., … Metter, E. (1997). A prospective study of estrogen replacement therapy and the risk of developing Alzheimer's disease: The Baltimore longitudinal study of aging. *Neurology, 48*(6), 1517–1521.

Keenan, P. A., Ezzat, W. H., Ginsburg, K., & Moore, G. J. (2001). Prefrontal cortex as the site of estrogen's effect on cognition. *Psychoneuroendocrinology*, *26*(6), 577–590.

Kemper, S., & McDowd, J. (2008). Dimensions of cognitive aging: Executive function and verbal fluency. In S. Hofer & D. Alwin (Eds.), *Handbook of cognitive aging: Interdisciplinary perspectives.* (pp. 181-193). Thousand Oaks, CA: SAGE Publications, Inc.

Kemper, S., & Sumner, A. (2001). The structure of verbal abilities in young and older adults. *Psychology and Ageing, 16*(2), 312–322.

Kempler, D., Teng, E. L., Dick, M., Taussig, I. M., & Davis, D. S. (1998). The effects of age, education, and ethnicity on verbal fluency. *Journal of the International Neuropsychological Society, 4*, 531–538.

Khwaileh, T., Body, R., & Herbert, R. (2014). A normative database and determinants of lexical retrieval for 186 Arabic nouns: Effects of psycholinguistic and morpho-syntactic variables on naming latency. *Journal of Psycholinguistic Research, 43*(6), 749-769.

Kimura, D. (1999). Sex and cognition. London: MIT Press.

Kimura, D., & Hampson, E. (1994). Cognitive pattern in men and women is influenced by fluctuations in sex hormones. *Psychological Science, 3*, 57-61.

Kircher, T., Nagels, A., Kirner-veselinovic, A., & Krach, S. (2011). Neural correlates of rhyming vs. lexical and semantic fluency. *Brain Research*, *1391*, 71–80.

Knight, R. G., McMahon, J., Green, T. J., & Skeaff, C. M. (2006). Regression equations for predicting scores of persons over 65 on the Rey auditory verbal learning test, the mini-mental state examination, the trail making test and semantic fluency measures. *The British Journal of Clinical Psychology, 45*, 393–402.

Kocoska-Maras, L., Zethraeus, N., Rådestad, A. F., Ellingsen, T., von Schoultz, B., Johannesson, M., & Hirschberg, A. L. (2011). A randomized trial of the effect of testosterone and estrogen on verbal fluency, verbal memory, and spatial ability in healthy postmenopausal women. *Fertility and Sterility*, *95*(1), 152–157.

Kok, H. S., Kuh, D., Cooper, R., van der Schouw, Y. T., Grobbee, D. E., Wadsworth, M. E., & Richards, M. (2006). Cognitive function across the life course and the menopausal transition in a British birth cohort. *Menopause, 13*, 19–27.

Kritz-Silverstein, D., & Barrett-Connor, E. (2002). Hysterectomy, oophorectomy, and cognitive function in older women. *Journal of American Geriatric Society, 50*, 55–61.

Kugaya, A., Epperson, C. N., Zoghbi, S., van Dyck, C. H., Hou, Y., Fujita, M., … Innis, R. B. (2003). Increase in prefrontal cortex serotonin 2A receptors following estrogen treatment in postmenopausal women. *The American Journal of Psychiatry*, *160*(8), 1522–1524.

LaBarge, E., Edwards, D., & Knesevich, J., W. (1986). Performance of normal elderly on the Boston naming test. *Brain and Language, 27*(2), 380–384.

Lacreuse, A., Wilson, M. E., & Herndon, J. G. (2002). Estradiol, but not raloxifene, improves aspects of spatial working memory in aged ovariectomized rhesus monkeys. *Neurobiology of Aging*, *23*(4), 589–600.

Lansing, A. E., Ivnik, R. J., Cullum, C. M., & Randolph, C. (1999). An empirically derived short form of the Boston naming test. *Archives of Clinical Neuropsychology, 14*(6), 481–487.

Lanting, S., Haugrud, N., & Crossley, M. (2009). The effect of age and sex on clustering and switching during speeded verbal fluency tasks. *Journal of the International Neuropsychological Society*, *15*(2), 196–204.

Laughlin, G. A., Kritz-Silverstein, D., & Barrett-Connor, E. (2010). Endogenous oestrogens predict 4-year decline in verbal fluency in postmenopausal women: The Rancho Bernardo study. *Clinical Endocrinology, 72*(1), 99–106.

Lebrun, C. E. I., van der Schouw, Y. T., de Jong, F. H., Pols, H. A. P., Grobbee, D. E., & Lamberts, S. W. J. (2005). Endogenous oestrogens are related to cognition in healthy elderly women. *Clinical Endocrinology*, *63*(1), 50–55.

Ledger, W. L. (2012). Ovarian and menstrual cycles. In D. K. Edmonds (Eds.), *Dewhurst's textbook of obstetrics and gynaecology* (pp. 487–494). West Sussex, UK: John Wiley and Sons, Ltd.

Lethaby, A., Hogervorst, E., Richards, M., Yesufu, A., & Yaffe, K. (2008). Hormone replacement therapy for cognitive function in postmenopausal women. *Cochrane Database of Systematic Reviews, 1*(Article CD003122).

Levelt, W. J., Roelofs, A., & Meyer, A. S. (1999). A theory of lexical access in speech production. *Behavioral and Brain Sciences*, *22*(1), 1–75.

Levelt, W. J. M., Schriefers, H., Vorberg, D., Meyer, A. S., Pechmann, T. & Havinga, J. (1991). The time course of lexical access in speech production : A study of picture naming, *98*(1), 122–142.

Lezak, M. D., Howieson, D., & Loring, D. W. (Ed.) (2004). *Neuropsychological assessment*. USA: Oxford University Press.

Lokken, K. L., & Ferraro, F. R. (2006). The relationship between menopausal status, phase of menstrual cycle, and replacement estrogen on cognition in healthy women without dementia. *The Journal of Psychology*, *140*(6), 533–547.

Loring, D. W., Meador, K. J., & Lee, G. P. (1994). Effects of temporal lobectomy on generative fluency and other language functions. *Archives of Clinical Neuropsychology, 9*(3), 229–238.

Linn, M. C., & Petersen, A. C. (1985). Emergence and characterization of sex differences in spatial ability: A meta-analysis. *Child Development*, *56*(6), 1479–1498.

Liu, Y., Julkunen, V., Paajanen, T., Westman, E., Wahlund, L.-O., Aitken, A., … Soininen, H. (2012). Education increases reserve against Alzheimer's disease-evidence from structural MRI analysis. *Neuroradiology, 54*(9), 929-938.

Lucas, J. A., Ivnik, R. J., Smith, G. E., Ferman, T. J., Willis, F. B., Petersen, R. C., & Graff-Radford, N. R. (2005). Mayo's older African Americans normative studies: Norms for the Boston naming test, controlled oral word association, category fluency, animal naming, token test, WRAT-3 reading, trail making test, stroop test, and judgement of line orientation. *The Clinical Neuropsychologist, 19*(2), 243–269.

Luetters, C., Huang, M. H., Seeman, T., Buckwalter, G., Meyer, P. M., Avis, N. E., …Greendale, G.A. (2007). Menopause transition stage and endogenous estradiol and follicle- stimulating hormone levels are not related to cognitive performance: Cross-sectional results from the study of women's health across the nation (SWAN). *Journal of Womens Health, 16*, 331–344.

Luine, V. N. (1985). Estradiol increases choline acetyltransferase activity in specific basal forebrain nuclei and projection areas of female rats. *Experimental Neurology, 89*(2), 484–490.

Luoto, R., Kaprio, J., & Uutela, A. (1994). Age at natural menopause and sociodemographic status in Finland. *American Journal of Epidemiology*, *139*(1), 64–76.

Maccoby, E. E., & Jacklin, C. N. (1974). *The psychology of sex differences*. Stanford, CA: Stanford University Press.

MacKay, D. G. (1987). *The organization of perception and action: A theory for language and other cognitive skills.* New York: Springer-Verlag.

MacKay, A. J., Connor, L. T., Albert, M. L., & Obler, L. K. (2002). Noun and verb retrieval in healthy aging. *Journal of the International Neuropsychological Society*, *8*(6), 764–770.

MacKay, A., Connor, L. T., & Storandt, M. (2005). Dementia does not explain correlation between age and scores on Boston naming test. *Archives of Clinical Neuropsychology, 20*(1), 129–133.

Marjoribanks, J., Farquhar, C., Roberts, H., & Lethaby, A. (2012). Long term hormone therapy for perimenopausal and postmenopausal women (Review). *Cochrane database of Systematic Reviews*, *7*(Article CD004143).

Maki, P. M. (2006). Hormone therapy and cognitive function: Is there a critical period for benefit? *Neuroscience*, *138*(3), 1027–1030.

Maki, P. M., Gast, M. J., Vieweg, A., Burriss, S. W., & Yaffe, K. (2007). Hormone therapy in menopausal women with cognitive complaints: A randomized, double-blind trial. *Neurology, 69*(13), 1322–1330.

Maki, P. M., & Resnick, S. M. (2000). Longitudinal effects of estrogen replacement therapy on PET cerebral blood flow and cognition. *Neurobiology of Aging*, *21*(2), 373–383.

Maki, P. M., & Resnick, S. M. (2001). Effects of estrogen on patterns of brain activity at rest and during cognitive activity: A review of neuroimaging studies. *NeuroImage*, *14*(4), 789–801.

Maki, P. M., Rich, J. B., & Rosenbaum, R. S. (2002). Implicit memory varies across the menstrual cycle: Estrogen effects in young women. *Neuropsychologia*, *40*(5), 518–529.

Maki, P. M., & Sundermann, E. (2009). Hormone therapy and cognitive function. *Human Reproduction Update*, *15*(6), 667–681.

Martin, R. C., Loring, D. W., Meador, K. J., & Lee, G. P. (1990). The effects of lateralized temporal lobe dysfunction on formal and semantic word fluency. *Neuropsychologia, 28*(8), 823–829.

Martin, A., Wiggs, C. L., Lalonde, F., & Mack, C. (1994). Word retrieval to letter and semantic cues: A double dissociation in normal subjects using interference tasks. *Neuropsychologia, 32*(12), 1487–1494.

McKinlay, S. M., Brambilla, D. J., & Posner, J. G. (2008). "Reprint of" The normal menopause transition. *Maturitas*, *61*(1-2), 4–16.

Matthews, K., Cauley, J., Yaffe, K., & Zmuda, J. M. (1999). Estrogen replacement therapy and cognitive decline in older community women. *Journal of the American Geriatrics Society, 47*(5), 518-523.

Mayr, U., & Kliegl, R. (2000). Complex semantic processing in old age: does it stay or does it go? *Psychology and Aging*, *15*(1), 29–43.

McCarthy, T. (1994). The prevalence of symptoms in menopausal women in the far east: Singapore segment. *Maturitas, 19*(3), 199–204.

McEwen, B. S. (2002). Estrogen actions throughout the brain. *Recent Progress in Hormone Research, 57*, 357–384.

McKenna, P., & Warrington, E. K. (1980). Testing for nominal dysphasia. *Journal of Neurology, Neurosurgery, and Psychiatry*, *43*(9), 781–788.

McLay, R. N., Maki, P. M., & Lyketsos, C. G. (2003). Nulliparity and late menopause are associated with decreased cognitive decline. *Journal of Neuropsychiatry and Clinical Neurosciences, 15*(2), 161–167.

Meinzer, M., Flaisch, T., Wilser, L., Eulitz, C., Rockstroh, B., Conway, T., Gonzalez-Rothi, L., & Crosson, B. (2009). Neural signatures of semantic and phonemic fluency in young and old adults. *Journal of Cognitive Neuroscience*, *21*(10), 2007–2018.

Messas, C. S., Mansur, L. L., & Castro, L. H. M. (2008). Semantic memory impairment in temporal lobe epilepsy associated with hippocampal sclerosis. *Epilepsy & Behavior*, *12*(2), 311–316.

Miceli, G., Caltagirone, C., Gainotti, G., Masullo, C., & Silveri, M. C., (1981). Neuropsychological correlates of localized cerebral lesions in non-aphasic brain damaged patients. *Journal of Clinical Neuropsychology, 3*(1), 53–63.

Micevych, P., & Dominguez, R. (2009). Membrane estradiol signalling in the brain. *Frontiers in Neuroendocrinology, 30*, 315–327.

Mietta, L. (2011a). *SpeCT*- The speech corpus toolkit for Praat. Retrieved from http://www.helsinki.fi/~lennes/praat-scripts/public/mark_pauses.praat

Mietta, L. (2011b). *SpeCT*- The speech corpus toolkit for Praat. Retrieved from http://www.helsinki.fi/~lennes/praat-scripts/public/calculate_segment_durations.praat

Miller, D. I., & Halpern, D. F. (2014). The new science of cognitive sex differences. *Trends in Cognitive Sciences*, *18*(1), 37–45.

Monsch, A. U., Seifritz, E., Taylor, K. I., Ermini-Funfschilling, D., Stahelin, H. B., & Spiegel, R. (1997). Category fluency is also predominantly affected in Swiss Alzheimer’s disease patients. *Acta Neurologica Scandinavica, 95*, 81–84.

Morris, D. H., Jones, M. E., Schoemaker, M. J., Ashworth, A., & Swerdlow, A. J. (2011). Secular trends in age at menarche in women in the UK born 1908-93: Results from the breakthrough generations study. *Paediatric and Perinatal Epidemiology, 25,* 394-400.

Morrison, C. M., Ellis, A.W., & Quinlan, P. T. (1992). Age of acquisition, not word frequency, affects object naming, not object recognition. *Memory and Cognition, 20*(6), 705–714.

Mortensen, L., Meyer, A. S., & Humphreys, G. W. (2006). Age-related effects on speech production: A review. *Language and Cognitive Processes*, *21*(1-3), 238–290.

Mulnard, R. I., Cotman, C. W., Kawas, C., van Dyck, C. H., Sano, M., Doody, R., … for the Alzheimer's Disease Cooperative Study. (2000). Estrogen replacement therapy for treatment of mild to moderate Alzheimer's disease: A randomized controlled trial. *The Journal of the American Medical Association, 283*(8), 1007–1015.

Nagels, A., Kircher, T., Dietsche, B., Backes, H., Marquetand, J., & Krug, A. (2012). Neural processing of overt word generation in healthy individuals: The effect of age and word knowledge. *NeuroImage*, *61*, 832–840.

National Health Services (2015, November 12). Menopause. Retrieved from http://www.nhs.uk/Conditions/Menopause/Pages/Introduction.aspx

National Institute on Aging. (2011). *Global health and aging* (NIH Publication No. 11-7737.

Neill, E., Gurvich, C., & Rossell, S. L. (2014). Category fluency in schizophrenia research: Is it an executive or semantic measure? *Cognitive Neuropsychiatry*, *19*(1), 81–95.

Neils, J., Baris, J. M., Carter, C., Dell'aira, A. L., Nordloh, S. J., Weiler, E., & Weisiger, B. (1995). Effects of age, education and living environment on Boston naming performance. *Journal of Speech and Hearing Research, 38*(5), 1143–1149.

Newcombe, F. (1969). *Missile wounds of the brain: A study of psychological deficits.* London: Oxford University Press.

Nicholas, L. E., Brookshire, R. H., MacLennan, D. L., Schumacher, J. G., & Porrazzo, S. A. (1989). Revised administration and scoring procedures for the Boston naming test and norms for non-brain-damaged adults. *Aphasiology, 3*(6), 569–580.

Nickels, L., & Howard, D. (1995). Aphasic naming: What matters? *Neuropsychologia, 33*(10), 1281–1303.

Norman, R. J., Dewailly, D., Legro, R. S., & Hickey, T. E. (2007). Polycystic ovary syndrome. *Lancet, 370*(9588), 685-697.

Oats, J., Abraham, S., & Llewellyn-Jones, D. (2010). *Fundamentals of Obstetrics and Gynaecology*. Elsevier Limited, UK.

Obler, L. K., & Albert, M. L. (1979). The Action naming test (experimental edition). Boston: VA Medical Centre.

Obler, L. K., Rykhlevskaia, E., Schnyer, D., Clark-Cotton, M. R., Spiro, A., III, Hyun, J., … Albert, M. L. (2010). Bilateral brain regions associated with naming in older adults. *Brain and Language*, *113*(3), 113–123.

Office for National Statistics. (2014, March 7). Highest levels of qualification across England and Wales infographic. Retrieved from http://www.ons.gov.uk/ons/rel/census/2011-census-analysis/local-area-analysis-of-qualifications-across-england-and-wales/info-highest-qualifications.html

Office for National Statistics. (2014, December 4). Childbearing for women born in different years, England and Wales, 2013. Retrieved from http://www.ons.gov.uk/ons/rel/fertility-analysis/childbearing-for-women-born-in-different-years/2013/stb-cohort-fertility-2013.html

Office for National Statistics. (2015, June 25). Annual mid-year population estimates, 2014. Retrieved from http://www.ons.gov.uk/ons/rel/pop-estimate/population-estimates-for-uk--england-and-wales--scotland-and-northern-ireland/mid-2014/stb---mid-2014-uk-population-estimates.html

Office for National Statistics. (2015, November 4). Life expectancy at birth and at age 65 by local areas in England and Wales, 2012 to 2014. Retrieved from http://www.ons.gov.uk/ons/rel/subnational-health4/life-expectancy-at-birth-and-at-age-65-by-local-areas-in-england-and-wales/2012-14/stb-life-2012-14.html

Office for National Statistics. (2015, November 9). Deaths registered in England and Wales (Series DR), 2014. Retrieved from http://www.ons.gov.uk/ons/rel/vsob1/mortality-statistics--deaths-registered-in-england-and-wales--series-dr-/2014/stb-mortality-stats-2014.html

Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia, 9,* 97–113.

Oldfield, R. C., & Wingfield, A. (1965). Response latencies in naming objects. *Quarterly Journal of Experimental Psychology, 17*, 273–281.

Opdebeeck, C., Nelis, S. M., Quinn, C., & Clare, L. (2015). How does cognitive reserve impact on the relationships between mood, rumination, and cognitive function in later life? *Aging & Mental Health*, *19*(8), 705–712.

Paganini-Hill, A., & Henderson, V. W. (1994). Estrogen deficiency and risk of Alzheimer's disease in women. *American Journal of Epidemiology, 140*(3)*,* 256–261.

Parent, A-S., Teilmann, G., Juul, A., Skakkebaek, N. E., Toppari, J., & Bourguignon, J-P. (2003). The timing of normal puberty and the age limits of sexual precocity: Variations around the world, secular trends, and changes after migration. *Endocrine Reviews, 24*(5), 668–693.

Parikh, P. K., Troyer, A. K., Maione, A. M., & Murphy, K. J. (2015). The impact of memory change on daily life in normal aging and mild cognitive impairment. *The Gerontologist*, *00*(00), 1–10.

Park, E., Bailey, J. D., & Cowell, C. A. (1983). Growth and maturation of patients with Turner's syndrome. *Pediatric Research, 17*, 1–7.

Parkin, A. J., & Java, R. I. (1999). Deterioration of frontal lobe function in normal aging: Influences of fluid intelligence versus perceptual speed. *Neuropsychology*, *13*(4), 539–545.

Pavio, A., Yuille, J. C., & Madigan, S. A. (1968*).* Concreteness, imagery and meaningfulness values for 925 words*. Journal of Experimental Psychology Monograph Supplement, 76*(1), 1-25.

Pefanco, M. A., Kenny, A. M., Kaplan, R. F., Kuchel, G., Walsh, S., Kleppinger, A., & Prestwood, K. (2007). The effect of 3-year treatment with 0.25 mg/day of micronized 17β-estradiol on cognitive function in older postmenopausal women. *Journal of the American Geriatrics Society, 55*(3), 426–431.

Peña-Casanova, J., Quiñones-Ubeda, S., Gramunt-Fombuena, N., Aguilar, M., Casas, L., Molinuevo, J. L., … Blesa, R. (2009a). Spanish multicenter normative studies (NEURONORMA Project): Norms for Boston naming test and token test. *Archives of Clinical Neuropsychology*, *24*(4), 343–354.

Peña-Casanova, J., Quiñones-Úbeda, S., Gramunt-Fombuena, N., Quintana-Aparicio, M., Aguilar, M., Badenes, D., … Blesa, R. (2009b). Spanish multicenter normative studies (NEURONORMA Project): Norms for verbal fluency tests. Archives of Clinical Neuropsychology, *24*(4), 395–411.

Perret, E. (1974). The left frontal lobe of man and the suppression of habitual responses in verbal categorical behaviour. *Neuropsychologia, 12*, 323-330.

Phillips, S. M., & Sherwin, B. B. (1992). Effects of estrogen on memory function in surgically menopausal women. *Psychoneuroendocrinology, 17*(5), 485–495.

Piras, F., Cherubini, A., Caltagirone, C., & Spalletta, G. (2011). Education mediates microstructural changes in bilateral hippocampus. *Human Brain Mapping, 32*, 282–289.

Ptok, U., Barkow, K., & Heun, R. (2002). Fertility and number of children in patients with Alzheimer's disease. *Archives of Women's Mental Health*, *5*(2), 83–86.

Randolph, C., Lansing, A., Ivnik, R. J., Cullum, C. M., & Hermann, B. P. (1999). Determinants of confrontation naming performance. *Archives of Clinical Neuropsychology, 14*(6), 489–496.

Rapoport, M., van Reekum, R., & Mayberg, H. (2000). The role of the cerebellum in cognition and behaviour. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *12*(2), 193–198.

Rapp, P. R., Morrison, J. H., & Roberts, J. A. (2003). Cyclic estrogen replacement improves cognitive function in aged ovariectomized monkeys. *The Journal of Neuroscience, 22*(13), 5708–5714.

Raskin, S. A., Sliwinski, M., & Borod, J. C. (1992). Clustering strategies on tasks of verbal fluency in Parkinson's disease. *Neuropsychologia, 30*(1), 95–99.

Raz, N., Lindenberger, U., Rodrigue, K. M., Kennedy, K. M., Head, D., Williamson, A., … Acker, J. D. (2005). Regional brain changes in aging healthy adults: general trends, individual differences and modifiers. *Cerebral Cortex*, *15*(11), 1676–1689.

Raz, N., & Rodrigue, K. M. (2006). Differential aging of the brain: patterns, cognitive correlates and modifiers. *Neuroscience and Biobehavioral Reviews*, *30*(6), 730–48.

Reiman, E. M., Armstrong, S. M., Matt, K. S., & Mattox, J. H. (1996a). The application of positron emission tomography to the study of the normal menstrual cycle. *Human Reproduction, 11*(12), 2799–2805.

Reitan, R. M. (1958). Validity of the trail making test as an indicator of organic brain damage. *Perceptual and Motor Skills, 8,* 271–276.

Rende, B., Ramsberger, G., & Miyake, A. (2002). Commonalities and differences in the working memory components underlying letter and category fluency tasks: A dual-task investigation. *Neuropsychology*, *16*(3), 309–321.

Resnick, S. M., Berenbaum, S. A., Gottesman, I. I., & Bouchard, T. J. (1986). Early hormonal influences on cognitive functioning in congenital adrenal hyperplasia. *Developmental Psychology, 22*(2), 191-198.

Resnick, S. M., Espeland, M. A., Jaramillo, S. A., Hirsch, C., Stefanick, M. L., Murray, A. M., … for the WHIMS Study. (2009). Postmenopausal hormone therapy and regional brain volumes: The WHIMS-MRI study. *Neurology, 72*(2), 135–142.

Resnick, S. M., & Henderson, V. W. (2002). Hormone therapy and risk of Alzheimer disease: A critical time. *The Journal of the American Medical Association, 288*(17), 2170-2172.

Resnick, S. M., Maki, P. M., Golski, S., Kraut, M. A, & Zonderman, A. B. (1998). Effects of estrogen replacement therapy on PET cerebral blood flow and neuropsychological performance. *Hormones and Behavior*, *34*(2), 171–182.

Resnick, S. M., Maki, P. M., Rapp, S. R., Espeland, M. A., Brunner, R., Coker, L.H., … for the WHISCA Investigators. (2006). Effects of combination estrogen plus progestin hormone treatment on cognition and affect. *The Journal of Clinical Endocrinology and Metabolism, 91*(5), 1802– 1810.

Roberts, J. E., & Bell, M. A. (2002). The effects of age and sex on mental rotation performance, verbal performance, and brain electrical activity. *Developmental Psychobiology*, *40*(4), 391–407.

Rocca, W. A, Grossardt, B. R., Shuster, L. T., & Stewart, E. A. (2012). Hysterectomy, oophorectomy, estrogen, and the risk of dementia. *Neurodegenerative Diseases*, *10*(1-4), 175–178.

Rodriguez-Aranda, C., & Martinussen, M. (2006). Age-related differences in performance of phonemic verbal fluency measured by controlled oral word association task (COWAT): A meta-analytic study. *Developmental Neuropsychology, 30*(2), 697–717.

Roelofs, A. (2002). Syllable structure effects turn out to be word length effects: Comment on Santiago et al. (2000). *Language and Cognitive Processes, 17*(1), 1–13.

Ryan, J., Carrière, I., Scali, J., Ritchie, K., & Ancelin, M.-L. (2009). Life-time estrogen exposure and cognitive functioning in later life. *Psychoneuroendocrinology*, *34*(2), 287–298.

Ryan, J., Stanczyk, F. Z., Dennerstein, L., Mack, W. J., Clark, M. S., Szoeke, C., Kildea, D., & Henderson, V. W. (2012). Hormone levels and cognitive function in postmenopausal midlife women. *Neurobiology of Aging*, *33*(7), 1138–1147.

Ruff, R. M., Light, R. H., Parker, S. B., & Levin, H. S. (1996). Benton controlled oral word association test: Reliability and updated norms. *Archives of Clinical Neuropsychology, 11*(4), 329–338.

Salthouse, T. A. (1996). The processing-speed theory of adult age differences in cognition. *Psychological Review*, *103*(3), 403–428.

Salthouse, T. A. (2010). Selective review of cognitive aging. *Journal of the International Neuropsychological Society*, *16*(5), 754–60.

Samil, R. S., & Wishnuwardhani, S. D. (1994). Health of Indonesian women, city-dwellers of perimenopausal age. *Maturitas, 19*(3), 191–197.

Santiago, J., MacKay, D. G., Palma, A., & Rho, C. (2000). Sequential activation processes in producing words and syllables: Evidence from picture naming. *Language and Cognition Processes, 15*(1), 1–44.

Satz, P. (1993). Brain reserve capacity on symptom onset after brain injury: A formulation and review of evidence for thresh- old theory. *Neuropsychology, 7,* 273–295.

Satz, P., Cole, M. A, Hardy, D. J., & Rassovsky, Y. (2011). Brain and cognitive reserve: mediator(s) and construct validity, a critique. *Journal of Clinical and Experimental Neuropsychology*, *33*(1), 121–130.

Sauzéon, H., Raboutet, C., Rodrigues, J., Langevin, S., Schelstraete, M. A., Feyereisen, P., Hupet, M., & N'Kaoua, B. (2011). Verbal knowledge as a compensation determinant of adult age differences in verbal fluency tasks over time. *Journal of Adult Development, 18*, 144–154.

Schmitter-Edgecombe, M., Vesneski, M., & Jones, D. W. R. (2000). Aging and word-finding: A comparison of spontaneous and constrained naming tests. *Archives of Clinical Neuropsychology*, *15*(6), 479–493.

Schwartz, S., & Baldo, J. (2001). Distinct patterns of word retrieval in right and left frontal lobe patients: A multidimensional perspective. *Neuropsychologia, 39*(6), 1209–1217.

Scott Killgore, W. D., & Adams, R. L. (1999). Prediction of Boston naming test performance from vocabulary scores: Preliminary guidelines for interpretation. *Perceptual and Motor Skills, 89*(1), 327-337.

Settnes, A., Andreasen, A. H., & Jorgensen, T. (2005). Hypertension is associated with an increased risk for hysterectomy: A Danish cohort study. *European Journal of Obstetrics and Gynecology and Reproductive Biology, 122*(2), 218–224.

Severens, E., Van Lommel, S., Ratinckx, E., & Hartsuiker, R. J. (2005). Timed picture naming norms for 590 pictures in Dutch. *Acta Psychologica, 119*, 159–187.

Shao, Z., Janse, E., Visser, K., & Meyer, A. S. (2014). What do verbal fluency tasks measure? Predictors of verbal fluency performance in older adults. *Frontiers in psychology, 5*(Article 772).

Shaywitz, S. E., Naftolin, F., Zelterman, D., Marchione, K. E., Holahan, J. M., Palter, S. F., & Shaywitz, B. A. (2003). Better oral reading and short-term memory in midlife, postmenopausal women taking estrogen. *Menopause, 10*, 420–426.

Shaywitz, S. E., Shaywitz, B. A., Pugh, K. R., Fulbright, R. K., Skudlarski, P., Mencl, W. E., … Gore, J. C. (1999). Effect of estrogen on brain activation patterns in postmenopausal women during working memory tasks. *The Journal of the American Medical Association, 281*(13), 1197–1202.

Sherwin, B. B. (2003). Estrogen and cognitive functioning in women. *Endocrine Reviews. 24*(2), 133–151.

Sherwin, B. B. (2005). Estrogen and memory in women: How can we reconcile the findings? *Hormones and Behavior, 47*(3), 371–375.

Sherwin, B. B. (2006). Estrogen and cognitive aging in women. *Neuroscience, 138*(3), 1021–1026.

Sherwin, B. B. (2007). The critical period hypothesis: Can it explain discrepancies in the oestrogen–cognition literature? *Journal of Neuroendocrinology, 19*(2), 77–81.

Sherwin, B. B. (2012). Estrogen and cognitive functioning in women: Lessons we have learned. *Behavioral Neuroscience*, *126*(1), 123–127.

Sherwin, B. B., & Henry, J. F. (2008). Brain aging modulates the neuroprotective effects of estrogen on selective aspects of cognition in women: A critical review. *Frontiers in Neuroendocrinology*, *29*(1), 88–113.

Sherwin, B. B., & Phillips, S. J. (1990). Estrogen and cognitive functioning in surgically menopausal women. *Annals of the New York Academy of Sciences, 592*, 474–475.

Shughrue, P. J., & Merchenthaler, I. (2000). Estrogen is more than just a "sex hormone": Novel sites for estrogen action in the hippocampus and cerebral cortex. *Frontiers in Neuroendocrinology, 21*(1), 95–101.

Shumaker, S. A., Legault, C., Kuller, L., Rapp, S. R., Thal, L., Lane, D. S., … for the WHIMS Investigators. (2004). Conjugated equine estrogens and incidence of probable dementia and mild cognitive impairment in postmenopausal women: Women's Health Initiative Memory Study. *The Journal of the American Medical Association*, *291*(24), 2947–2958.

Shumaker, S. A., Legault, C., Rapp, S. R., Thal, L., Wallace, R. B., Ockene, J. K., … for the WHIMS Investigators. (2003). Estrogen plus progestin and the incidence of dementia and mild cognitive impairment in postmenopausal women: The Women's Health Initiative Memory Study. *The Journal of the American Medical Association*. *289*(20), 2651–2662.

Shumaker, S. A., Reboussin, B. A., Espeland, M. A., Rapp, S. R., Mcbee, W. L., Dailey, M., … for the WHIMS Investigators. (1998). The Women's Health Initiative Memory Study (WHIMS): A trial of the effect of estrogen therapy in preventing and slowing the progression of dementia. *Controlled Clinical Trials, 19*, 604–621.

Shuster, L. T., Rhodes, D. J., Gostout, B. S., Grossardt, B. R., & Rocca, W. A. (2010). Premature menopause or early menopause: Long-term health consequences. *Maturitas*, *65*(2), 161–166.

Silva, I., Mello, L. E., Freymuller, E., Haider, M. A., & Baracat, E. C. (2003). Onset of estrogen replacement has a critical effect on synaptic density of CA1 hippocampus in ovariectomized adult rats. *Menopause, 10*(5), 406–411.

Singh, R. P., & Carr, D. H. (1966). The anatomy and histology of XO human embryos and fetuses. *The Anatomical Record, 155*(3), 369–383.

Singh-Manoux, A., Kivimaki, M., Glymour, M. M., Elbaz, A., Berr, C., Ebmeier, K. P., Ferrie, J. E., & Dugravot, A. (2012). Timing of onset of cognitive decline: Results from the Whitehall II prospective cohort study. *BMJ, 344*, d7622.

Singh-Manoux, A., Marmot, M. G., Glymour, M., Sabia, S., Kivimäki, M., & Dugravot, A. (2011). Does cognitive reserve shape cognitive decline? *Annals of Neurology*, *70*(2), 296–304.

Smail, P. J., Reyes, F. I., Winter, J. S. D., & Faiman, C. (1981). The fetal hormone environment and its effect on the morphogenesis of the genital system. In S.J. Kogan & E.S.E. Hafez (Eds.), *Pediatric Andrology* (pp 9-20). Martinus Nijhoff: The Hague.

Smith, Y. R., Love, T., Persad, C. C., Tkaczyk, A., Nichols, T. E., & Zubieta, J. K. (2006). Impact of combined estradiol and norethindrone therapy on visuospatial working memory assessed by functional magnetic resonance imaging. *The Journal of Clinical Endocrinology and Metabolism, 91*(11), 4476–4481.

Smith, C. A, McCleary, C. A, Murdock, G. A, Wilshire, T. W., Buckwalter, D. K., Bretsky, P., … Buckwalter, J. G. (1999). Lifelong estrogen exposure and cognitive performance in elderly women. *Brain and Cognition*, *39*(3), 203–218.

Snodgrass, J. G., & Vanderwart, M. (1980). A standardized set of 260 pictures: Norms for name agreement, image agreement, familiarity, and visual complexity. *Journal of Experimental Psychology: Human Learning and Memory*, *6*(2), 174–215.

Sobow, T., & Kloszewska, I. (2004). Modulation of age at onset in late-onset sporadic Alzheimer's disease by estrogen-related factors: The age of menopause and number of pregnancies. *German Journal of Psychiatry, 6,* 49–55.

Sowers, M. R., & Pietra, M. T. La. (1995). Menopause : Its epidemiology and potential association with chronic diseases. *Epidemiologic Reviews, 17*(2), 287–302.

Spieler, D. H., & Balota, D. A. (2000). Factors influencing word naming in younger and older adults. *Psychology and Aging, 15,* 225–231.

Spreen, F.O., & Benton, A.L. (1977). Manual of instructions for the neurosensory center comprehensive examination for aphasia. Victoria, British Columbia, Canada: University of Victoria.

Steinberg, B. A, Bieliauskas, L. A, Smith, G. E., & Ivnik, R. J. (2005). Mayo's older Americans normative studies: Age- and IQ-adjusted norms for the trail-making test, the Stroop test, and MAE controlled oral word association test. *The Clinical Neuropsychologist*, *19*(3-4), 329–377.

Steiner, V. A. G., Mansur, L. L., Brucki, S. M. D., & Nitrini, R. (2008). Phonemic verbal fluency and age: A preliminary study, *2*(4), 328–332.

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society*, *8*(3), 448–460.

Tang, M. X., Jacobs, D., Stern, Y., Marder, K., Schofield, P., Gurland, B., … Mayeux, R. (1996). Effect of oestrogen during menopause on risk and age at onset of Alzheimer's disease. *The Lancet, 348*(9025), 429-32.

Tang, Y., Janssen, W. G. M., Hao, J., Roberts, J. A., McKay, H., Lasley, B., … Morrison, J. (2004). Estrogen replacement increases spinophilin-immunoreactive spine number in the prefrontal cortex of female rhesus monkeys. *Cerebral Cortex, 14*(2), 215–223.

Temple, C. M. (2002). Oral fluency and narrative production in children with Turner's syndrome, *Neuropsycholgia, 40*, 1419–1427.

Temple, C. M., & Shephard, E. E. (2012). Exceptional lexical skills but executive language deficits in school starters and young adults with Turners syndrome: Implications for X chromosome effects on brain function. *Brain and Language*, *120*(3), 345–359.

Thilers, P. P., Macdonald, S. W. S., Nilsson, L.-G., & Herlitz, A. (2010). Accelerated postmenopausal cognitive decline is restricted to women with normal BMI: Longitudinal evidence from the Betula project. *Psychoneuroendocrinology*, *35*(4), 516–524.

Thomas, J. C., Fozard, J. L., & Waugh, N. C. (1977). Age-related differences in naming latency. *The American Journal of Psychology*, *90*(3), 499–509.

Toglia, M. P., & Battig, W. R. (1978). *Handbook of semantic word norms.* New York: Erlbaum.

Tombaugh, T. N., & Hubley, A. M. (1997). The 60-item Boston naming test: Norms for cognitively intact adults aged 25 to 88 years. *Journal of Clinical and Experimental Neuropsychology, 19*, 922–932.

Tombaugh, T. N., Kozak, J., & Rees, L. (1999). Normative data stratified by age and education for two measures of verbal fluency: FAS and animal naming. *Archives of Clinical Neuropsychology*, *14*(2), 167–177.

Toran-Allerand, C. D. (2005). Estrogen and the brain: Beyond ER-α, ER-β, and 17β-estradiol. *Annals of the New York Academy of Sciences, 1052*, 136–144.

Tröster, A I., Fields, J. A., Testa, J. A., Paul, R. H., Blanco, C. R., Hames, K. A, … Beatty, W. W. (1998). Cortical and subcortical influences on clustering and switching in the performance of verbal fluency tasks. *Neuropsychologia*, *36*(4), 295–304.

Troyer, A. K., Moscovitch, M., & Winocur, G. (1997). Clustering and switching as two components of verbal fluency: Evidence from younger and older healthy adults. *Neuropsychology*, *11*(1), 138–146.

Troyer, A. K., Moscovitch, M., Winocur, G., Alexander, M. P., & Stuss, D. (1998a). Clustering and switching on verbal fluency: The effects of focal frontal- and temporal-lobe lesions. *Neuropsychologia*, *36*(6), 499–504.

Troyer, A. K., Moscovitch, M., Winocur, G., Leach, L., & Freedman, M. (1998b). Clustering and switching on verbal fluency tests in Alzheimer's and Parkinson's disease. *Journal of the International Neuropsychological Society*, *4*(2), 137–143.

Tsang, H.-L., & Lee, T. M. C. (2003). The effect of ageing on confrontational naming ability. *Archives of Clinical Neuropsychology*, *18*(1), 81–89.

Tupak, S. V., Badewien, M., Dresler T., Hahn, T., Ernst, L. H., Herrmann, M. J., Fallgatter, A. J., & Ehlis, A.-C. (2012). Differential prefrontal and frontotemporal oxygenation patterns during phonemic and semantic verbal fluency. *Neuropsychologia, 50*, 1565–1569.

United Nations, Department of Economic and Social Affairs, Population Division (2013). *Pathways to low fertility: European perspectives* (Expert Paper No. 2013/8). Retrieved from http://www.un.org/en/development/desa/population/publications/pdf/expert/2013-8_Sobotka_Expert-Paper.pdf

Van der Elst, W., Van Boxtel, M. P. J., Van Breukelen, G. J. P., & Jolles, J. (2006). Normative data for the animal, profession and letter *m* naming verbal fluency tests for Dutch speaking participants and the effects of age, education, and sex. *Journal of the International Neuropsychological Society*, *12*(1), 80–89.

Van Gorp, W. G., Satz, P., Kiersch, M. E., & Henry, R. (1986). Normative data on the Boston naming test for a group of normal older adults. *Journal of Clinical and Experimental Neuropsychology, 8*, 702–705.

Valenzuela, M. J., & Sachdev, P. (2006). Brain reserve and cognitive decline: A non-parametric systematic review. *Psychological Medicine*, *36*(8), 1065–1073.

Venegas, M. J., & Mansur, L. L. (2011). Verbal fluency: Effect of time on item generation. *Dementia & Neuropsychologia, 5*(2), 104-107.

Verhaegen, P. (2003). Aging and vocabulary scores: A meta-analysis. *Psychology and Aging*, *18*(2), 332–339.

Verhaegen, C., & Poncelet, M. (2013). Changes in naming and semantic abilities with aging from 50 to 90 years. *Journal of the International Neuropsychological Society*, *19*(2), 119–126.

Verghese, J., Kuslansky, G., Katz, M. J., Sliwinski, M., Crystal, H. A., Buschke, H., & Lipton, R. B. (2000). Cognitive performance in surgically menopausal women on estrogen. *Neurology*, *55*(6), 872–874.

Vihko, R., & Apter, D. (1984). Endocrine characteristics of adolescent menstrual cycles : Impact of early menarche. *Journal of Steroid Biochemistry, 20*(1), 231–236.

Virtala, A., Kunttu, K., Huttunen, T., & Virjo, I. (2006). Childbearing and the desire to have children among university students in Finland. *Acta Obstetricia et Gynecologica Scandinavica*, *85*(3), 312–316.

Viscoli, C. M., Brass, L. M., Kernan, W. N., Sarrel, P. M., Suissa, S., & Horwitz, R. I. (2005). Estrogen therapy and risk of cognitive decline: Results from the Women's Estrogen for Stroke Trial (WEST). *American Journal of Obstetrics and Gynecology*, *192*, 387–393.

Vitevitch, M. S. (2002). The influence of phonological similarity neighbours on speech production. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 28*, 735–747.

Voyer, D., Voyer, S., & Bryden, M. P. (1995). Magnitude of sex differences in spatial abilities: A meta-analysis and consideration of critical variables. *Psychological Bulletin, 117*(2), 250–270.

Wadnerkar, M. B. (2008). *Sex differences and menstrual cycle effects on speech and related behaviours* (Unpublished doctoral dissertation). The University of Sheffield, Sheffield.

Wadnerkar, M. B., Cowell, P. E., & Whiteside, S. P. (2006). Speech across the menstrual cycle: A replication and extension study. *Neuroscience Letters, 408*, 21-24.

Wadnerkar, M. B., Whiteside, S. P., Cowell, P. E. (2008, June). Verbal fluency performance and cognitive strategy as a function of sex and menstrual cycle phase. Organization for the Study of Sex Differences. Annual Meeting, New Orleans, Louisiana, USA.

Wai, J., Cacchio, M., Putallaz, M., & Makel, M. C. (2010). Sex differences in the right tail of cognitive abilities: A 30 year examination. *Intelligence*, *38*(4), 412–423.

Waite, M. (Ed.). (2009). Oxford thesaurus of English. Oxford: Oxford University Press.

Wallace, M., Luine, V., Arellanos, A., & Frankfurt, M. (2006). Ovariectomized rats show decreased recognition memory and spine density in hippocampus and prefrontal cortex. *Brain Research, 1126*(1)*,* 176–182.

Wang, A. C. J., Hara, Y., Janssen, W. G. M., Rapp, P. R., & Morrisson, J. H. (2010). Synaptic estrogen receptor-α levels in prefrontal cortex in female rhesus monkeys and their correlation with cognitive performance. *Journal of Neuroscience, 30*, 12770–12776.

Wang, P. N, Liao, S. Q., Liu, R. S., Liu, C. Y., Chao, H. T., Lu, S. R. … Liu, H. C. (2000). Effects of estrogen on cognition, mood, and cerebral blood flow in AD: A controlled study. *Neurology, 54*(11), 2061-2066.

Waring, S. C., Rocca, W. A., Petersen, R. C., O'Brien, P. C., Tangalos, E. G., & Kokmen, E. (1999). Postmenopausal estrogen replacement therapy and risk of AD: A population-based study. *Neurology, 52*(5), 965–970.

Wasti, S., Robinson, S. C., Akhtar, Y., Khan, S., & Badaruddin, N. (1993). Characteristics of menopause in three socioeconomic urban groups in Karachi, Pakistan. *Maturitas, 16*(1), 61–69.

Weber, M. T., Maki, P. M., & McDermott, M. P. (2014). Cognition and mood in perimenopause: A systematic review and meta-analysis. *Journal of Steroid Biochemistry and Molecular Biology*, *142*, 90-98.

Weber, M. T., Rubin, L. H., & Maki, P. M. (2013). Cognition in perimenopause: The effect of transition stage. *Menopause: The Journal of The North American Menopause Society, 20*(5), 511–517.

Wechsler, D. (1958). *The measurement and appraisal of adult intelligence*. Baltimore, MD: Williams & Wilkins.

Wechsler, D. (1987). *Wechsler memory scale–revised: Manual.* New York: The Psychological Corporation.

Wechsler, D. (1999). *Wechsler abbreviated scale of intelligence (WASI)*. San Antonio: The Psychological Corporation, Harcourt Brace.

Weis, S., Hausmann, M., Stoffers, B., & Sturm, W. (2011). Dynamic changes in functional cerebral connectivity of spatial cognition during the menstrual cycle. *Human Brain Mapping*, *32*(10), 1544–1556.

Weis, S., Hausmann, M., Stoffers, B., Vohn, R., Kellermann, T., & Sturm, W. (2008). Estradiol modulates functional brain organization during the menstrual cycle: an analysis of interhemispheric inhibition. *The Journal of Neuroscience*, *28*(50), 13401–13410.

Weiss, E. M., Ragland, J. D., Brensinger, C. M., Bilker, W. B., Deisenhammer, E. A, & Delazer, M. (2006). Sex differences in clustering and switching in verbal fluency tasks. *Journal of the International Neuropsychological Society*, *12*, 502–509.

Weiss, E., Siedentopf, C., Hofer, A., Deisenhammer, E. A., Hoptman, M. J., Kremser, C., … Delazer, M. (2003). Brain activation pattern during a verbal fluency test in healthy male and female volunteers: A functional magnetic resonance imaging study. *Neuroscience Letters*, *352*, 191–194.

Welch, L. W., Doineau, D., Johnson, S., & King, D. (1996). Educational and gender normative data for the Boston naming test in a group of older adults. *Brain and Language, 53*(2), 260–266.

White, P. C., & Speiser, P. W. (2000). Congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *Endocrine Reviews, 21*(3), 245–291.

Whiteside, S. P., Hanson, A., & Cowell, P. E. (2004). Hormones and temporal components of speech: Sex differences and effects of menstrual cyclicity on speech. *Neuroscience Letters, 367*, 44-47.

Whitney, C., Weis, S., Krings, T., Huber, W., Grossman, M., Kircher, T. (2009). Task-dependent modulations of prefrontal and hippocampal activity during intrinsic word production. *Journal of Cognitive Neuroscience, 21*, 697–712.

Wierenga, C. E., Benjamin, M., Gopinath, K., Perlstein, W. M., Leonard, C. M., Rothi, L. J. G., … Crosson, B. (2008). Age-related changes in word retrieval: Role of bilateral frontal and subcortical networks. *Neurobiology of Aging*, *29*(3), 436–451.

Wixted, J. T., & Rohrer, D. (1994). Analyyzing the dynamics of free recall: An integrative review of the empirical literature. *Psychonomic Bulletin and Review, 1*(1), 89–106.

Wolf, O., Heinrich, A. B., Hanstein, B., & Kirschbaum, C. (2005). Estradiol or estradiol/progesterone treatment in older women: No strong effects on cognition. *Neurobiology of Aging, 26*(7), 1029–1033.

World Health Organization (1996). Research on the menopause in the 1990s: Report of a WHO scientific group. *World Health Organization technical report series, 866,* 1–107.

World Health Organization (2015). Health in 2015: From MDGs, millennium development goals to SDGs, sustainable development goals. Retrieved from http://www.who.int/gho/publications/mdgs-sdgs/en/

Worrall, L. E., Yiu, E. M.-L., Hickson, L. M. H., & Barnett, H. M. (1995). Normative data for the Boston naming test for Australian elderly. *Aphasiology, 9*(6), 541–551.

Xu, J., Bartoces, M., Neale, A. V., Dailey, R. K., Northrup, J., & Schwartz, K. L. (2005). Natural history of menopause symptoms in primary care patients: A MetroNet study. *Journal of the American Board of Family Medicine, 18*(5), 374–382.

Yaffe, K., Vittinghoff, E., Ensrud, K. E., Johnson, K. C., Diem, S., Hanes, V., & Grady, D. (2006). Effects of ultra-low-dose transdermal estradiol on cognition and health-related quality of life. *Archives of Neurology, 63*(7), 945–950.

Zandi, P. P., Carlson, M. C., Plassman, B. L., Welsh-Bohmer, K. A., Mayer, L. S., Steffens, D. C., & Breitner, J. C. (2002) Hormone replacement therapy and incidence of Alzheimer's disease in older women: The Cache county study. *The Journal of the American Medical Association,* 288, 2123–2129.

Zec, R. F., Burkett, N. R., Markwell, S. J., & Larsen, D. L. (2007a). A cross-sectional study of the effects of age, education, and gender on the Boston naming test. The Clinical Neuropsychologist, 21, 587–616.

Zec, R. F., Burkett, N. R., Markwell, S. J., & Larsen, D. L. (2007b). Normative data stratified for age education and gender on the Boston naming test. The Clinical Neuropsychologist, 21, 617–637.

Zec, R. F., Markwell, S. J., Burkett, N. R., & Larsen, D. L. (2005). A longitudinal study of confrontation naming in the "normal" elderly. *Journal of the International Neuropsychological Society*, *11*, 716–726.

Zec, R. F., & Trivedi, M. A. (2002). The effects of estrogen replacement therapy on neuropsychological functioning in postmenopausal women with and without dementia: A critical and theoretical review. *Neuropsychology Review*, *12*(2), 65–109.

Zhao, Q., Guo, Q., & Hong, Z. (2013). Clustering and switching during a semantic verbal fluency test contribute to differential diagnosis of cognitive impairment. *Neuroscience Bulletin*, *29*(1), 75–82.

Zimmermann, N., Parente, M., A. M. P., Joanette, Y., & Fonseca, R. P. (2014). Unconstrained, phonemic and semantic verbal fluency: Age and education effects, norms and discrepancies. *Psicologia: Reflexão e Crítica, 27*(1), 1-9.

Appendix 1

Table 1
Means (± SEM) for total number of words, number of switches and mean cluster size across Letters (F, A, S) and Time (T1, T2 and T3) for the letter fluency task as a function of menstrual cycle phase

		Dependent variable								
		Total number of words			Number of switches			Mean cluster size		
Menstrual cycle phase	Letter	T1	T2	T3	T1	T2	T3	T1	T2	T3
Menstrual phase (*n* = 7)	F	7.43 (0.72)	5.00 (1.00)	3.86 (0.96)	1.14 (0.46)	1.23 (0.89)	0.23 (0.29)	1.39 (0.13)	0.78 (0.21)	0.97 (0.50)
	A	7.57 (0.92)	5.00 (1.35)	4.71 (1.06)	2.00 (0.69)	2.00 (0.76)	0.86 (0.55)	0.86 (0.14)	0.69 (0.25)	0.80 (0.21)
	S	8.86 (0.83)	5.43 (0.57)	5.43 (0.78)	2.28 (0.89)	2.00 (0.65)	1.00 (0.43)	1.03 (0.19)	1.55 (0.71)	0.96 (0.17)
Periovulatory phase (*n* = 6)	F	11.00 (0.89)	5.83 (1.35)	6.50 (1.61)	4.33 (1.17)	2.00 (1.00)	1.00 (0.82)	1.76 (0.55)	2.43 (0.87)	1.25 (0.31)
	A	9.00 (1.21)	4.83 (0.70)	3.83 (0.48)	2.17 (1.08)	1.83 (1.28)	0.50 (0.50)	1.15 (0.30)	1.25 (0.30)	0.67 (0.33)
	S	11.33 (0.92)	6.00 (1.15)	6.50 (1.20)	1.33 (0.56)	2.50 (0.56)	1.17 (0.60)	1.74 (0.40)	1.12 (0.48)	1.56 (0.44)
Midluteal phase (*n* = 7)	F	8.86 (0.63)	4.71 (0.64)	3.71 (0.84)	1.86 (0.51)	2.00 (0.49)	0.14 (0.14)	1.26 (0.10)	1.23 (0.27)	2.17 (0.81)
	A	8.00 (1.05)	4.57 (0.84)	3.71 (0.68)	1.57 (0.48)	1.14 (0.55)	0.71 (0.47)	1.43 (0.20)	1.50 (0.65)	1.15 (0.51)
	S	9.43 (0.92)	6.43 (1.17)	5.00 (0.93)	2.00 (0.82)	2.86 (0.59)	1.00 (0.49)	1.79 (0.51)	1.24 (0.46)	1.57 (0.37)
Mean (*N* = 20)	F	9.00 (0.52)	5.15 (0.56)	4.60 (0.68)	2.35 (0.50)	1.75 (0.45)	0.45 (0.27)	1.45 (0.17)	1.43 (0.31)	1.47 (0.35)
	A	8.15 (0.59)	4.80 (0.56)	4.10 (0.45)	1.90 (0.42)	1.65 (0.48)	0.70 (0.28)	1.14 (0.13)	1.14 (0.27)	0.88 (0.21)
	S	9.80 (0.54)	5.95 (0.55)	5.60 (0.54)	1.90 (0.44)	2.45 (0.34)	1.05 (0.28)	1.51 (0.23)	1.31 (0.32)	1.35 (0.20)

Appendix 2a

Screening questionnaire

Participant Number: **Telephone screening**	
1. Date of Telephone Screening	
2. Name	
3. Contact Details Address Phone/Mobile/Email	
4. Date of birth (~1932-1967) Place of birth Residence for past 10 years	
5. Native Speaker of British English?	Y / N
6. Current medications: Screen for oral contraceptives, any hormonally based medications, hormone replacement therapy (HRT), antidepressants.	
7. Past medications: Screen for oral contraceptives, hormone replacement therapy and other hormonally based medications up to 1 year prior	
8. History of major illnesses and hospitalisations	
9. Typical length of menstrual cycle (from onset of one bleeding phase to the onset of the next). (Should be 26-30 days pre menopause)	
10. Regularity of menstrual cycle (does it occur on a monthly basis)	
11. Start date of most recent menstrual period (i.e., onset of the bleeding phase)	
12. Pregnancy or lactation in past year.	
13. Delay/absence of menstrual cycle in past year (> 4 days)	
14. Pattern of delay, absence or change in relation to age or peri-menopause	
15. Date of last menstrual period in relation to menopause (months or years since last period).	

Appendix 2a (continued)

Interview questionnaire

Participant Number: **Interview ~ Test session**	
16. a. Date of Test Session b. Notation of menopausal status	
17. Review items from telephone screening.	Date any changes or additional notes. Confirm that participant has not skipped meals, and is not feeling tired or unwell.
18. Years of formal education (highest educational attainment and date)	
19. Occupation	
20. a. Handedness b. Has this always been the case? c. Left handedness in 1st degree relatives	
21. History of substance abuse (drugs, alcohol)	
22. History of head injury or loss of consciousness (black outs, concussion, coma)	
23. Vision or hearing problems (ok if corrected)	
24. History of mental illness or psychological problems (depression, anxiety, schizophrenia, personality disorder; seen by psychologist, psychiatrist)	
25. History of emotional problems (periods of prolonged sadness, panic attacks)	
26. History of movement disorder (e.g., loss of feeling/movement coordination, involuntary movements)	
27. History of cognitive disorder in adulthood (e.g., problems paying attention, remembering things)	
28. Language/learning delay or disorder as child (e.g., dyslexia, difficulties in school, ADD)	
29. Age at first menstrual period (has your period been regular since this age?)	
30. Number of pregnancies and age at which pregnant	
31. Number of children	
32. History of endocrine, hormonal dysfunction or illness (reproductive system, obstetric-gynaecological, thyroid, adrenal)	

Appendix 2a (continued)

Screening questionnaire: Email version

Participant Number: **Volunteer background screening**	
1. Date of Screening	
2. Name	
3. Contact Details: Address Phone/Mobile/Email	
4. Date of birth Place of birth Residence for past 10 years	
5. Are you a native speaker of British English? If No, i. Are you fluent in English? ii. At what age did you start learning English?	Yes / No
6. Current medications: i. Are you taking any oral contraceptives? ii. Are you taking any hormonally based medications or hormone replacement therapy (HRT)? iii. Are you taking any thyroid medications? iv. Are you taking any antidepressants?	
7. In the past one year, i. Did you take any oral contraceptives? ii. Did you take any hormonally based medications or hormone replacement therapy (HRT)? iii. Did you take any thyroid medications? iv. Did you take any antidepressants?	
8. Have you ever had any major medical illnesses, hospitalisations or surgeries? If yes, please list them	
9. Are you still having menstrual periods? If yes, please answer questions 10 through 14 below. If no, go to question 15	Yes / No
10. What is the typical length of your menstrual cycle (from onset of one bleeding phase to the onset of the next)?	
11. If you are still having menstrual cycles, do they occur on a regular basis?	
12. What was the start date of your most recent menstrual period (i.e., onset of the bleeding phase)?	
13. Have you been pregnant or lactating in past year?	Yes / No
14. Have you had any delay/absence of menstrual cycle in past year (> 4 days) If yes, please describe the pattern of delay, absence or change.	
15. If you have already gone through the menopause, when was the last time you experienced a menstrual period?	

Appendix 2b

Ethics approval form

ETHICS REVIEWER'S COMMENTS FORM

This form is for use when ethically reviewing a research ethics application form.

1. Name of Ethics Reviewer:	Richard Body Silke Fricke Sarah Spencer
2. Research Project Title:	Effects of menopause and age on word processing
3. Principal Investigator (or Supervisor):	Ramya Maitreyee
4. Academic Department / School:	Human Communication Sciences
5. I confirm that I do not have a conflict of interest with the project application	

6. I confirm that, in my judgment, the application should:

Be approved:	Be approved with *suggested* amendments in '7' below: and/or	Be approved providing *requirements* specified in '8' below are met:	NOT be approved for the reason(s) given in '9' below:
✓			

7. Approved with the following suggested, optional amendments (i.e. it is left to the discretion of the applicant whether or not to accept the amendments and, if accepted, the ethics reviewers do not need to see the amendments):

8b. Approved providing the following, compulsory requirements are met (ethics reviewers need to see the required changes, which should be highlighted in the resubmitted form):

9. Not approved for the following reason(s):

10. Date of Ethics Review: 13 November 2012

Signature of reviewer:

Appendix 3

Multiple linear regression analyses were performed to determine if any of the demographic (age, number of years of education, vocabulary scores) and reproductive factors (age at menarche, menstrual cycle length, age at first childbirth, number of children, age at menopause, number of years since menopause and number of reproductive years) were significant predictors of category and letter fluency. These analyses were conducted on postmenopausal women only. Prior to conducting regressions, correlations were used to determine predictors to be used in the statistical models. A variable was chosen as a predictor if it was associated with performance and it did not strongly correlate with another potential predictor.

3.1. Predictors of category fluency performance

A linear stepwise multiple regression analysis was performed after excluding women with hysterectomies (because a significant effect of Age group on category fluency was found when these women were excluded) to determine significant predictors of task performance. Category fluency was found to be significantly associated with age, vocabulary, number of years of education, age at menarche, number of years since menopause and number of reproductive years. Age, number of years of education, age at menarche and number of reproductive years were entered as predictors in the final model after accounting for multicollinearity issues. The mean of total number of words produced across the three categories (animals, fruits, vehicles) was the dependent variable. The regression analysis confirmed that number of years of education and age at menarche were significant predictors of category fluency performance (see Table 1).

Table 1

Predictors of category fluency performance in postmenopausal women aged 48-79 years (n = 53)

Variable	B	SE B	β	95% CI
Constant	20.03	7.09		[5.80, 34.27]
Education	0.59	0.22	0.34**	[0.15, 1.02]
Age at menarche	-0.88	0.41	-0.27*	[-1.71, -.05]
R^2	0.24			

Note. CI = confidence interval

***p* = .009, **p* = .037.

3.2. Predictors of letter fluency performance

Pearson correlations showed that vocabulary and number of years of education were significantly correlated with performance. Age had a weak nonsignificant trend. Age and number of years of education were entered as predictors in the model. The mean of total number of words produced across the three letters (F, A, S) was the dependent variable. The analysis confirmed that education was a significant predictor of letter fluency performance (see Table 2).

Table 2

Predictors of letter fluency performance in postmenopausal women aged 48-79 years (n = 58)

Variable	B	SE B	β	95% CI
Constant	2.12	7.65		[-13.22, 17.43]
Age	0.02	0.07	0.03	[-0.13, 0.16]
Education	0.84	0.26	0.45**	[0.32, 1.36]
R^2	0.19			

Note. CI = confidence interval ***p* = .002.

Appendix 4

As mentioned in Chapter 7, the latency data for picture naming and naming-to-auditory-definitions were trimmed. Analysis was also conducted on the untrimmed data. The results are presented in section 4.1.

4.1. Results from the untrimmed data

4.1.1. Pearson correlations between picture naming latency, naming-to-auditory definitions latency, demographic and reproductive variables

Pearson correlations were conducted to examine the associations between the dependent measures (picture naming latency, naming-to-auditory-definitions latency), demographic variables (Table 1) and reproductive variables (Table 2).

Table 1

Correlations between picture naming latency, naming-to-auditory-definitions and demographic variables as a function of menopause stage, age group and time since menopause

Dependent variable	Independent variable	Group	*n*	Demographic variable		
				Vocabulary T score	Education (in years)	Age (in years)
Picture naming latency	Menopause stage	Premenopause	9	-.71*	-.53	.21
		Perimenopause	11	-.52	-.06	-.30
		Postmenopause	12	-.15	-.63*	.24
	Age group	Group I (46-55 years)	32	-.58**	-.36*	-.24
		Group II (56-65 years)	24	-.06	.05	-.18
		Group III (70-79 years)	22	-.25	-.32	.44*
	Time since menopause	Recent menopausal	16	-.16	-.43	.14
		Longer-term menopausal	42	-.11	-.20	.43**
Naming-to-auditory-definitions latency	Menopause stage	Premenopause	9	-.51	-.61	-.11
		Perimenopause	11	-.57	.09	-.17
		Postmenopause	12	-.17	-.31	-.11
	Age group	Group I (46-55 years)	32	-.45	-.17	-.18
		Group II (56-65 years)	24	.09	.09	-.17
		Group III (70-79 years)	22	.03	-.04	-.27
	Time since menopause	Recent menopausal	16	.06	-.12	.41
		Longer-term menopausal	42	-.02	-.06	.07

†$p < .10$. *$p < .05$. **$p < .01$.

Table 2

Correlations between picture naming latency, naming-to-auditory-definitions latency and reproductive markers as a function of menopause stage, age group and time since menopause

Dependent variable	Independent variable	Group	*n*	Reproductive marker						
				Age at menarche	Menstrual cycle length	Age at first childbirth+	Number of children	Age at menopause	Number of years since menopause	Number of reproductive years
Picture naming latency	Menopause stage	Premenopause	9	-.39	-.21	-.80	.15	-	-	-
		Perimenopause	11	.00	.39	.15	.03	-	-	-
		Postmenopause	12	.24	-.21	.09	-.09	.17	-.19	.05
	Age group	Group I (46-55 years)	32	-.10	.02	-.11	.12	.17	-.19	.05
		Group II (56-55 years)	24	.14	.12	.36	-.44*	-.26	.04	-.31
		Group III (70-79 years)	22	.30	.11	.39	-.15	-.32	.45*	-.41
	Time since menopause	Recent menopausal	16	.33	-.21	.32	-.05	.09	.16	-.04
		Longer-term menopausal	42	.24	.26	-.02	-.09	-.36*	.49**	-.44
Naming-to-auditory-definitions latency	Menopause stage	Premenopause	9	-.04	-.12	.25	-.10	-	-	-
		Perimenopause	11	.03	.34	.25	-.20	-	-	-
		Postmenopause	12	.35	-.33	-.21	.74**	-.14	.05	-.26
	Age group	Group I (46-55 years)	32	.10	-.01	.16	.13	-.14	.05	-.26
		Group II (56-55 years)	23	.25	-.16	.28	-.01	-.07	-.09	-.20
		Group III (70-79 years)	21	.08	.28	.18	-.21	.17	-.24	.12
	Time since menopause	Recent menopausal	16	.35	-.35	-.26	.76**	.34	.25	.16
		Longer-term menopausal	40	.18	.16	.12	-.19	-.03	.07	-.11

Note. +*Sample size for age at first childbirth variable*, **Picture naming**: Premenopause: 6, Perimenopause: 10, Postmenopause: 8; Group I: 24, Group II: 23, Group III: 21; Recent menopausal: 12, Longer-term menopausal: 40. **Naming-to-auditory-definitions**: Premenopause: 6, Perimenopause: 10, Postmenopause: 8; Group I: 24, Group II: 22, Group III: 20; Recent menopausal: 12, Longer-term menopausal: 38. †$p < .10$. *$p < .05$. **$p < .01$.

4.1.2. ANOVAs and ANCOVAs comparing women across Age groups, Menopause stages and Time since menopause for picture naming latency and naming-to-auditory-definitions latency

Separate ANOVAs were performed with picture naming latency as the dependent measure and Age group (46-55, 56-65, 70-79 years) or Menopause stage (pre, peri, postmenopause) or Time since menopause (recent, longer-term) as the between-group factor.

4.1.2.1. Picture naming latency

Age group comparisons

There was a significant effect of Age on picture naming latency, $F(2, 75) = 3.79$, $p = .027$. Post hoc independent *t*-tests with Bonferroni corrections ($\alpha = .05/3 = .017$) showed that women age 70-79 years had significantly longer latencies than women aged 56-65 years, $t(44) = -2.90$, $p = .006$. Women aged 46-55 years did not significantly vary from women aged 56-65 and 70-79 years.

Menopause stage comparisons

Women across the three menopause stages did not significantly differ in their picture naming latency.

Time since menopause comparisons

The Levene's test was significant, $F(1, 56) = 9.31$, $p = .003$; therefore results from the Welch's test are reported. The analysis showed that recent-menopausal women had shorter latencies than longer-term menopausal women, $F(1, 57) = 8.79$, $p = .005$.

4.1.2.2. Naming-to-auditory-definitions latency

An ANOVA with Frequency (High and Low) and Neighbourhood density (High and Low) as repeated measures and Age group (46-55, 56-65, 70-79 years) or Menopause stage (pre, peri, postmenopause) or Time since menopause (recent, longer-term) as the between-group factor was conducted to examine mean differences in latency.

Age group comparisons

Women across the three Age groups did not differ significantly in naming-to-auditory-definitions latency. There was a significant effect of Frequency, $F(1, 73) = 25.52$, $p < .001$, Neighbourhood density, $F(1, 73) = 5.81$, $p = .018$, and Frequency x Neighbourhood density interaction, $F(1, 73) = 4.76$, $p = .032$ for latency. High frequency words took longer to be produced than low frequency words. Low neighbourhood density words took longer to be produced than high neighbourhood density words. No other significant findings were seen.

Menopause stage comparisons

There was no significant effect of menopause stage on latency. There was a significant effect of Frequency, $F(1, 29) = 4.51$, $p = .042$, and Neighbourhood density, $F(1, 29) = 9.30$, $p = .005$ on latency. High frequency words took longer to be produced than low frequency words; and low neighbourhood density words took longer to be produced than high neighbourhood density words. No significant interactions were seen.

Time since menopause comparisons

Recent and longer-term menopausal women were comparable for naming-to-auditory-definitions latencies. There was a significant effect of Frequency, $F(1, 54) = 31.34$, $p < .001$, but not of Neighbourhood density. High frequency words took longer to be produced than low frequency words.

4.2. Predictors of picture naming and naming-to-auditory-definitions

Multiple linear regression analyses were performed to determine whether any of the demographic (age, number of years of education, vocabulary scores) and reproductive factors (age at menarche, menstrual cycle length, age at first childbirth, number of children, age at menopause, number of years since menopause and number of reproductive years) were significant predictors of naming accuracy or latency. These analyses were conducted on postmenopausal women only. Prior to conducting regressions, correlations were used to determine predictors to be used in the statistical models. A variable was chosen as a predictor if it was associated with performance and it did not strongly correlate with another potential predictor.

4.2.1. Predictors of picture naming accuracy and latency

Accuracy

Picture naming accuracy was significantly associated with age, vocabulary, education, age at menopause, number of years since menopause and reproductive years. No other reproductive variables were significantly correlated. After examining the intercorrelations between these six variables (see Chapter 5), age, number of years of education and number of reproductive years were included in the linear multiple regression model. Education was the only significant predictor of picture naming accuracy (see Table 3).

Table 3

Predictors of picture naming accuracy in postmenopausal women aged 48-79 years (n = 58)

Variable	B	SE B	β	95% CI
Constant	44.17	7.29		[-29.56, 58.78]
Age	-0.06	0.05	-0.15	[-0.16, 0.05]
Education	0.46	0.19	0.33*	[0.08, 0.85]
Reproductive years	0.21	0.12	0.22	[-0.03, 0.45]
R^2	0.27			

*p = .019, *Note*. n = 58, CI = confidence interval

The regression analysis plots indicated that two outliers. When these two women were excluded and the analysis was re-run, the results were the same as above, with education was the only significant predictor.

Latency (results from trimmed data)

Picture naming latency correlated significantly with age, years of education, age at menarche, age at menopause, number of years since menopause and reproductive years. For the regression analysis, age, education, age at menarche and number of reproductive years were considered in order to avoid problems arising from multi-collinearity. Age was the only significant predictor of picture naming latency (see Table 4). With every one-year increase in age, the latency increased by approximately 15 msec.

Table 4

Predictors of picture naming accuracy in postmenopausal women aged 48-79 years (n =58)

Variable	B	SE B	β	95% CI
Constant	796.77	832.59		[-873.19, 2466.74]
Age	14.84	4.58	0.42**	[5.64, 24.03]
Education	-7.33	16.70	-0.06	[-40.82, 26.16]
Age of menarche	29.53	28.65	0.13	[-27.94, 87.00]
Reproductive years	-17.49	11.10	0.20	[-39.75, 4.78]
R^2	.35			

**p = .002, *Note.* CI = confidence interval

4.2.2. Predictors of naming-to-auditory-definitions accuracy and latency

<u>*Accuracy*</u>

The variables that were found to be associated with accuracy were age, vocabulary T score, number of years of education, age at menarche, menstrual cycle length, number of years since menopause and reproductive years. A multiple linear regression was conducted with naming-to-auditory-definitions total accuracy score (sum of accuracy scores on all the four lists) as the dependent variable and age, number of years of education, age at menarche, menstrual cycle length and number of reproductive years as predictors. The results showed that education and menstrual cycle length were significant predictors of accuracy (see Table 5). An additional year of education increased the accuracy by 0.47 units and an increase of one day in menstrual cycle length increased it by 0.90 units.

Table 4

Predictors of naming-to-auditory-definition accuracy scores in postmenopausal women between 48-79 years of age (n = 56)

Variable	B	SE B	β	95% CI
Constant	24.02	12.21		[-0.51, 48.54]
Age	-0.10	0.06	-0.19	[-0.22, 0.03]
Number of years of education	0.47	0.23	0.26*	[0.00, 0.94]
Age at menarche	-0.59	0.39	-0.18	[-1.37, 0.21]
Menstrual cycle length	0.90	0.26	0.39**	[0.38, 1.42]
Number of reproductive years	0.19	0.15	0.15	[-0.12, 0.49]
R^2	.40			

$^{**}p < .01$, $^{*}p < .05$. *Note.* CI = confidence interval

Latency (results from trimmed data)

No linear regression analysis was conducted to determine predictors of naming-to-auditory-definitions latency as none of the variables were significantly related to performance in this subsample of postmenopausal women.

Appendix 5

5.1. Exploratory analysis investigating the interactive effects of demographic and reproductive factors on word-finding performance in a subgroup of women from the study sample

As discussed in Chapter 8, exploratory analysis was conducted in a subsample of women from the data set to examine the relationships between word-finding performance, demographic and reproductive variables. This section presents the initial multivariate analyses that were conducted prior to finalizing the final model.

5.1.1. Results from the initial multivariate analyses

5.1.1.1. Age analysis in women aged 48-79 years (n = 45)

Women who had not had hysterectomy and had had a child or children were considered for this analysis.

Model 1

Dependent variables: Category fluency total words, Letter fluency total words, 4-series switch rate, 3-series switch cost, Picture naming latency, Naming-to-definitions accuracy

Covariates: Age, number of years of education, age at menarche, menstrual cycle length, age at first childbirth, number of children, reproductive years.

Results: Age, $V = 0.52$, $F(6, 32) = 5.77$, $p < .001$, menstrual cycle length, $V = 0.44$, $F(6, 32) = 4.14$, $p = .003$, age at first childbirth, $V = 0.39$, $F(6, 32) = 3.37$, $p = .011$, and number of reproductive years, $V = 0.32$, $F(6, 32) = 2.52$, $p = .041$, were significantly associated with overall word-finding performance, $V = 0.29$, $F(6, 32) = 2.22$, $p = .067$. Education showed a nonsignificant trend. Therefore, these covariates were retained in the final model, and age at menarche and number of children were excluded. The dependent variables mentioned above were included in the final model, except 4-series switch rate because it was not significantly associated with any of the covariates. The results of the final model are discussed in Chapter 8 (section 8.4.1.1).

5.1.1.2. Age analysis in women aged 46-55 years (n = 24)

Women who had not had hysterectomy and had had a child or children were considered for this analysis.

Model 1

Dependent variables: Category fluency total words, Letter fluency total words, 4-series switch rate, Picture naming latency, Naming-to-definitions accuracy,

Covariates: Age, number of years of education, age at menarche, menstrual cycle length, age at first childbirth, number of children, menopause stage (pre vs peri, pre vs post). For details on how menopause stages variables were created, see section 8.4.1.2.

Results: None of the variables was significantly associated with word-finding performance. Age, $V = 0.47$, $F(5, 11) = 7.66$, $p = .163$, and menstrual cycle length, $V = 0.53$, $F(5, 11) = 7.66$, $p = .096$, showed nonsignificant trend of associations with performance. Therefore, the final included the same set of dependent variables are mentioned above and age, menstrual cycle length and menopause stage as covariates. The results of the final model are presented in section 8.4.1.2.