The Early Cognitive Profile and the Interactions Between Health and Cognition in Children with Down Syndrome

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Abstract

This thesis aimed to examine the development of cognitive, linguistic and adaptive skills in children with Down syndrome, with a particular emphasis on the interactions between health and these outcomes. Chapters 3, 4 and 5 describe a longitudinal study in which the cognitive, adaptive and linguistic skills of four- to five-year-old children with Down syndrome were traced over 15 months. Parental interviews about health enabled examination of the links between health and cognitive outcomes. Chapter 6 reports a vocabulary training study, which aimed to look at the relationship between sleep and vocabulary consolidation; a more specific health-cognition link.

Chapters 3 and 4 showed that the cognitive, linguistic and adaptive profile associated with older children and adults with Down syndrome had fully emerged by the age of four, although there was a large degree of variability in the expression of the profile at the individual level. The relationships between different cognitive domains in the children with Down syndrome were largely similar to those in the typically developing group, suggesting that development is delayed rather than disordered. The only exception was the relationship between grammar and vocabulary which was atypical in the children with Down syndrome. Chapter 4 showed that parent-report measures of language can be reliably used as predictors of later objectively measured linguistic skill. In a more detailed investigation of vocabulary skills, Chapter 6 found that children with Down syndrome were able to consolidate new vocabulary over time, achieving similar levels of performance to language matched typically developing controls.

To address questions about the links between health and cognition, Chapter 5 found that childhood hearing difficulties and congenital heart defects were associated with poorer language outcomes between the ages of four- and six-years-old in children with Down syndrome. However, there were no reliable relationships between cognition and either sleep or hospitalisation measures. Furthermore, Chapter 6 failed to find a relationship between sleep and vocabulary consolidation. Implications, both for practitioners and for theoretical models of developmental disability, are discussed.

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Author's Declaration

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1 Development of Children with Down Syndrome: The Cognitive Profile

1.1 Introduction to Down Syndrome

Down syndrome is the most common genetic disorder resulting in intellectual disability with a prevalence of 1.08 per 1000 live births (Irving, Basu, Richmond, Burn, & Wren, 2008). In 95% of cases Down syndrome is caused by full trisomy 21 where an individual has an extra, third, copy of chromosome 21 in all cells. More rarely the disorder occurs through mosaicism or translocation of portions of chromosome 21. Down syndrome is often associated with certain physical features, puts individuals at an increased risk of a variety of health problems (Roizen & Patterson, 2003) and results in an intellectual impairment that ranges from mild to severe. Language and motor skills are impaired relative to nonverbal abilities and social skills (Chapman & Hesketh, 2000; Silverman, 2007). However, despite the typical profile that is documented in the literature, it is important to note that there are wide individual differences in ability levels and, to a degree, within the profile of cognitive strengths and weaknesses (Tsao & Kindelberger, 2009). Thus, it is important to identify key factors that determine aspects of this variability.

Down syndrome is a complex disorder with multiple developmental outcomes in different domains. Despite having a clear genetic origin, there is still much to learn about precisely how causal mechanisms operate in Down syndrome to produce the observed behavioural outcomes. Understanding these is key to designing effective interventions to support individuals with Down syndrome. This thesis is concerned with the issue of how health and cognition interact during the development of young children with Down syndrome. To this end, theoretical frameworks within which to consider cognitive development will be evaluated and a detailed description of development in Down syndrome at the cognitive (Chapter 1) and biological (Chapter 2) levels will be presented. This will provide the foundation for considering the interactions between health and cognitive abilities in Down syndrome.

1.2 Frameworks for Considering Atypical Development

Development is a multifaceted, dynamic process and a major challenge for research has been to establish a framework within which to consider all the relevant interacting factors that influence development. Such frameworks are important for considering both typical and atypical development. A further challenge in the study of

atypical development has been enabling representations of the causal pathways that lead to developmental difficulties within such a framework. In an attempt to address these issues, Morton (2004) proposed an atheoretical framework in which to model the causes of developmental disorders, known as Developmental Causal Modelling. Within this framework, there are three levels of description for causes and outcomes: biological (genetic and brain level), cognitive and behavioural. Morton (2004) also accounts for the influence of the environment at each of these levels. Guided by theory, different features of a disorder can be introduced at the appropriate level and the causal relationships between them modelled using a specified notation system. Morton (2004) argues that depicting relationships in this way is clearer than trying to describe them linguistically. Figure 1.1 illustrates the notation approach. Developmental Causal Modelling places biology as the top level of explanation followed by the cognitive and then behavioural levels with causal chains largely operating in this direction. However, other researchers have noted the importance of allowing for bidirectional influences between the different levels where, for example, behaviour can influence biology or the environment as well as the other way around (Cebula, Moore, & Wishart, 2010).

Developmental Causal Modelling (Morton, 2004) provides a very useful method for conceptualising the difficulties in different developmental disorders (e.g. Hulme & Snowling, 2009). The idea of integrating different levels of explanation is particularly important for considering development in disorders with clear biological origins, such as Down syndrome, as the links between biology and cognition can be more distinctly drawn. This approach encourages the synthesis of research focussing on both biological and cognitive aspects of Down syndrome, which are often dealt with in relatively separate bodies of literature. Morton (2004) intended Developmental Causal Modelling to be applied to disorders that involve specific deficits, such as dyslexia and conduct disorder, although he notes that it can also be useful for modelling specific strengths or difficulties in disorders that involve general difficulties and cognitive delay, such as autism or Down syndrome (pp.102-103). For example, there has been an attempt to model the causal pathways involved in social cognition in Down syndrome using a variant of Developmental Causal Modelling (Cebula et al., 2010), demonstrating that this framework can be applied to the study of cognitive skills in Down syndrome.

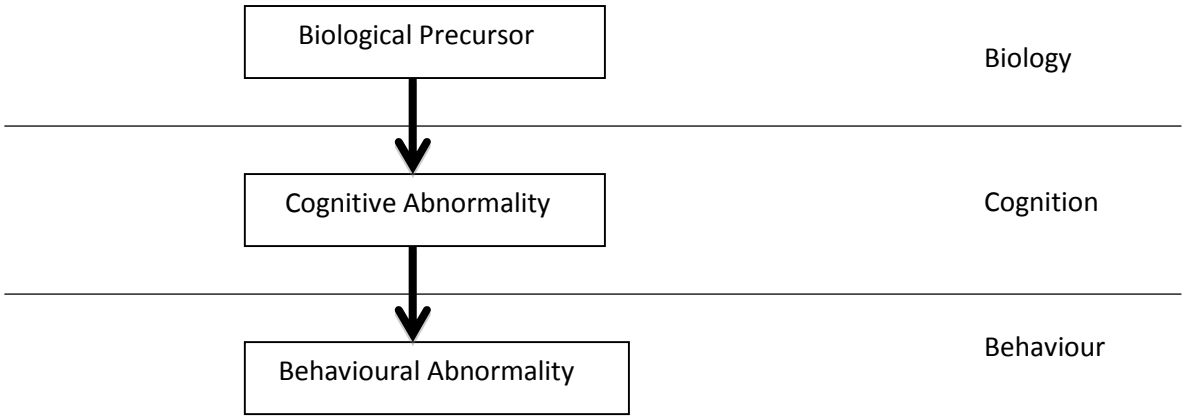


Figure 1.1. An illustration of the Developmental Causal Modelling approach, adapted from Morton (2004).

The Developmental Causal Modelling approach is limited by the fact that it produces very static models that can't encapsulate the changing nature of interactions between different levels of explanation over time. Other approaches to development, such as neuroconstrucitivsm (for review see Westermann et al., 2007), suggest that developmental outcomes are not pre-programmed and, from a highly interconnected infant brain, specialisations emerge through a dynamic process of epigenesis where the nature of interactions between genes, the brain, behaviour and the environment change throughout development (Karmiloff-Smith, 2007). Thus, the nature of developmental influences and causal chains can change over time, casting doubt on the utility of static models within this field of research. Certainly, modular approaches to developmental disorders, derived from literature on adult acquired brain injury, have faced increasing criticism (Bishop, 1997) with questions raised about the validity of considering disorders as a static collection of strength and impairments. On the other hand, a neuroconstructivist approach posits that small, general differences in constraints on brain development in infancy can lead to the widely varying phenotypic outcomes seen in different developmental disorders as these constraints interact differently with various intrinsic and extrinsic influences on development (Karmiloff-Smith, 1998). Therefore, the emphasis is placed on carefully tracking and understanding development by examining children within a narrow age range at specific points in time and then analysing data using either a trajectory approach (Thomas, Ansari, Jarrold, & Karmiloff-Smith, 2009) or a connectionist modelling approach (Oliver, Johnson, Karmiloff-Smith, & Pennington, 2000). These approaches lose the clarity of the simple visual notation system advocated by Developmental Causal Modelling and require statistical analyses that are methodologically challenging to apply to clinical populations where sample sizes are necessarily small.

Nevertheless, it is clearly important to incorporate recognition of developmental changes over time when considering how best to integrate levels of explanation for developmental disorders.

In an attempt to synthesise both of the above approaches, Moore and George (2011) have recently adapted the Developmental Causal Modelling visual notation system to incorporate an appreciation for the time-course of changing interactions using a framework named ACORNS. They do this by adding a horizontal time axis along which linear or non-linear skill trajectories can be depicted. While this framework becomes rather complex due the addition of notations for rate and variance of development in skills, the addition of a time axis does allow a more developmental approach to causal modelling in developmental disorders. An earlier incarnation of this framework has been applied to modelling social cognition in Down syndrome (Cebula et al., 2010) but it remains to be seen whether this framework can be usefully and widely adopted by researchers looking at the causes of developmental difficulties.

In sum, while there is no universally accepted framework for considering causal models of developmental disorders, most approaches emphasise the interactions between genes, brain, cognition and the environment as critical for understanding development. While Morton (2004)'s Developmental Causal Modelling approach has provided a clear way of depicting these relationships, it's static nature masks the importance of changing causal relationships throughout development, as highlighted by the neuroconstructivist approach (Karmiloff-Smith, 1998). Although there have been recent attempts to adapt developmental frameworks to recognise changes over time, it remains to be seen whether such models can be practically applied to the study of developmental disorders. Bearing in mind the overlap of these frameworks, however, a logical starting point for consideration of the causal mechanisms operating in Down syndrome would be to examine the features of the disorder at the different levels of explanation.

1.3 Cognitive Phenotype in Down Syndrome

Understanding how biology may influence cognitive development in a particular disorder requires a clear overview of what is known about cognition in that disorder in order to guide theory about which biological systems to examine in relation to the disorder. Thus, the literature concerning the cognitive strengths and weaknesses seen in Down syndrome will be summarised to provide a context within which to consider wider developmental influences. The Developmental Causal Modelling approach advocates the

separation of the cognitive and behavioural levels of explanation in development. Morton (2004) argues that this division is important because cognitive processes and behaviours don't map precisely onto one another: a particular behaviour is likely to be explained by multiple cognitive processes and a cognitive process could cause multiple behavioural outcomes. However, as is common in developmental cognitive research, the evidence and conclusions concerning cognitive skills in Down syndrome is largely inferred from behavioural tasks making cognition and behaviour very difficult to separate. Thus, for the present summary, cognition and behaviour will be considered together in order to build a more comprehensive picture of the phenotype commonly seen in children with Down syndrome.

1.3.1 General Cognitive Development

When examining the development of cognitive skills in any developmental disorder, a key consideration is whether the rate and order of acquisition of developmental milestones are merely delayed relative to typical development or are disordered in some way (Hulme & Snowling, 2009). In Down syndrome the sequence in which developmental milestones are acquired is broadly similar to that in typical development but there are certain skill areas, such as expressive language, verbal memory and fine motor skills, which are delayed to a greater extent (Chapman & Hesketh, 2000). This results in a characteristic profile of cognitive strengths and weaknesses. Furthermore, the degree of cognitive delay increases over time as the rate of development in Down syndrome is slower than in typical development. For example, Miller (1988) notes that language delays relative to general developmental level are more frequent in the third than second year of life in a group of children with Down syndrome. Detailing more precisely how the delay in different skill areas progresses in the early years, before the delay becomes too severe, would provide valuable information about the possible nature and timing of effective interventions aimed at remediating skills.

It is important to note that the rate of development and overall skill levels attained vary widely in Down syndrome. For example, while the average IQ of adults with Down syndrome is 50, this can vary from 30 to 70 (Chapman & Hesketh, 2000). Identifying predictors of this variability is a fundamental challenge for researchers in this area. While it is important to bear these individual differences in mind, understanding the apparent consistencies and characteristics of the cognitive phenotype in Down syndrome provides an essential background for making sense of variation between individuals. In general,

language skills are impaired relative to nonverbal ability with additional specific weaknesses in articulation, verbal short term memory and fine motor skill (Silverman, 2007). Social skills and functional day-to day abilities, also known as adaptive skills, remain a relative strength. Development within the key domains of language, nonverbal, motor and social and adaptive skills will be considered in turn in more detail. There will be a particular emphasis on the complexities of the language profile as this is both the most widely researched domain and a central issue for this thesis.

1.3.2 Language Profile

The finding that language skills are impaired relative to nonverbal ability in individuals with Down syndrome is consistent across many studies (e.g. Chapman, Seung, Schwartz, & Bird, 1998; Price, Roberts, Vandergrift, & Martin, 2007 and for reviews see Chapman, 1995; Fowler, 1998). This is true when language is assessed using both objective, behavioural measures and parent-report measures (Fidler, Hepburn, & Rogers, 2006). These delays appear to become more pronounced as children get older (Miller, 1988) although aspects of pre-linguistic communication, such as the emergence of speech sounds and the development of joint attention, are also delayed (Abbeduto, Warren, & Conners, 2007).

However, it is not the case that all language domains are affected uniformly. Many studies have noted that individuals with Down syndrome face greater difficulties with expressive than receptive language (e.g. Fidler et al., 2006; Sigman & Ruskin, 1999). Although the age at which children with Down syndrome say their first word is not always delayed, the rate of spoken expressive vocabulary growth then progresses more slowly, with between 10 and 20% of three- to five-year old children with Down syndrome saying fewer than 10 words, and progression to combining words also delayed (Berglund, Eriksson, & Johansson, 2001). These expressive language delays continue into later childhood and adolescence. For example, Chapman et al. (1998) found that the mean length of utterance (MLU), total number of words and number of different words produced by individuals with Down syndrome during conversational and narrative language samples were significantly reduced compared to controls matched for nonverbal ability.

Vocabulary and morphosyntactic abilities are also affected to different extents with individuals with Down syndrome showing greater impairments in morphosyntax (Berglund et al., 2001; Laws & Bishop, 2003; Vicari, Caselli, & Tonucci, 2000). Individuals with Down syndrome have been found to produce shorter sentences and demonstrate poorer use of

morphological markers compared to nonverbal-ability and vocabulary matched typically developing controls on a variety of measures including parent report (Berglund et al., 2001; Vicari et al., 2000) and objective measures derived from samples of natural language, such as MLU (Laws & Bishop, 2003) and frequency of production of tense markers and inflections (Eadie, Fey, Douglas, & Parsons, 2002).

Across most studies, receptive vocabulary emerges as a relative strength within the language profile in Down syndrome. There is some debate in the literature as to where receptive vocabulary lies within the overall cognitive profile in Down syndrome. Many studies find that receptive vocabulary levels are in line with nonverbal ability (Fidler et al., 2006; Laws & Bishop, 2003), even for the majority of very young children with Down syndrome (Miller, 1988), while others find that receptive vocabulary is weaker (Caselli, Monaco, Trasciani, & Vicari, 2008) or stronger (Chapman, 2006) than nonverbal ability matched controls. These divergent findings could be a result of the various measures of receptive vocabulary used. For example Chapman (2006) suggests that individuals tested with the Peabody Picture Vocabulary Test (PPVT) and its British equivalent may score higher than those assessed with other receptive vocabulary tests due to the high imageability and frequency of items on the PPVT. The different nonverbal measures used to match the groups with Down syndrome and the control groups may also account for some of these divergent findings. However, while there is debate surrounding the extent to which receptive vocabulary is a strength within the overall cognitive profile, the balance of evidence certainly supports the idea that it is the strongest linguistic skill for individuals with Down syndrome.

1.3.2.1 Speech and articulation difficulties

In trying to understand the causes of the language difficulties in Down syndrome, particularly within the expressive domain, the role of speech and articulation problems has been examined. There are anatomical skeletal and muscular differences that influence how well children with Down syndrome are able to produce speech sounds (Leddy, 1999), although neurological control of speech has been proposed as the more important determinant of comprehensible speech (Miller & Leddy, 1999). Poor speech intelligibility is commonly observed in Down syndrome, with Kumin (1994) reporting that over half of children with Down syndrome have difficulty making themselves understood according to parental report. Poor oromotor control is also a contributory factor to speech difficulties (Barnes, Roberts, Mirrett, Sideris, & Misenheimer, 2006). Cleland, Wood, Hardcastle,

Wishart and Timmins (2010) investigated whether speech and oromotor problems were related to the broader language difficulties in 9- to 18-year-old children with Down syndrome. They found that speech and oromotor measures were correlated with each other but not with wider language and cognitive measures, suggesting that the language difficulties in Down syndrome cannot be entirely accounted for by issues with speech and articulation. They also found that articulation errors showed a disordered rather than a delayed pattern, suggesting that speech and phonological development progresses differently in Down syndrome compared to typical development. However, their data are from an adolescent sample and as such, the possibility that speech, articulation and broader language measures are more interdependent in early development cannot be ruled out.

1.3.2.2 Verbal short-term memory and word learning

In line with the pattern seen in the overall cognitive profile, within the domain of memory verbal short-term memory is impaired to a greater extent than visual short-term memory (Brock & Jarrold, 2005). Among individuals with Down syndrome verbal short-term memory deficits have been well replicated (for a review see Jarrold, Baddeley, & Phillips, 1999). Verbal short-term memory has been shown to play a critical role in learning new vocabulary in typically developing children (Gathercole & Baddeley, 1990). Thus, given the slow vocabulary growth in Down syndrome, it seems logical to predict that verbal short-term memory deficits may underlie language learning difficulties. Indeed, verbal short-term memory has been shown to predict receptive vocabulary and grammar comprehension in children with Down syndrome (Laws & Gunn, 2004).

However, somewhat paradoxically, experimental studies of word learning suggest that children with Down syndrome do not have specific difficulties with the immediate acquisition of new vocabulary words. In comparison to typically developing peers matched for language ability, children with Down syndrome show no impairments in the immediate acquisition of verbal labels, as assessed in fast mapping paradigms (Chapman, Kay-Raining Bird, & Schwartz, 1990; Chapman, Sindberg, Bridge, Gigstead, & Hesketh, 2006; Kay-Raining Bird, Chapman, & Schwartz, 2004). Furthermore, in more explicit experimental training studies, individuals with Down syndrome still perform at the same level as language- (Mosse & Jarrold, 2011) or reading-matched controls (Mengoni, Nash, & Hulme, 2013), with only one exception (Jarrold, Thorn, & Stephens, 2009). This is all the more surprising given that the typically developing comparison group tend to have stronger verbal short-

term memory skills meaning that the children with Down syndrome are showing better vocabulary learning than would be expected given their verbal short-term memory capacity (Mosse & Jarrold, 2011). This suggests that poor verbal short-term memory can't fully account for the language problems associated with Down syndrome, although it may be a contributory factor. An open question remains concerning why individuals with Down syndrome show a slow rate of vocabulary growth in the face of relatively unimpaired immediate vocabulary acquisition, at least in experimental settings.

1.3.2.3 Similarities to specific language impairment

In an attempt to gain a further insight into the complex language difficulties in Down syndrome, some researchers have drawn comparisons with the language profile associated with specific language impairment. Specific language impairment is a developmental disorder in which language skills are impaired in the presence of broadly normal nonverbal IQ and in the absence of any known physical, environmental or neurological cause (Bishop, 2006). Similarly to children with Down syndrome, children with specific language impairment tend to have greater difficulty with expressive than receptive language and grammatical skills are more impaired than vocabulary (Laws & Bishop, 2003, 2004; Ypsilanti & Grouios, 2008). These similarities have led to speculation that the language difficulties in Down syndrome may be a type of specific language impairment that is somewhat independent from general cognitive difficulties. Thus, drawing parallels between the two disorders may lead to the discovery of a common causal factor.

However, while on the surface the language profiles share many similarities, studies directly comparing the language abilities of children with Down syndrome and children with specific language impairment have found subtle differences. For example, Laws and Bishop (2003) found that while both groups were impaired at producing grammatical morphemes, the group with Down syndrome were only impaired at producing the regular past tense, whereas the group with specific language impairment were also impaired at producing the irregular past tense. The same pattern was seen for the production of the irregular and regular third person singular in children with Down syndrome (Eadie et al., 2002). Laws and Bishop (2003) speculate that this may be due to the slightly higher vocabulary levels in the group with Down syndrome, as irregular morphemes don't follow a consistent pattern and may be learnt more as isolated, individual vocabulary items. This is supported by the correlation between irregular past tense production and receptive vocabulary found in their study.

As of yet there has been no convincing evidence to suggest that the language problems associated with Down syndrome and specific language impairment share a common causal factor. However, the available research does suggest that perhaps there are features of language, such as grammar and expression, which are more vulnerable than others to a host of risk factors resulting in many surface profile similarities between the two groups (Laws & Gunn, 2004).

1.3.2.4 Summary: language profile

The language profile in Down syndrome has been extensively researched and findings converge to suggest that expressive language is impaired relative to receptive language, and grammatical skills are impaired to a greater extent than vocabulary. However, understanding what underpins the development of this profile has proved more challenging. While poor articulation and poor verbal short-term memory may contribute to aspects of the profile, neither can account fully for the pattern of langauge abilities associated with Down syndrome. Furthermore, while comparisons with SLI have yielded useful observations about the precise nature of the language profile in Down syndrome, they do not provide strong evidence for a unified underlying cause. More research is needed to clarify how the language profile develops over time and what its crucial cognitive underpinnings may be.

1.3.3 Nonverbal Ability

The majority of studies examining language and cognition in Down syndrome make reference to nonverbal ability as a unitary construct observing that, in general, it is a strength relative to language (e.g. Chapman et al., 1998). In comparison to the multitude of studies unpicking the details of the language profile, very few studies have looked at whether different components of nonverbal ability are differentially spared or impaired. To an extent this may be because there is less consistency in the ways that nonverbal ability is fractionated into component skills. However, there is some suggestion that within the nonverbal domain, individuals with Down syndrome may show particular strengths in visuospatial construction skills in comparison to nonverbal reasoning skills (Klein & Mervis, 1999). However, a recent review concluded that visuospatial skills are not a strength relative to general cognitive ability, they are just a relative strength in comparison to areas of particular impairment, such as language (Yang, Conners, & Merrill, 2014). Furthermore, Yang et al. (2014) suggest that in Down syndrome there is a discrepancy in the way that

different visuospatial skills are affected, with greater impairments in visuospatial working memory than sequential spatial memory, for example.

It is also interesting to note that within the nonverbal domain there is some limited evidence of a different, rather than simply delayed, pattern of development relative to typically developing children. Gunn and Jarrold (2004) found that individuals with Down syndrome make different types of errors on the Raven's matrices task compared to typically developing children matched for either task performance or overall mental age. In line with this, Vakil and Lifshitz-Zehavi (2012) also find that the pattern of eye movements made by adults with Down syndrome during the Raven's matrices task differs from matched typically developing controls. Whether these differences reflect a different course of nonverbal development or more fundamental differences in strategy use requires further clarification. In sum, less is known about nonverbal ability in Down syndrome relative to the evidence base about language skills. While it is consistently found that, in general, nonverbal abilities are stronger than language abilities there is emerging evidence that there may be specific strengths and weaknesses within the nonverbal domain itself and it has been speculated that nonverbal development may progress atypically in Down syndrome.

1.3.4 Motor Skills

In addition to cognitive delays, individuals with Down syndrome have delays in both fine and gross motor skills (Connolly & Michael, 1986). The balance of evidence suggests that although there is a delayed rate of motor skill acquisition, motor milestones are usually acquired in the same order as in typical development (Palisano et al., 2001; Tudella, Pereira, Basso, & Savelsbergh, 2011). However, it has been noted that there are greater delays for more complex, later developing motor skills (Palisano et al., 2001; Pereira, Basso, Lindquist, Silva, & Tudella, 2013). Although there has been no systematic investigation into the pattern of motor impairments in Down syndrome, it is generally assumed that fine motor movements are impaired to a greater degree than gross motor movements due to their increased complexity. Indeed, at a functional level individuals with Down syndrome have greater difficulty with activities requiring fine as opposed to gross motor skills (Dolva, Coster, & Lilja, 2004). Furthermore, it is assumed that the motor impairments in Down syndrome are largely a result of the decreased muscle tone (hypotonia) that is an almost universal feature of the disorder (Vicari, 2006). However, the

extent to which this is true has yet to be determined and it is possible that aspects of these motor difficulties actually arise from different, neurological origins.

On the surface it may seem unusual to include motor skills as a domain when examining the cognitive profile. However, there is evidence to suggest that motor and cognitive skills may be related in both typical and atypical populations and at a neural level, it has been posited that this relationship may be mediated by the cerebellum and prefrontal cortex (Diamond, 2000). Furthermore, a recent meta-analysis has found that children with language impairments are more likely to have co-morbid motor difficulties (Rechetnikov & Maitra, 2009). Given the argument that children with Down syndrome have a language impairment, it stands to reason that there is value in examining the role of motor impairments in relation to their linguistic and broader cognitive difficulties as part of the same cognitive profile.

1.3.5 Social and Adaptive Skills

Social and adaptive skills have frequently been highlighted as a strength for individuals with Down syndrome and, indeed, there is a common perception that children with Down syndrome are inherently sociable (see Fidler & Nadel, 2007 for review). In some contexts children with Down syndrome have been shown to have relatively unimpaired nonverbal communication and play skills (Sigman & Ruskin, 1999). Observational studies too, have confirmed that in one-to-one play, the social competence of children with Down syndrome does not differ from matched typically developing controls (Guralnick, Connor, & Johnson, 2011). Social skills in Down syndrome have also been examined within the context of more general adaptive behaviour. Adaptive behaviour is commonly measured using a parent-report interview measure called the Vineland Adaptive Behaviour Scales (Sparrow, Cicchetti, & Balla, 2005). This assesses functioning in four domains: communication, daily living skills, socialisation and motor skills. On this measure, children with Down syndrome show strengths in socialisation relative to communication and motor skills, and sometimes in relation to daily living skills (Dykens, Hodapp, & Evans, 2006; Fidler et al., 2006; Rodrigue, Morgan, & Geffken, 1991).

However, there have been some recent caveats to conclusions of spared social skills in Down syndrome. Guralnick et al. (2011) found that, in comparison to one-to-one play situations, children with Down syndrome showed social impairments in larger group play situations. Furthermore Cebula et al. (2010) review research into the cognitive skills underpinning social competence and note that in several areas of social cognition, such as

emotion recognition, individuals with Down syndrome show impairments. Thus, while the evidence does suggest that social skills are a strength in relation to some of the more stark impairments in Down syndrome, there are still some subtle socio-cognitive weaknesses that bear consideration and may explain why children's social competence differs across varied social contexts. This also highlights the importance of the dissecting the underlying cognitive components of skills within the cognitive and adaptive profile in order to better understand the cognitive difficulties in Down syndrome.

1.3.6 Cognitive Profile in Down Syndrome: A Summary

Much work to date has detailed the cognitive and adaptive profile associated with Down syndrome. Generally speaking nonverbal ability and social skills are strengths in comparison to language and motor skills. However, even within the nonverbal and social domains there are more subtle impairments that may shed light on the cognitive underpinnings of Down syndrome. The language profile is particularly complex, with greater impairments in expressive than receptive language and in grammatical skills than vocabulary. However, efforts to establish what gives rise to this pattern of linguistic impairments have met with mixed success. While verbal short-term memory and articulation impairments may contribute, neither accounts for the full pattern of strengths and weaknesses. Despite surface similarities, studies have failed to confirm that individuals with Down syndrome could be said to have a 'specific language impairment' although they do suggest that expressive language and grammatical skills could be particularly vulnerable language domains. There are elements of delayed and disordered development in all cognitive domains and future studies would benefit from examining the development of the cognitive profile over time in order to gain further insight into the causes of the cognitive difficulties in Down syndrome and distinguish between delayed and disordered development.

1.4 Studying Cognitive Development in Down Syndrome: Longitudinal Designs

The vast majority of studies looking at the cognitive phenotype in Down syndrome have utilised static designs that examine the phenotype at one point in time, averaged across a group that vary widely in age. While this is informative for gaining a broad picture of the cognitive strengths and weaknesses in Down syndrome, the design is not sensitive enough to detect subtle changes that may occur across development or between children of similar ages. For this, studies that focus on children within narrow age bands and follow

participants over time are necessary. Longitudinal designs can also speak to questions about possible causal mechanisms underlying cognitive difficulties in Down syndrome.

There have been relatively few longitudinal studies of cognitive development in Down syndrome. The of these focussed on changes in an overall intelligence or developmental quotient measure (IQ/DQ) (Carr, 1992; Sigman & Ruskin, 1999). These studies found that overall IQ or DQ decreased over time, becoming more homogenous the older the sample became (Sigman & Ruskin, 1999). However, given what is known about the discrepancy between component skills in Down syndrome, using an overall quotient measure provides limited information about precisely what is changing and at what rate. More recently, research has focussed on tracking domain-specific measures of performance over time and sometimes comparing them (Byrne, MacDonald, & Buckley, 2002; Chapman, Hesketh, & Kistler, 2002; Couzens, Haynes, & Cuskelly, 2012; Cupples & Iacono, 2000; Hick, Botting, & Conti-Ramsden, 2005; Hulme et al., 2012). A meta-analysis examining the outcomes of these studies found that scores on tests of phonology and short-term memory improve less over time than tests of receptive language and word reading, in line with findings about the strengths and weaknesses in the static profile (Patterson, Rapsey, & Glue, 2013). However, there were generally raw score improvements across time on all tests.

Patterson et al. (2013) highlight that most existing longitudinal studies utilise small samples of children from a wide age range, making it hard to draw conclusions about how improvements in different skills may vary with age. Chapman, Hesketh and Kistler (2002) used hierarchical linear modelling to analyse individual differences in syntax development in Down syndrome and found that language comprehension improved in younger children but there was evidence of decline in older children. This demonstrates the importance of examining skills at different stages of development rather than taking group averages across wide age ranges. Understanding when the critical periods of development occur in different skill areas will aid in the design of effective interventions. Patterson et al. (2013) also show that there is a lot of overlap in the age ranges studied in longitudinal research of Down syndrome, with most covering middle childhood and adolescence. However, very few include children below the age of five. Given the importance of intervening early to ameliorate educational difficulties, understanding how the cognitive profile in Down syndrome develops in the early years would provide vital information for both researchers and practitioners.

1.4.1 Use of Comparison Groups

There has been much debate over the most appropriate comparison groups to use when examining the cognitive profile in groups with developmental disorders, and the way in which they should be selected. As many disorders are characterised by general cognitive delay, comparisons with age-matched typically developing children are of limited utility as those in the clinical group will be weaker on all variables, making it difficult to look at relative strengths and weaknesses within the profile. Therefore, one approach has been to match an individual from each group on a variable that is thought to provide a good general estimate of intellectual ability in the clinical population. Thus, when performance on another skill is above or below that of the control group, it can be said to be an atypical cognitive strength or weakness. In studies looking at development in Down syndrome, participants are usually matched to the control group on a measure of nonverbal ability as this skill is not thought to be selectively impaired within the cognitive profile. This is known as nonverbal mental-age matching and is a method that has been employed in many similar studies (e.g. Fidler et al., 2006; Hick et al., 2005; Vicari, Caselli, & Tonucci, 2000).

However, problems have been noted with the pairwise matching method (Jarrold & Brock, 2004). In particular, strategic selection of the typically developing controls may result in a group that aren't fully representative of the population from which they're drawn, which could complicate the interpretation of results. This can be avoided if a larger, representative typically developing sample within the appropriate age range are recruited so that there is no significant difference between the group means on the variable of interest but they haven't been explicitly matched (Jarrold, Thorn, & Stephens, 2009). However, Facon, Magis and Belmont (2011) argue that similar group means can result from very different data distributions and variances and individual matching is preferable. One approach that avoids matching groups altogether is analysis of developmental trajectories, as advocated by Thomas et al. (2009), which plots how skills develop over time in a disordered and typically developing group. However, this approach requires a very large sample that spans a wide age range, which is not always feasible.

1.5 The Development of the Cognitive Profile in Down Syndrome: A Summary

Down syndrome is a genetic disorder associated with a unique profile of cognitive strengths and weaknesses primarily characterised by relative strengths in nonverbal ability and social skills and weaknesses in language and motor skills. Neuroconstructivist frameworks of development emphasise the importance of tracing development over time

and examining narrow developmental windows. To date, most of the research into the cognitive profile in Down syndrome has examined one point in time using samples covering a broad age range, making it difficult to draw conclusions about how individual skills develop over time. There is debate over how the cognitive profile should be determined with respect to control group selection. While developmental trajectories can be a novel and informative approach they require large sample sizes and there is still value in designs that match children on an appropriate variable, provided the limitations of this method are acknowledged. Developmental Causal Modelling highlights the importance of studying the cognitive profiles of different developmental disorders. Such frameworks suggest that the best way to understand causal pathways in development is to draw links between biology, cognition and the environment. In order to do this detailed descriptions of cognition throughout development are required and these are best determined through well-designed longitudinal studies focussing on groups of children who are of a similar age.

2 Development of Children with Down Syndrome: Biology and Health

2.1 Genetics of Down Syndrome

In order to better understand causal pathways in developmental disorders, links are often sought between cognition and biology, typically at the level of genetics and brain development (Hulme & Snowling, 2009; Morton, 2004). There has been a recent drive towards understanding the function of certain genes by examining associations between behaviourally defined developmental disorders, such as dyslexia and autism, and genetic variations (Fisher, 2006). However, tracing the relationships backwards from cognition, which can be subject to arbitrary diagnostic cut-offs, results in mixed findings at the genetic level that are difficult to interpret (e.g. Neale et al., 2010). A disorder such as Down syndrome provides a relatively unique opportunity to look at the relationship in the 'forwards' direction, as its clear genetic origins allow speculation about the function of a specific chromosome through a detailed understanding of the cognitive phenotype. Down syndrome is caused by an extra, third copy, of chromosome 21. In around 95% of individuals there is trisomy of the full chromosome but a small number of cases also result from partial trisomy (Patterson, 2007).

Despite understanding the basic genetic cause of Down syndrome, it has been more challenging than one might expect to draw conclusions about the function of chromosome 21. There is still some disagreement about the mechanism by which trisomy 21 results in the characteristic phenotypic outcomes (for a review see Contestabile, Benfenati, & Gasparini, 2010). One leading theory is known as the "dosage imbalance hypothesis" which posits that the increased expression of specific genes on chromosome 21, some of which are dosage-sensitive, results in the characteristic phenotype associated with Down syndrome (Korenberg et al., 1990). However, there is a contrasting proposal known as the "genetic homeostatic hypothesis", which states that triplication of any genetic material, not necessarily specific to chromosome 21, can result in altered gene expression at a wider level that could explain the phenotype (Shapiro, 1983). More recently, a combined view has been favoured, which attributes some aspects of the phenotype to gene dosage effects that are specific to chromosome 21 and others to more general effects of genetic triplication (Roper & Reeves, 2006). Understanding genotype-phenotype relationships in Down syndrome is further complicated by the moderating effects of other genes that are inherited from parents, just as in the typical population (Patterson, 2007). Thus, while there has been much progress in identifying small, critical

regions of chromosome 21 that are linked in key ways to the phenotype in Down syndrome (Lana-Elola, Watson-Scales, Fisher, & Tybulewicz, 2011), there is still much work to be done to understand the complex genetic background that results in the cognitive phenotype described in the previous chapter.

2.2 Brain Development in Down Syndrome

Another avenue of research has explored the biological basis of Down syndrome in terms of underlying neuroanatomical abnormalities. Some of these will be, in part, due to the genetic origins of the disorder. However, it is important to remember that the brain develops in structure and function throughout an individual's lifespan and is influenced by gene-environment interactions. Therefore, the neuroanatomy in Down syndrome will not be the result solely of trisomy 21 but will also depend on individuals' experienced environmental factors (Karmiloff-Smith, 2007). There is a great deal of variability in the way that the brain develops between individuals with Down syndrome, similarly to cognitive skills. However, there are some consistent patterns of brain abnormalities that have emerged.

During prenatal development and in the first few months of postnatal development, there are minimal differences in the brains of infants with Down syndrome compared to typically developing infants, although they tend to be at the bottom end of the average range on some measures, such as myelination (for a review see Fidler & Nadel, 2007). However, as development progresses clear differences emerge. Children and adults with Down syndrome tend to show reduced brain volume, which particularly affects the hippocampus and the cerebellum (Aylward et al., 1999; Carducci et al., 2013; Pinter et al., 2001; Pinter, Eliez, Schmitt, Capone, & Reiss, 2001).

These neuroanatomical differences are consistent with the cognitive difficulties associated with Down syndrome. The importance of the cerebellum for both motor and higher cognitive functions has been highlighted (Diamond, 2000). Its potential importance for linguistic skills, particularly grammatical ability and speech production, has also been noted (Silveri, Leggio, & Molinari, 1994) and thus there has been speculation that smaller cerebellar volumes in Down syndrome could be linked to the impairments that are typically seen in the motor and linguistic domains (Pinter et al., 2001).

Reduced hippocampal volumes, too, are in line with the performance of children with Down syndrome on neuropsychological tests. The hippocampus plays an important

role in learning and memory. Pennington, Moon, Edgin, Stedron and Nadel (2003) gave 28 children with Down syndrome a battery of tests that tapped hippocampal and prefrontal functions. They found that the children with Down syndrome were specifically impaired on the hippocampal, but not prefrontal, tests compared to typically developing children matched for nonverbal ability. More recent work has found impairments in executive functions that rely on the prefrontal cortex (Lanfranchi, Jerman, Dal Pont, Alberti, & Vianello, 2010; Rowe, Lavender, & Turk, 2006) indicating that there are functional deficits in both the hippocampus and the prefrontal cortex in Down syndrome.

The neural mechanisms underlying these brain deficits have been explored. It is widely accepted that, particularly during early development, individuals with Down syndrome generate fewer new neurons, a process known as neuronal genesis (Contestabile et al., 2010; Guidi et al., 2008). There is also evidence that in some areas of the brain, such as the hippocampus, there is a higher than expected rate of cell death in Down syndrome (Guidi et al., 2008). Furthermore, abnormalities in neuronal dendrites and synapses have been noted (e.g. Takashima, Iida, Mito, & Arima, 1994). However, the process by which these neuronal abnormalities lead to the characteristic functional impairments seen in Down syndrome remains unknown.

In general it is difficult to draw definite conclusions about causal pathways from brain abnormalities to cognitive impairments in Down syndrome. Although structural brain differences have been noted which align logically with difficulties in cognitive skills that are known to depend on those brain regions, very few studies have looked directly at the relationship between structural and functional impairments. A recent study by Menghini, Costanzo and Vicari (2011) aimed to address this by correlating grey matter volumes in different brain regions with performance on cognitive tests. They replicated findings that overall brain volume is reduced in Down syndrome alongside notable reductions in hippocampal, cerebellar and temporal brain regions. They found that there were many positive correlations between brain volume and cognitive functioning but that these were not always in the expected regions, particularly for linguistic skills, suggesting that brain organisation may differ in some ways in Down syndrome. For example, grey matter density in the bilateral orbitofrontal cortex was related to verbal memory amongst the adults with Down syndrome on tasks that do not usually recruit these brain areas in the typical population. While this study is one of the first to link neurological and cognitive findings in Down syndrome, it is important to note that causal links cannot be drawn from such a

design. It is possible that differences in cognition and the environment across development influence factors that affect brain volume rather than the reverse. The study was conducted on adolescents at one point in time but longitudinal studies with a younger sample would be necessary to answer questions about causality.

In sum, recent technological advances have enabled examination of brain differences across development in Down syndrome. Most of these have focussed on structural differences, finding reduced brain volumes overall and in specific areas; most notably in the cerebellum and hippocampus. It is not clear what underlies these differences at the neuronal level although reductions in neuronal genesis and increases in cell death may contribute. Elucidating the links between these structural impairments and cognitive difficulties is complex and although associations have been shown between reduced brain volumes and cognitive impairments, there is not yet evidence to support the interpretation that this link is causal. However, there are many promising avenues of research for future studies to explore using longitudinal designs.

2.2.1 Alzheimer's Disease

There is one cognitive consequence of Down syndrome that has provided a unique opportunity for researchers to make clear connections between genetic, neurological and behavioural features of the disorder. Rather strikingly, evidence suggests that all individuals with Down syndrome over the age of 35 develop neuropathological features associated with Alzheimer's disease (Nieuwenhuis-Mark, 2009). However, not all will go on to develop the clinical symptoms of dementia although the estimates as to what proportion do develop the full pathology ranges from 7 to 50% (Zigman, Schupf, Sersen, & Silverman, 1996). There are difficulties associated with establishing criteria for diagnosing dementia in a population that suffers from intellectual disability, which may account for the differing estimates (Nieuwenhuis-Mark, 2009). However, in those that go on to develop the full pathology of Alzheimer's disease there are many common behavioural features to those with the disease in the typical population such as confusion, impairments of recent memories and forgetfulness (Deb, Hare, & Prior, 2007).

At the neurobiological level, Alzheimer's disease is characterised by a build up of β-amyloid deposits known as Aβ plaques and an accumulation of neurofibrillary tangles (Glenner & Wong, 1984; Lee & Trojanowski, 1992). The Aβ plaques are derived from a protein (β-amyloid precursor protein) which is encoded in a gene on chromosome 21 (Goate et al., 1991). Individuals with Down syndrome therefore have an extra copy of this

gene and as a result nearly all will show evidence of these plaques by the age of 30 (Wisniewski, Ghiso, & Frangione, 1994). Furthermore, there are correlations between the number of these plaques and the severity of the cognitive symptoms associated with Alzheimer's disease (Contestabile et al., 2010). Thus, research into Down syndrome has informed research into Alzheimer's disease and vice versa helping to disentangle the complex relationships between genes, brain and cognition in both disorders. The links between the domains may not always be so straightforward but these findings emphasise the importance of looking for causal connections between biology and cognition.

2.3 Health in Down Syndrome

Alzheimer's disease has clear links with cognition given its neurological origins and perhaps this is why researchers have looked at the disease to draw links between health, biology and cognition in Down syndrome. However, individuals with Down syndrome are at an increased risk for many other health conditions that don't have a neurological basis (Roizen & Patterson, 2003). It is plausible to predict, based on evidence from typical populations, that non-neurological health problems can still have an impact on cognitive skills and as such it is surprising that there is so little research investigating the influence of health on cognitive development in Down syndrome.

2.3.1 Overview of Health Status

To date several large-scale studies have investigated the nature of health difficulties associated with Down syndrome (Roizen et al., 2014; Schieve, Boulet, Boyle, Rasmussen, & Schendel, 2009; Schieve, Boulet, Kogan, Van Naarden-Braun, & Boyle, 2011; Turner, Sloper, & Adrian, 1990; Yam et al., 2008). These studies highlight the increased risk of cardiovascular, gastrointestinal and respiratory problems, hypothyroidism, diabetes and celiac disease in Down syndrome. There is a particularly elevated risk of congenital heart defects with around half of infants with Down syndrome affected (Freeman et al., 1998; Roizen et al., 2014). In the majority of cases these present as a type of septal defect, affecting the wall of tissue between the two sides of the heart (Freeman et al., 1998; Yam et al., 2008). Visual and hearing difficulties are also very commonly reported (Marcell & Cohen, 1992; Turner et al., 1990). An emerging literature has also established a high incidence of sleep disorders in individuals with Down syndrome (Carter, McCaughey, Annaz, & Hill, 2009; Levanon, Tarasiuk, & Tal, 1999). Perhaps unsurprisingly given the range of health problems associated with Down syndrome, there are higher rates and lengths of hospitalisations among those with Down syndrome compared to those without (Hung, Lin,

Wu, & Lin, 2011; So, Urbano, & Hodapp, 2007). In sum, individuals with Down syndrome suffer a greater number and range of health problems than the typically developing population, which has a negative impact on their daily functioning (Schieve et al., 2011).

2.3.2 Links Between Health and Cognition

While health is not explicitly part of the Developmental Causal Modelling approach (Morton, 2004), it clearly has influences at both the biological and environmental levels of explanation. Consequently, in populations where health is a particular issue, there is value in examining whether it plays a role in the causal pathway of cognitive difficulties. In this section, specific health concerns associated with Down syndrome and their possible links to cognition in both those with Down syndrome and other populations will be reviewed in turn. One study has looked very generally at the relationship between health and cognition in Down syndrome. Määttä, Kaski, Taanila, Keinänen-Kiukaanniemi, and Iivanainen (2006) found a positive correlation between the weight of hard-copy medical records and the severity of intellectual disability. While this indicates that health and cognition are related in Down syndrome, the measures used were very broad and cannot answer questions about which aspects of health are interacting with which aspects of cognition. Health concerns need to be broken down into component parts in order to address this issue.

2.3.2.1 Congenital heart defects

There is a growing body of evidence to suggest that children born with congenital heart defects, even in the absence of other health or developmental problems, have poorer neurocognitive skills in some areas despite overall IQ generally being in the low-average range (Miatton, De Wolf, François, Thiery, & Vingerhoets, 2006). Weaknesses are more pronounced in the motor domain, particularly in early childhood (Snookes et al., 2010), although there is still evidence of psychomotor difficulties at eight years of age (Bellinger et al., 2003; Miatton, De Wolf, François, Thiery, & Vingerhoets, 2007). It has been proposed that general motor slowness underpins these difficulties as opposed to problems with motor planning or control (van der Rijken, Hulstijn, Hulstijn-Dirkmaat, Daniëls, & Maassen, 2011). Language and executive control weaknesses have also been noted in children with congenital heart defects (Bellinger et al., 2003; Miatton et al., 2006; Miatton et al., 2007). Children who take part in these studies have typically undergone early surgical intervention. However, recent evidence suggests that neurocognitive impairments are also seen in children who are still awaiting surgery indicating that it is not surgery per se that is causing these difficulties (van der Rijken et al., 2010). In fact, the precise mechanisms that

link heart defects and neurocognitive impairments are still unclear but common genetics, prenatal brain abnormalities and environmental factors have all been discussed (Majnemer et al., 2009).

In Down syndrome, despite the known motor and language weaknesses, only two studies have investigated the link between such difficulties and the congenital heart defects that so many children are born with. Visootsak et al. (2011) found that a group of 12 one-year-old children with Down syndrome who were born with an atrioventricular septal defect (AVSD) performed significantly more poorly on the motor composite of the Bayley Scales than a group without heart defects. Although the differences did not reach significance, they also achieved lower scores on the language and general cognitive sub-scales. In a second study Visootsak, Hess, Bakeman and Adamson (2013) found that a different group of two- to three-year-old children born with Down syndrome and a congenital heart defect were significantly weaker on some parent-report measures of language and showed a trend towards weaker language scores on the Mullen's Scales than those born without a heart defect. The group with heart defects also showed lower scores on the visual and motor subdomains of the Mullen's Scales but the differences between the groups were smaller than on the language tests. Taken together, these studies suggest that having a congenital heart defect can put children with Down syndrome at greater risk of cognitive difficulties and the domains that are most affected are language and motor skills. Future research would benefit from examining whether these group differences continue throughout development and whether any other health or cognitive factors might be mediating the relationship between heart defects and cognitive difficulties.

2.3.2.2 Sleep problems

The links between sleep and cognition are well established in both adults and children. Sleep apnoea is a condition characterised by pauses in breathing during sleep and is a common concern for children with Down syndrome (Levanon et al., 1999; Shott et al., 2006). In children who are otherwise developing typically, sleep apnoea and other types of sleep-disordered breathing are related to cognitive difficulties, particularly in the domains of attention and memory (Blunden & Beebe, 2006; Blunden, Lushington, Kennedy, Martin, & Dawson, 2000; Gottlieb et al., 2004). However, despite showing weaknesses relative to controls, performance on cognitive tests still tends to be within the average range for their age, suggesting that any cognitive difficulties are subclinical.

There is some evidence that in adolescents and adults with Down syndrome, those who suffer from sleep apnoea have greater cognitive difficulties. A small scale study by Andreou, Galanopoulou, Gourgoulianis, Karapetsas and Molyvdas (2002) assessed the nonverbal ability of twelve adults with Down syndrome using the Ravens Progressive Matrices (RPM) and looked at the relationship with night time sleep apnoea. They found that the average number of apnoeas an individual with Down syndrome suffered within an hour was negatively related to their RPM score, but only on item set A, which specifically taps visuoperceptual skills through pattern completion. However, no sleep measures were related to the sets assessing analogic reasoning. Furthermore, Chen, Spanò and Edgin (2013) found that caregiver reports of sleep apnoea were related to executive functioning in adults with Down syndrome, particularly tasks of verbal fluency and inhibition. Thus, although causation cannot be inferred, there is evidence of relationships between sleep apnoea in Down syndrome and both executive function and visuoperceptual skills in adults. A recent study by Breslin et al. (2014) extended these research questions to children, rather than adults, with Down syndrome and included linguistic measures in their cognitive assessment. They found that 9-year-old children with Down syndrome who suffered sleep apnoea had significantly lower verbal IQ and showed executive functioning difficulties. Although these research designs cannot determine causality, there is evidence of an association between sleep apnoea and certain cognitive abilities in Down syndrome, which bears further consideration. It is not yet known how early in development these associations may emerge or if the link is underpinned by the apnoea events per se or the consequent differences in overall sleep architecture.

The precise nature of the link between sleep and cognition has been a question of great interest and there is mounting evidence that sleep plays an active and crucial role in memory consolidation processes (Stickgold, 2005). In typically developing adults and children sleep is linked to improvements in recall for many types of information, particularly explicit, factual information (declarative memory) (Backhaus, Hoeckesfeld, Born, Hohagen, & Junghanns, 2008; Diekelmann, Wilhelm, & Born, 2009; Wilhelm, Metzkow-Mészàros, Knapp, & Born, 2012). To add further weight to these findings, children with sleep difficulties, either with (Prehn-Kristensen et al., 2011) or without (Kheirandish-Gozal, de Jong, Spruyt, Chamuleau, & Gozal, 2010) comorbid developmental disorders, show impairments in consolidating declarative information. Vocabulary learning is often conceptualised as a type of declarative learning task and, indeed, in both children and adults sleep has been shown to have an essential role in consolidating memories of

new words and establishing them as part of the 'mental dictionary' (Dumay & Gaskell, 2007; Henderson, Weighall, Brown, & Gaskell, 2012). As reviewed in section 1.3.2.2, children with Down syndrome do not show the expected weaknesses in the immediate acquisition of new vocabulary, particularly given the extent of their verbal difficulties. Therefore, it is plausible to predict that the verbal difficulties may be related to difficulties in consolidating new vocabulary over time, instead, particularly given the sleep difficulties often associated with Down syndrome. This hasn't yet been investigated experimentally but would be an interesting avenue for future research that is trying to specify the mechanisms that link sleep and cognitive impairments in Down syndrome.

2.3.2.3 Hearing impairments

Children with Down syndrome are at a much higher risk of developing hearing losses, typically transitory conductive losses due to frequent ear infections (Marcell & Cohen, 1992; Shott, Joseph, & Heithaus, 2001). Prevalence estimates range between 40% and 80% (Laws & Hall, 2014). There has been some debate surrounding the extent to which these hearing problems contribute to cognitive difficulties, particularly in the linguistic domain. Evidence suggests that childhood middle ear infections associated with fluctuating hearing loss, known as otitis media, are unrelated to typical language development (Roberts, Rosenfeld, & Zeisel, 2004). However, given the language impairment associated with Down syndrome, it is possible that the relationship between hearing and language could differ in this population.

Several studies with a focus on the language profile in Down syndrome have assessed the relationship between hearing levels (measured either through audiometry or a speech discrimination task) and language or other cognitive tasks. Some find that there is no relationship between hearing levels and receptive language (Abbeduto et al., 2003; Marcell & Cohen, 1992; Miolo, Chapman, & Sindberg, 2005) whereas others find a significant but relatively weak association (Chapman, Schwartz, & Bird, 1991; Jarrold & Baddeley, 1997; Laws & Gunn, 2004). The findings are similarly inconsistent when expressive language is used as the outcome measure (Chapman, Seung, Schwartz, & Kay-Raining Bird, 2000; Laws, 2004 vs. Cairns & Jarrold, 2005; Jarrold & Baddeley, 1997). However, the majority of these studies excluded children with moderate to severe hearing loss, a strategy which may artificially diminish the strength of the relationship between hearing and language development. Furthermore, these studies are conducted with older

children and adults and only take into account hearing levels at the time of language assessment.

The fluctuating nature of hearing difficulties, and their increased prevalence in the early years, invites questions concerning the role of more general hearing history in early childhood, which is a key period for language development. In order to address this issue, Laws and Hall (2014) collected the hearing histories from ages 2 to 4, retrospectively, of 41 children with Down syndrome and related them to later language abilities. Children were allocated to the hearing impaired group (N=16) if they had a history of serious or non-fluctuating hearing problems or had required grommets or hearing aids. Otherwise they were allocated to the non-hearing impaired group (N=25). The group with hearing difficulties performed significantly worse on tests of both receptive and expressive language even once age and nonverbal ability were accounted for. Thus, while there is mixed evidence about the contribution of concurrent hearing difficulties to the language abilities of older children and adults with Down syndrome who have mild or possibly fluctuating hearing loss, childhood hearing history may relate to later language difficulties.

2.3.3 Health in Down Syndrome: A Summary

Alongside cognitive impairments, individuals with Down syndrome are also at an increased risk of a wide array of health problems across the lifespan. Almost half of individuals will suffer a congenital heart defect, the majority will also experience hearing losses and frequent hospitalisations and then, in middle age, many will also experience symptoms of Alzheimer's disease. With the exception of research into Alzheimer's disease in Down syndrome, there is relatively little research exploring the impact that these health concerns may have on cognitive development. There is some tentative evidence that health in a very general sense is linked to degree of intellectual disability (Määttä et al., 2006) and some small scale studies suggest that congenital heart defects may impact on early language and motor skills (Visootsak et al., 2013; Visootsak et al., 2011). There is also evidence to suggest that a childhood history of hearing problems and sleep apnoea may be related to aspects of cognition. However, the field lacks comprehensive investigations attempting to link multiple health and cognitive factors within the same sample to determine the nature of the relationship between health and cognition.

2.4 The Role of Biology and Health in Development in Down Syndrome: A Summary

The genetic origins of the disorder and the well-established associated neural abnormalities highlight the central role of biology in understanding development in Down syndrome. Developmental Causal Modelling approaches advocate drawing links between genes, brain and cognition. In Down syndrome, these links are currently clearest in research on Alzheimer's disease. Trisomy of chromosome 21 results in a build up of β-amyloid deposits in the brain, which consequently results in cognitive symptoms associated with dementia in many individuals. This example highlights the advantages of synthesising research findings across the biological and cognitive levels of explanation. There is a growing body of evidence showing that individuals with Down syndrome suffer from a range of health complaints. However, research attempting to link health factors to cognitive factors is much less common. Within the Developmental Causal Modelling framework, health could have potential influences at both the biological and environmental levels. While the biological influences are more intuitive, given that health problems often impact on basic biological functions, poor health can also result in environmental differences (for example if children stay at home rather than go to school, or are frequently in hospital), which would also be considered important within the framework. Thus, there is theoretical as well as practical interest in determining the ways in which health and cognition might interact in Down syndrome. There is some evidence to suggest that health may explain some of the variability in certain cognitive outcomes in Down syndrome although more research is certainly required to unpick the nature of the relationship. If health factors were found to be important for cognitive development, it could help to identify children at risk of the greatest degree of cognitive impairment as well as informing theories about how and why certain cognitive strengths and weaknesses emerge in Down syndrome.

2.5 Research Aims

The overarching aim of this thesis was to investigate the development of cognitive and linguistic skills in individuals with Down syndrome and examine the role of health factors in accounting for variability between individuals. This question was addressed through three primary research aims.

2.5.1 Development of the Cognitive and Adaptive Profile in Young Children with Down Syndrome

Previous research has established that individuals with Down syndrome have language and motor weaknesses in comparison to nonverbal ability and, in terms of adaptive functioning, show strengths in social skills in comparison to language, motor and daily living skills (Chapman & Hesketh, 2000). However, this profile has largely been determined using studies that investigated abilities at one point in time and utilised a sample that varied widely in age and consisted primarily of older children and adolescents. The difficulties in drawing conclusions about the development of different skill areas from such study designs has been noted and longitudinal studies focussing on narrow periods of development have been advocated (Patterson et al., 2013). Such an approach would be compatible with frameworks for considering atypical development, most of which emphasise the importance of carefully documenting how the development of different skills changes over time.

To address these gaps in the research literature, the central study in this thesis investigated the development of cognitive and adaptive skills in four- to five-year-old children with Down syndrome longitudinally over the course of fifteen months. In this way, detailed descriptions of cognition and adaptive behaviour could be drawn for this age group to inform developmental models of Down syndrome. Cognitive and adaptive performance was compared to a typically developing group of children matched for nonverbal ability in order to determine the pattern of cognitive and adaptive strengths and weaknesses in Down syndrome. Inclusion of this control group also allowed consideration of whether the relationships between different skill areas over time were similar for children with Down syndrome and those with typical development.

In the extant literature, parent-report and objective cognitive measures are often used interchangeably to draw conclusions about the cognitive and adaptive profile in Down syndrome. However, the comparability of these two methods of assessment has not yet been established. A further novel aim of this thesis was to compare the utility of parent-report and objective measures in assessing the cognitive and adaptive skills of young children with Down syndrome, a question which is relevant to both researchers and practitioners.

2.5.2 The Relationship Between Health and Cognition in Down Syndrome

The wide array of health conditions that are associated with Down syndrome have been well established (Roizen & Patterson, 2003). Models of development that emphasise the links between biology and cognition suggest that there would be value in exploring the links between health and cognition. However, there have been limited attempts to do this for Down syndrome. This is surprising given the variability in cognitive outcomes seen in the disorder and the potential for health variables to account for some of this variability. There is evidence to suggest that broad, indirect measures of health are related to overall level of cognitive impairment in Down syndrome (Määttä et al., 2006). More specific investigations have found evidence of cognitive weaknesses in children with Down syndrome who also have a congenital heart defect, childhood history of hearing difficulties or sleep apnoea (see section 2.3.2 for a review). However, no investigation to date has looked in a more integrated way at the relationships between health and cognition.

This thesis aimed to investigate the relationships between cognitive skills and each of these different health factors in children with Down syndrome. This was primarily addressed through the central longitudinal study by interviewing parents about their child's medical history and then relating this to children's cognitive and adaptive assessment results. This is the first study to look comprehensively at the potential links between health and cognition in young children with Down syndrome, within a narrow age range.

2.5.3 The Nature of the Language Impairment in Down Syndrome

The complex nature of the linguistic difficulties in Down syndrome has drawn considerable research interest. It is well established that individuals with Down syndrome tend to have weaknesses in expressive compared to receptive language and in grammatical skills compared to vocabulary (Abbeduto et al., 2007). However, the emergence of this profile has not been thoroughly investigated using young samples within a narrow age range and following children over time. This thesis addressed this question in the central longitudinal study, looking in detail at the language profile and how it developed between the ages of four- and six-years-old. A further aim was to examine the relationships between language and other domains of functioning to see if there were any differences that could inform theories about language development in Down syndrome, in comparison to typical development.

One puzzling aspect of the language impairment in Down syndrome is reconciling findings about word learning with findings of slow vocabulary growth (see section 1.3.2.2).

Individuals with Down syndrome are relatively unimpaired at immediately acquiring novel labels for novel items and, in fact, can perform such tasks at a level beyond that expected given their verbal short-term memory, even in the expressive domain (Mosse & Jarrold, 2011). However, despite this preserved ability, expressive vocabulary remains a weakness in the language profile. Thus, it is possible that poor long-term consolidation of new vocabulary learning underpins these difficulties. This hypothesis gains indirect support from evidence of sleep difficulties in Down syndrome given the well-established importance of sleep for vocabulary consolidation in typically developing children (Henderson et al., 2012). Thus, a final study aimed to draw together two of the central concerns in this thesis; health and the language profile in Down syndrome. Consolidation of vocabulary in Down syndrome was investigated in an experimental context and possible links with sleep difficulties were explored with the intention of clarifying the nature of the language impairment in Down syndrome and the possible role of sleep disorders.

2.5.4 Overall Thesis Structure

In a comprehensive, novel investigation of cognitive and adaptive development in young children with Down syndrome, a longitudinal study examined development over fifteen months in four- to five-year-old children with Down syndrome. As part of this longitudinal study parent-report and objective assessment methods were compared and the impact of health on cognition was explored. Detailed descriptions of the language profile in the early years were obtained. A separate experimental word learning study investigated vocabulary consolidation in Down syndrome and the potential role that sleep difficulties might play. The results of these studies will inform developmental models of Down syndrome by detailing the development of cognitive, adaptive and linguistic skills over a specific period of time. This thesis also provides the first comprehensive investigation of the links between health and cognition in Down syndrome, both in a general sense and in the more specific context of the role that sleep difficulties might play in vocabulary consolidation.

3 Longitudinal Study Investigating the Cognitive Profile in Young Children with Down Syndrome

3.1 Introduction

3.1.1 The Cognitive Profile in Down Syndrome

As discussed in Chapter 1, evidence indicates that there is a unique and uneven cognitive profile in Down syndrome. Understanding the development of this specific pattern of cognitive strengths and weaknesses is important for informing theoretical models of cognitive development in Down syndrome and for establishing effective age-appropriate interventions. On the whole, individuals with Down syndrome show weaknesses in language and motor skills compared to nonverbal ability (Chapman, Seung, Schwartz, & Bird, 1998; Pueschel, Gallagher, Zartler, & Pezzullo, 1987; Vicari, 2006). However, skills within the language domain are not uniformly affected with relative strengths in receptive language compared to expressive language and in vocabulary compared to morphosyntactic skill (Abbeduto et al., 2007). This pattern tends to be based on group averages and the majority of research has been conducted with older children and adolescents. Thus, relatively little is known about the emergence of this cognitive phenotype and how it varies at the individual level.

One study has looked at the full cognitive profile in Down syndrome in the early years. Fidler, Hepburn and Rogers (2006) administered the Mullens Scales of Early Learning to eighteen two- to three-year-old children with Down syndrome, alongside a typically developing control group matched for nonverbal mental age and a group of age-matched children with different developmental delays. They found that the toddlers with Down syndrome, as a group, showed evidence of the characteristic profile of strengths and weaknesses, with difficulties in expressive language and motor control when compared to nonverbal ability. However, at this age, the differences were small and the profile was not statistically distinct from the control groups, perhaps in part because it is difficult to assess nonverbal and language ability at such a young age. The authors conclude that at this stage the phenotype is ‘emerging’.

While Fidler et al. (2006) provide a useful analysis of the profile in the early years, the profile is examined at only one time point and so cannot provide information about how skills develop beyond that. Longitudinal designs are considered more informative as they allow the development of skills to be mapped over time (Thomas et al., 2009).

Longitudinal studies of cognitive development in Down syndrome have tended to focus on middle to late childhood and use samples that vary widely in age (for a review see section 1.4 and Patterson, Rapsey, & Glue, 2013). Patterson et al. (2013) recommend that future studies focus on narrower age bands in order to provide more detailed descriptions about developmental progress at different stages. They state that it is only through precise descriptions of cognition at different ages that educational interventions can be properly and effectively evaluated. In line with these recommendations, the present study will track the cognitive development of a group of four- to five-year-old children with Down syndrome over fifteen months.

3.1.2 Cognitive Variability in Down Syndrome

Comparisons at the group level are very important for establishing consistencies in the cognitive profile in Down syndrome. However, this approach often ignores variability between participants. There have been suggestions that variability in the level of cognitive attainment amongst individuals with Down syndrome is substantial (Patterson et al., 2013; Silverman, 2007). However, little research has examined whether the profile of relative cognitive strengths and weaknesses is also variable across the population. Tsao and Kindelberger (2009) aimed to address this question in a sample of 88 six- to eleven-year-old children with Down syndrome. They looked specifically at the relationship between a nonverbal and a language composite. Using cluster analysis they found that participants were fairly evenly distributed between four clusters. Two clusters showed the typical profile for individuals with Down syndrome, with language skills weaker than nonverbal ability but one group had a higher overall ability than the other. However, another cluster showed the reverse pattern, with stronger language than nonverbal skills, and participants in the final cluster did not show a difference between the domains. Although these findings require replication they indicate that not all children with Down syndrome show the same cognitive pattern, despite the consistent profile that emerges at the group level. This could have implications for drawing strong links between cognition and other domains such as the environment and health on the basis of the average profile. It also highlights the need for research that examines factors which predict this variability between individuals.

3.1.3 Relationship Between Grammar and Vocabulary

Longitudinal studies provide a unique opportunity to look at how different skills relate to each other across development. The language profile in Down syndrome raises several interesting questions, which can be addressed using longitudinal designs. For

example, the impairment in grammar relative to vocabulary in Down syndrome (Chapman et al., 1998; Vicari, Caselli, & Tonucci, 2000) could signal different developmental pathways for these skills in comparison to typical development. In typical early language acquisition there are moderate to strong correlations between vocabulary and grammatical skill (Bates & Goodman, 1997; Dale, Dionne, Eley, & Plomin, 2000; Dionne, Dale, Boivin, & Plomin, 2003). It has been widely suggested that early grammar development builds on a critical mass of vocabulary words in a process known as lexical bootstrapping (Bates & Goodman, 1997). However, while this may still hold true, more recent evidence has indicated that between the ages of 2 and 3 the relationship between vocabulary and grammar is actually bidirectional, indicating that lexical and syntactic bootstrapping are occurring simultaneously (Dionne et al., 2003; Moyle, Ellis Weismer, Evans, & Lindstrom, 2007). The authors interpret these findings as suggesting that general linguistic brain processes are more likely to be operating than distinct modules for grammar and vocabulary in early language development.

In Down syndrome, the relationship has been much less extensively studied. However, research with four- to seven-year-old children with Down syndrome has found significant correlations between measures of vocabulary and grammar, both from parental report and from analysis of speech during play, suggesting that the two skills are not entirely independent (Vicari, Caselli, Gagliardi, Tonucci, & Volterra, 2002; Vicari et al., 2000; Zampini & D'Odorico, 2011). No studies have yet investigated these relationships longitudinally. Moyle et al. (2007) showed that, in a sample of late talkers, there was still a co-occurrence of lexical and syntactic bootstrapping, but at a later point in development than for typically developing children. It is possible that, given their delays in vocabulary production, children with Down syndrome would show a similar pattern. Alternatively, it is also possible that even if concurrent relationships between grammar and vocabulary are seen in Down syndrome, their apparent dissociation in the overall language profile may indicate atypical, independent developmental pathways and thus there would be a weaker relationship between them over time.

3.1.4 Relationship Between Language, Nonverbal and Motor Ability

Another indirect way to address the question of whether the cognitive deficits seen in Down syndrome are more likely to arise from selective impairments or more general constraints on development is to examine whether development in the language domain relates more or less strongly than expected to development in other skill domains. An

example of one such relationship would be that between language and nonverbal ability. In early typical development there tends to be modest correlations between language and nonverbal ability and, while the simple correlations remain fairly stable, there is evidence that between the ages of 2 and 4 these two domains exhibit an increasing degree of overlap at the genetic level (Price, Dale, & Plomin, 2004). Thus, in typical development, language and nonverbal ability are not entirely dissociable. However, it is not yet clear how these skills relate in individuals with Down syndrome. Van der Schuit, Segers, van Balkom and Verhoeven (2011) found that nonverbal ability was a significant longitudinal predictor of both syntactic and vocabulary development between the ages of 4 and 5 in a group of heterogeneous children with intellectual disabilities, but not in an age matched typically developing group. Furthermore, Estigarribia, Martin and Roberts (2012) found that nonverbal mental age was a significant predictor of concurrent syntax in a sample of older children with Down syndrome and Fragile X syndrome. However, Chapman et al. (2002) addressed this question specifically for Down syndrome and found that nonverbal pattern construction ability was not a predictor of syntactic development. Thus, further research is needed to specify whether the relationship between nonverbal and language ability differs in Down syndrome compared to typical development.

There have also been suggestions that motor ability may be linked to language skills. Motor ability and cognitive skills are typically studied separately but there is some recognition that there are interrelationships between them in the typical population, perhaps in part because of shared neural substrates (Diamond, 2000). Furthermore, motor difficulties are more common than expected in children that have language difficulties, suggesting that these two domains may be more strongly linked in such populations (Hill, 2001). Thus far no known studies have looked at the relationship between motor and language ability in Down syndrome despite co-occurring impairments in both areas.

3.1.5 Aims of the Current Study

The current study aimed to examine the cognitive profile in a sample of three- to four-year-old children with Down syndrome using a typically developing control group of younger children matched for nonverbal mental age. The samples were individually matched to ensure similar variance and distributions of scores across groups. Although there have been criticisms of pairwise matching (Jarrold & Brock, 2004), the sample size in the present study precluded the use of developmental trajectories (Thomas et al., 2009) and, in an attempt to ensure that the control group were not atypical by nature of the

selection process, any typically developing child whose standard score on the matching variable was outside the normal range was excluded.

In a longitudinal design, the children in this study were assessed again after approximately one year. This study targeted the period of development immediately following that studied by Fidler et al. (2006) and encompassed the start of formal schooling. It is during the school years that children with Down syndrome receive educational intervention and therefore this could be a particularly important period in which to understand the development of the cognitive profile. It was expected that the overall profile would look similar to that seen in studies with older children and that the group differences would be more apparent than for the younger children in the Fidler et al. (2006) study.

This study also aimed to examine variability in the cognitive profile, which has seldom been addressed in previous research. In line with Tsao and Kindelberger (2009), it was expected that not all individuals would conform to the profile seen at the group level although the extent of this variability remained an open question. It was also expected that the group with Down syndrome would show more overall variability on the standardised tests compared to the typically developing children on the basis of the observations about larger standard deviations in test scores for individuals with Down syndrome noted in the meta-analysis by Patterson et al. (2013).

As this study traced development over time it also addressed questions of how different skills relate to each other in children with Down syndrome over this period of development. In particular, the relationship between vocabulary and grammar concurrently and longitudinally was examined. As this was the first study to look at this relationship longitudinally, no strong predictions were made. It was predicted that there would either be little association between the two due to their dissociation in the overall language profile or that there would be a similar pattern to late-talkers whereby the relationship emerges at a later point in development, when a certain level of expressive vocabulary has been reached (Moyle et al., 2007). The relationships between language and both nonverbal and motor skills were also examined. Although these questions have not been addressed before, research with other populations who have developmental disabilities suggests that there may be stronger links between language and these other domains in children with Down syndrome than in typically developing children (van der Schuit et al., 2011).

3.2 Method

3.2.1 Design

This study utilised a longitudinal design with two data collection points, approximately one year apart (T1, T2). A group of children with Down syndrome and a comparison group of typically developing children, matched for nonverbal ability, completed a battery of nonverbal, language and motor tests at both time points. Information about the children's health and background was obtained through a semi-structured face-to-face interview with the primary caregiver (see section 5.2.3.1.).

3.2.2 Participants

3.2.2.1 Children with Down syndrome

The participants with Down syndrome were recruited through the Children with Down Syndrome Study (CDSS), a multi-centre birth cohort study based at the Epidemiology and Genetics Unit in the University of York. The CDSS recruited an epidemiological sample of babies with Down syndrome, born between May 2006 and September 2011. The babies were recruited through their hospital of birth and the project aimed to trace the health and development of the children from birth onwards. The current study was granted NHS ethical approval as part of a major amendment to the main CDSS study protocol. In addition, approval of the amendment was sought from the Research and Development departments of the 15 individual NHS trusts who had initially recruited the children approached for this part of the study. The study was also given approval from the Research Ethics committee at the Department of Psychology in the University of York.

One aim of the current study was to clarify the behavioural phenotype of young children with Down syndrome and at the critical phase of having just started, or being about to start school. This requires a sample with a narrow age range and thus, families involved in the CDSS whose child was born between May 2006 and March 2007 were contacted with information about the study. Furthermore, only families that lived within 100 miles of York were approached because of the logistical challenges of multiple assessment visits. In the initial stages of the CDSS, children were recruited primarily from the Yorkshire Regional Neonatal Network so most families eligible for the current study lived in the target area. No other inclusion criteria were set forth in terms of the abilities or health of the children as it was important to retain the advantages of an epidemiological sample and examine the full picture of variability amongst these children.

Thirty-nine families were sent an information pack about the study, which included an information leaflet about the project and a consent form for them to fill in if they were happy for their child to participate. In total, 24 families consented. However, two children did not complete the standardised cognitive assessment, one due to the degree of their cognitive impairment and another due to repeated task refusal. This resulted in a final sample of 22 children, with a mean age of 4 years, 9 months (ranging from 4 years, 4 months to 5 years, 1 month). The gender distribution of both groups is given in Table 3.1. According to parental interview, 19 of the children had trisomy 21, one child had the translocation form of Down syndrome and the precise form of Down syndrome was unknown for the remaining two participants. One of the children assessed at T1 could not be contacted to participate in the follow-up assessment at T2.

At T1, nine participants were attending mainstream primary schools, ten were attending mainstream nurseries (one in conjunction with a private nursery placement) and three were attending private nurseries (one in conjunction with a special needs nursery placement). At T2, 20 of the participants were attending mainstream primary schools and one was attending a special primary school. Children with Down syndrome are at an increased risk of visual (Pueschel & Gieswein, 1993) and hearing (Shott et al., 2001) difficulties. Paediatric healthcare guidelines recommend that children with Down syndrome have their hearing checked every year in the preschool years and their vision checked every two years (Down Syndrome Medical Interest Group, 2011). At both time points all children had attended vision and hearing tests within the preceding 12 months meaning that their hearing and visual difficulties were known and corrected, where appropriate. Thirteen of the participants had visual problems that were corrected with glasses at both T1 and T2. At T1 two children had hearing impairments that warranted the use of hearing aids and three further participants had recent grommets inserted to improve hearing. At T2 one child had a hearing impairment that required hearing aids and a further two had recently had grommets inserted. No parents felt that, with the appropriate aids in use, their child's hearing status would be a concern during the cognitive assessment.

The sample covered a wide geographical area including Yorkshire, Lincolnshire, Tyne and Wear, Greater Manchester, Nottinghamshire and Leicestershire and the children had a variety of social backgrounds. The Office of National Statistics ascribes a multiple deprivation score to geographical areas of varying size, according to postcode. For all participants, this score was obtained for their home address at the 'super output area'

level, which are often used in countrywide comparisons. The mean deprivation score is given in Table 3.1 with a higher score indicating a higher degree of deprivation and 88 being the highest deprivation score ascribed to any UK area.

Table 3.1.

Gender ratio of participants in both groups, and the means, standard deviations and group differences in nonverbal mental age and social background.

	Children with Down syndrome (N=22)	Typically developing children (N=22)	Significant difference
Gender ratio (male:female)	13:9	15:7	
Nonverbal mental age (years;months)	3;01 (0;05)	3;03 (0;04)	t=- .98, *p*= .331
Social deprivation score	18.21 (14.85)	11.11 (10.68)	t= 1.81, *p*= .078

3.2.2.2 Typically developing children

The typically developing group were recruited to be at a similar level of nonverbal ability to the children with Down syndrome. To ensure that the appropriate age bracket was targeted, the typically developing children were recruited after the nonverbal mental age of the majority of children with Down syndrome had been calculated from their first assessment. Typically developing children whose chronological ages corresponded to the range of nonverbal mental ages in the group with Down syndrome (2 years, 0 months to 3 years, 11 months) were invited to be part of an initial screening procedure.

Consent was sought from all parents of two- to four-year-old children at five nurseries across York and Leeds. For the screening procedure, 41 children (24 males, 17 females) were administered both of the Leiter-R nonverbal tests (see section 3.2.3.1.1) to get an estimate of nonverbal mental age. From these children, 22 were invited to take part in the full longitudinal study as their mental age could be pair-wise matched to one of the participants with Down syndrome within three months, with the exception of one pair who could only be matched within seven months. Table 3.1 confirms that there was no significant difference between the two groups in nonverbal mental age. The average chronological age of the typically developing children was 2 years, 10 months (ranging from 2 years, 4 months to 3 years, 9 months). All 22 participants were seen at both T1 and T2.

Due to the nature of recruitment, all typically developing participants were attending mainstream nurseries and T1. At T2 one child had progressed to mainstream primary school but the remaining sample still attended mainstream nurseries. Table 3.1 shows that, on average, the typically developing children were from less deprived areas than the children with Down syndrome, although this difference did not reach significance.

3.2.3 Assessment Battery

3.2.3.1 Nonverbal abilities

In order to gain a comprehensive picture of nonverbal ability, three tests assessing different aspects of nonverbal ability were administered at both T1 and T2 and an additional test was administered at just T2.

3.2.3.1.1 Leiter-R

The Leiter International Performance Scale-Revised (Leiter-R; Roid & Miller, 1997) was designed to assess the nonverbal abilities of people ranging in age from 2 to 20, particularly those with communication difficulties. The battery includes a Brief Visualisation IQ Scale consisting of four subtests that give an estimate of an individual's nonverbal IQ, which can be converted into an age equivalent or 'nonverbal mental age'. This method of estimating nonverbal mental age has been previously used with individuals with Down syndrome (e.g. Roberts et al., 2005). Two of the subtests in the Leiter-R IQ scale primarily assessed visualisation ability and two primarily assessed nonverbal reasoning. Given the age and thus limited attention levels of the sample, combined with the number of tests in the complete assessment battery, only one subtest from each domain was administered in the current study: the *Figure Ground* test assessed visualisation ability and the *Repeated Patterns* test assessed nonverbal reasoning. The raw scores on these subtests can be translated into age equivalent scores and the average age equivalent across both subtests was taken as an estimate of the child's nonverbal mental age.

In the *Figure Ground* test children pointed to embedded figures in larger scenes and were awarded one point for each figure they correctly locate. There were 31 figures to search for giving a maximum raw score of 31. Testing was discontinued after six cumulative incorrect responses (internal consistency reliability coefficient of .75). In the *Repeated Patterns* test children completed a given pattern by placing two, three or four foam shapes or response cards in the correct order. Item response options included zero, one or two distractor items. Participants were awarded one point for each item in the sequence that

was correctly placed. There were 12 patterns to complete with a maximum raw score of 27 (internal consistency reliability coefficient of .76). Testing was discontinued after six cumulative incorrect responses. Both tests were administered at T1 and T2.

The Leiter-R subtests were designed to be administered nonverbally and while efforts were made to adhere to these standardised nonverbal instructions, the age and ability levels of the children in the sample meant that they were surprised and confused by the pantomimed instructions. Thus, as permitted by the Leiter-R manual in exceptional circumstances (p.23), brief verbalisations were used as a supplement to the nonverbal instructions for all children in both groups. This ensured that children's attention remained directed towards the task and gave participants the greatest opportunity to comprehend the task demands and perform to the best of their abilities. The same adaptations to administration have been necessary in previous research with individuals with Down syndrome (Glenn & Cunningham, 2005).

3.2.3.1.2 WPPSI-III^{UK}

The *Object Assembly* subtest from the Wechsler Pre-school and Primary Scale of Intelligence III^{UK} (WPPSI-III^{UK}; Wechsler, 2003) was administered at T1 and T2. This test was designed to assess nonverbal skills in preschool children and taps visuo-construction abilities, which is not assessed explicitly by the Leiter-R tests. This test required children to complete jigsaws of increasing numbers of pieces and complexity. Children received one point for every correct juncture in a particular jigsaw with a maximum score of 37 points. Testing was discontinued after three consecutive scores of zero (internal consistency reliability coefficient .85).

The *Block Design* subtest from the WPPSI-III^{UK} was administered at T2 only, as a more challenging assessment of visuo-construction abilities. This test required children to replicate patterns using a set of red and white blocks. The patterns were initially built by the experimenter using real blocks and later presented as two-dimensional diagrams for participants to copy. Children received two points for every design copied correctly (rotations are permitted for the first 10 items) and one point for some of the early items if they could correctly reproduce the design after a second attempt. The maximum score was 40 points. Testing was discontinued after three consecutive scores of zero (internal consistency reliability coefficient .84).

3.2.3.2 Language abilities

The language profile of children with Down syndrome was of particular interest given the aims of this study and so both receptive and expressive language tasks were included tapping concrete vocabulary knowledge, word and nonword repetition, and understanding of more abstract, conceptual language.

3.2.3.2.1 Receptive vocabulary

The Receptive One Word Picture Vocabulary Test (ROWPVT; Brownell, 2000) was used at T1 and T2 to assess understanding of concrete words. Participants were required to point to the picture that matched the verbally presented word from four response options. A basal was established with eight consecutive correct responses and the test was discontinued after reaching a ceiling of six incorrect responses in eight consecutive items. All items before the basal were scored as correct and all items after the ceiling were scored as incorrect. The raw score was the total number of correct responses with a maximum raw score of 170 (internal consistency reliability coefficient of .96 and test-retest reliability coefficient of .84).

3.2.3.2.2 Expressive vocabulary

The *Expressive Vocabulary* subtest of the Clinical Evaluation of Language Fundamentals-Preschool 2^{UK} (CELF-Preschool 2^{UK}; Wiig, Secord, & Semel, 2006) was administered to assess production of words at T1 and T2. Participants were asked to name a series of 20 pictures ranging from "carrot" to "scales" and responses were audio recorded for later scoring. A correct response scored two points, a semantically related response that did not include the target vocabulary received one point and an incorrect response scored zero points. The maximum possible raw score was 40. The test was discontinued after seven consecutive incorrect responses (internal consistency reliability coefficient .82, test-retest reliability coefficient .90). Children with Down syndrome have specific difficulties in articulation (Cleland et al., 2010); in order not to disadvantage these children on an expressive test, allowances were made for children's articulation errors. Thus, a response was scored as correct as long as the word was recognisable to the examiner. The test was administered towards the end of the session enabling the examiner to become more familiar with the child's speech before scoring. In the majority of cases, the responses were also audio-recorded to help with scoring ambiguous items. However, as much of the scoring was done online as possible so that children's oromotor movements could be taken into account. Young children with Down syndrome often use forms of sign language to

communicate, particularly in the early stages of language development (Clibbens, 2001). However, the purpose of this test was to assess children's verbal expression of words and so only verbal responses were scored and children were encouraged to give their responses verbally if possible. The expressive signing vocabulary of the children was considered separately through parental questionnaires (see section 4.2.1.2).

3.2.3.2.3 Receptive language

The *Basic Concepts* subtest of the CELF-Preschool 2^{UK} was used at T1 and T2 to assess understanding of complex relational concepts such as "bigger", "same" and "at the bottom". Children were required to point to the picture that best represents the verbally presented concept from a choice of three with a maximum score of 18. Testing was discontinued after five consecutive incorrect responses (internal consistency reliability coefficient .77, test-retest reliability coefficient .86).

At T2, the *Sentence Structure* subtest of the CELF-Preschool 2^{UK} was also included as a more advanced assessment of receptive language. This test evaluates children's ability to understand spoken sentences that increase in length and complexity. Children were required to point to the picture that best represents a spoken sentence, such as "the bear is in the wagon", from a choice of four. The maximum score was 22 and testing was discontinued after 5 consecutive incorrect responses (internal consistency reliability coefficient .78, test-retest reliability coefficient .79).

3.2.3.2.4 Expressive language

A 10-minute sample of natural language during play was elicited at T1 and T2 so that measures of language complexity, such as mean length of utterance (MLU) could be calculated. This method is commonly used to assess the expressive language abilities of young children and children with language weaknesses (e.g. Rice et al., 2010). The experimenter and the child played with a set of food and park-related toys for approximately 10 minutes. If a child did not speak much during play the experimenter asked open-ended questions such as "what happened there?" in an attempt to elicit narrative responses. The language samples were both video and audio recorded for later transcription and analysis of the child's utterances. However, MLU is only an appropriate measure once children reach a certain level of productive language. For example, Fowler (1988) only used language sample measures with individuals with Down syndrome who commonly used two or more words in their utterances. As data collection progressed, it became clear that the majority of the children with Down syndrome had not yet reliably

passed the single word stage, limiting the utility of this type of measure. Therefore, this task was not transcribed and scored and was not included in the analysis.

3.2.3.2.5 Phonological short-term memory

In order to assess children's memory for phonological forms the Preschool Repetition (PSRep) Test from the Early Repetition Battery (ERB; Seef-Gabriel, Chiat, & Roy, 2008) was administered at T1 and T2. Children repeated a series of 18 real words and 18 phonologically matched nonwords, spoken one at a time by the examiner using an animal puppet to make the task more enjoyable for the young participants. Responses were audio recorded for later scoring. There were six one-syllable words, six two-syllable words and six three-syllable words. The nonwords were all prosodically and phonologically similar to a real word from the word list but with a vowel changed or some of the phonemes transposed (e.g. "dalla" for "ladder"). Having multiple items which contained the same phonemes permitted examination of consistent speech errors made by children, which were taken into account when scoring the test. This test was scored using two criteria: the number of words and nonwords with all phonemes repeated correctly and the number of individual syllables within a word or nonword repeated correctly. The maximum score for correct repetitions at the word level was 18 for both words and nonwords and at the syllable level the maximum raw score for each was 36 (internal consistency reliability coefficient .89, test-retest reliability coefficient .81).

3.2.3.3 Motor skills

Two subtests from the Movement Assessment Battery for Children-2 (Movement ABC-2; Henderson, Sugden, & Barnett, 2007) battery were used at T1 and T2 to assess fine motor skills. The *Posting Coins* task required the child to post six coins into a money box as quickly as possible and the time taken, to the nearest second, was recorded by the experimenter. The child was given a practice trial with each hand and then completed a timed trial with each hand. At the start the experimenter noted the child's preferred hand according to either parental report or, if they were able to use a pencil, which hand they draw with. For all children the task was completed with the preferred hand first followed by the other hand (reliability coefficient .77).

The *Bike Trails* task was used to assess children's pencil skills. Children traced a route carefully with a pencil. The examiner demonstrated the task by tracing half of the route and the child then finished that route as a practice trial. The participant then completed one route independently and the raw score was calculated as the number of

errors that a child made during the route. An error was counted every time the child went outside the lines of the route and an extra error was counted for every additional ½ inch that a child remained outside of the lines. If a child made no visible attempt to trace the route then it was considered unscorable and awarded a maximum score of 26, which a child would obtain if they drew the whole route outside of the trail (reliability coefficient .77).

Table 3.2.

The content of the assessment battery, and the order of test administration, at each time point.

	T1		T2	
Cognitive Domain	Test	Order	Test	Order
Nonverbal	Repeated Patterns	2	Repeated Patterns	6
	Figure Ground	5	Figure Ground	3
	Object Assembly	8	Object Assembly	1
	-		Block Design	7
Language	ROWPVT	4	ROWPVT	5
	Expressive Vocab	6	Expressive Vocab	8
	Basic Concepts	1	Basic Concepts	2
	Language Sample	10	Language Sample	12
	Nonword Repetition	7	Nonword Repetition	9
	-		Sentence Structure	10
Motor	Coin Posting	3	Coin Posting	4
	Bike Trails	9	Bike Trails	11

3.2.4 Procedure

T1 took place between May 2011 May 2012 and T2 took place between August 2012 and April 2013. The average length of time between T1 and T2 was longer for the participants with Down syndrome, at 14.29 months, compared to 12.95 months for the typically developing children. An independent t-test confirmed that this difference was significant (t= 3.68(32.04), *p*= .001). The reason for this difference was due to data collection time constraints towards the end of the project, when the typically developing group were being followed up. It is important to note, also, that one aim of the study was to look at improvement over time. Cognitive development is known to be slower in Down

syndrome and is not directly comparable to typical development over the same time period. Thus, giving the children with Down syndrome the maximum possible time between assessment points was prioritised over closely matching the groups on this variable.

Depending on age and parental preference, the children were seen either in a quiet room at their school or nursery, or at home. For all assessments, there was typically a teaching assistant or parent present. The tests that were administered at each time point, and the order of administration, are shown in Table 3.2. Given the age of the participants, it was necessary that the order of administration be somewhat flexible and the primary aim was always engaging the participants with as many of the tests as possible. Thus, the tests were not administered in precisely the same order for all children although the standard order was always attempted. Children were seen for either one or two sessions (no more than 4 weeks apart) lasting for 45-60 minutes, depending on the child's attention levels and interest in the tasks. Participants were given as many breaks as they needed during the session.

The interview about the child's background and development was conducted face-to-face with the primary caregiver or both parents, usually at the parents' home after their child had been assessed and typically lasting for around half an hour.

3.3 Results

3.3.1 Cognitive Profile at Time 1

The first aim of this study was to examine the early cognitive profile in Down syndrome, its stability over time and the variability between children. In order to do this, the scores of the group of children with Down syndrome on the cognitive test battery will be compared to the group of typically developing children matched on nonverbal ability. These comparisons will demonstrate which skills are strengths and weaknesses for children with Down syndrome, in relation to their nonverbal ability.

Descriptive statistics for both groups on all measures from the cognitive test battery at T1 are shown in Table 3.3. All children in both groups completed the *Leiter-R* nonverbal tasks, the *ROWPVT*, *Basic Concepts* and *Expressive Vocabulary* tasks. However, two of the children with Down syndrome didn't complete the *Object Assembly* task. Furthermore, six of the participants with Down syndrome and four of the typically developing participants didn't complete the *Nonword Repetition* task, due to task refusal.

The task was not fully administered to a further three of the children with Down syndrome who were not yet consistently producing clear words in their natural language, as this may have caused undue frustration. These children were given a score of zero for the task and were included in further analyses. On the *Bike Trails* task, six children with Down syndrome and three typically developing children refused to complete the trail. On the *Posting Coins* task one of the participants with Down syndrome was unable to comfortably post a single coin, which is the requirement for the practice trial of the task. Another child with Down syndrome took over two and a half minutes to post the coins (a length of time more than three standard deviations above the group mean) and it was unclear whether the speeded element of the task had been fully understood. Thus, both of these children were excluded from analyses involving this task.

Inspection of histograms, Kolmogorov-Smirnoff tests of normality, and skewness and kurtosis statistics highlighted that the distribution of scores in both groups deviated from normality on several of the tasks. On the *Object Assembly* task the distribution of scores was positively skewed in both groups, with the majority of children achieving scores at the lower end of the distribution. However, this was largely due to a couple of children in each group achieving noticeably higher scores than the rest. Similarly, the distributions of scores for both groups of participants on the *Posting Coins* task were positively skewed with the majority of participants posting the coins at the faster end of the distribution but with some notable exceptions in both groups. On the *Expressive Vocabulary* test there was evidence of floor effects in the group of children with Down syndrome, with 7 of the 22 children scoring zero on the task, although some children did score considerably higher. Similarly, 10 of the 16 children with Down syndrome who completed the *Bike Trails* task scored the maximum possible number of errors, indicating large floor effects in this group on this task as well. Finally, on the *Nonword Repetition* task, assessed at the syllable and the whole-word level, the distribution of scores were positively skewed for the children with Down syndrome, with the majority achieving low scores on the task. As scoring by syllable did not affect the distribution of scores on the measures, scores at the whole-word level were used in analyses as this is the scoring method recommended in the manual of the test.

Table 3.3 displays the results of group comparisons on each of the cognitive measures. For the measures where the distributions deviated from normality, Mann-Whitney U tests were used and for all other measures independent t-tests were used to

Table 3.3.

Means, standard deviations and group differences on all measures at T1

	DS N=22	TD N=22	Group difference
Nonverbal mental age (in months)	37.36 (4.95)	38.68 (3.87)	t= -.98, *p*=.331
Object Assembly raw score (max=37)	6.30 (6.20)	9.95 (5.47)	*U*= 110.00, *p*=.005
Receptive Vocabulary raw score (max=170)	26.86 (10.10)	33.00 (11.03)	t= -1.93, *p*=.061
Basic Concepts raw score (max=18)	8.05 (2.36)	10.77 (2.39)	t= -3.81, *p*<.001
Expressive Vocabulary raw score (max=40)	4.50 (4.76)	10.68 (5.66)	*U*= 92.50, *p*<.001
Nonword Repetition raw score (max=18)	3.12 (3.56) N=16	9.50 (3.67) N=18	*U*= 31.00, *p*<.001
Coin Posting with preferred hand (s)	34.20 (17.37) N=20	15.41 (4.37)	*U*= 36.50 , *p*<.001
Bike Trails number of errors (max = 26)	24.31 (3.46) N=16	18.47 (5.38) N=19	*U*= 53.00, *p*= .001

detect group differences. The alpha level used for all statistical tests was .05. Table 3.3 shows that the typically developing group generally performed better on all of the cognitive tasks. However, the groups did not differ significantly in nonverbal mental age, which is to be expected given the explicit matching procedure. The difference between the groups on the receptive vocabulary measure was also not significant, although the typically developing children had higher scores on average. On all other language and motor tasks the typically developing children performed significantly better than the children with Down syndrome. This is in line with previous research which has demonstrated that receptive vocabulary is a linguistic strength for children with Down syndrome, in line with their nonverbal ability, but fine motor skill and both expressive language and more complex linguistic understanding are relative weaknesses (Chapman & Hesketh, 2000).

While group comparisons give an indication of areas of strength or weakness, they don't provide information about the extent to which different skills are impaired in relation to each other. To examine the language phenotype in the sample of children with Down syndrome, and explore the hypothesis that grammar is impaired to a greater extent than vocabulary, z-score analysis was utilised. This allows comparison of the performance on different tests from different assessment batteries. For each participant with Down syndrome a z-score was calculated for nonverbal mental age and the *ROWPVT*, *Expressive Vocabulary* and *Basic Concepts* tests. These z-scores were based on the mean score and standard deviation of the typically developing group on that measure. This essentially uses the group of typically developing children as a standard against which the performance of each child with Down syndrome is compared. The *ROWPVT* and *Expressive Vocabulary* z-scores were then averaged to form a vocabulary composite and the *Basic Concepts* z-score was used as a proxy for grammatical skill. Nonverbal ability was included to see if either language domain was in line with nonverbal skill or if both were impaired. However, z-scores assume that variables are normally distributed and so the *Object Assembly* task was excluded as it was not normally distributed in either group. Thus, nonverbal mental age was used as the sole nonverbal measure.

Figure 3.1 shows that both vocabulary and grammar were weaker than nonverbal ability, but grammar more so than vocabulary. In fact, grammar ability (as assessed by *Basic Concepts*) is more than 1 standard deviation below the typically developing group, which on a standardised test would be classified as impairment. Furthermore, the vocabulary composite consists of both an expressive and receptive test. While this gives a more

balanced picture of overall vocabulary ability, the expressive language weaknesses in the sample precluded the use of an equivalent expressive measure in the grammar variable. As individuals with Down syndrome have greater weaknesses in expressive than receptive language, comparing two language domains where only one includes an expressive measure may mask differences between the domains. Indeed, it is apparent from Figure 3.2 that when the receptive vocabulary measure, which is directly comparable to the grammar measure, is examined alone, the discrepancy between the vocabulary and grammar domains is even greater. Expressive vocabulary is in line with the receptive grammar measure. Figure 3.2 also shows that receptive vocabulary is almost in line with nonverbal ability, which supports the findings of the group comparisons above. In sum, these analyses indicate that the expected group-level cognitive profile is seen in four- to five-year-old children with Down syndrome, in line with previous evidence.

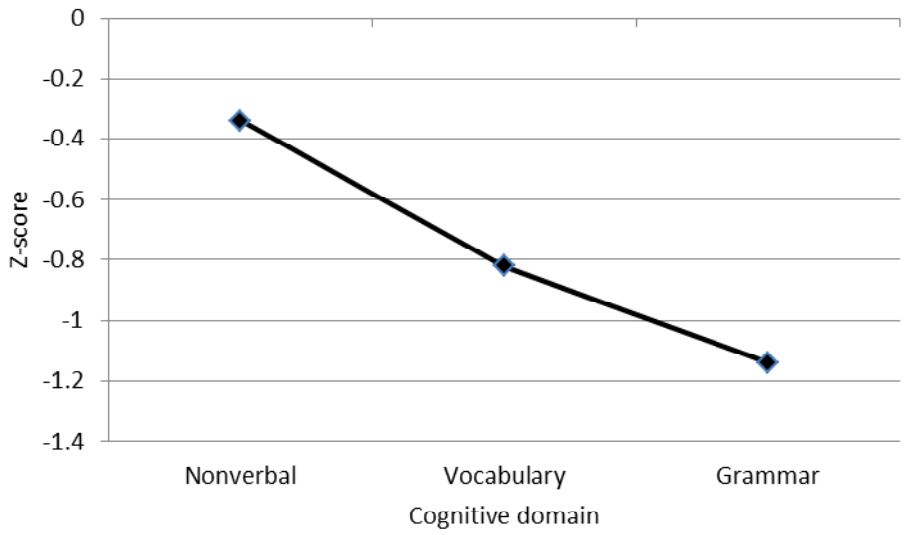


Figure 3.1. Graph showing the mean z-score of the group of children with Down syndrome in the nonverbal, vocabulary and grammar domains, based on the mean performance of the typically developing group.

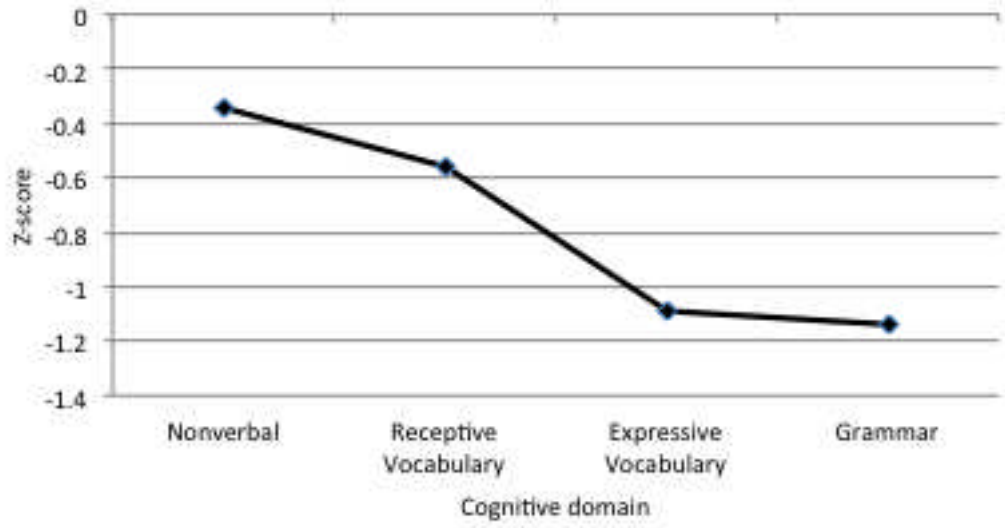


Figure 3.2. Graph showing the mean z-score for the group of children with Down syndrome in the nonverbal, receptive vocabulary, expressive vocabulary and grammar domains, based on the mean performance of the typically developing group

3.3.2 Variability in the T1 Cognitive Profile

In order to examine whether the cognitive profile typically associated with Down syndrome is also true for the majority of children at the individual level, the profile of cognitive strengths and weaknesses was calculated for each child according to their z-scores on the relevant assessment tasks or composites. The profile was calculated using a series of binary comparisons, all of which have been highlighted as areas in which there should be a discrepancy for children with Down syndrome. Children were deemed to have shown the expected profile if their expressive vocabulary, grammar and motor z-scores were lower than their z-scores for nonverbal mental age, if their grammar z-score was lower than their vocabulary z-score and if their expressive vocabulary z-score was lower than their receptive vocabulary z-score. As it is unclear, both in previous studies and in the results about the group-level profile in the current study, whether receptive vocabulary should be in line with nonverbal mental age or weaker than it, this comparison was not used in determination of the expected profile. Z-scores were calculated for the Leiter-II nonverbal mental age estimate, the ROWPVT (Receptive Vocabulary), CELF Expressive Vocabulary and Basic Concepts (Grammar). The z-score for the vocabulary composite was calculated in the same way as in Section 3.3.1. The motor composite was calculated by taking an average of the z-scores on the Coin Posting and Bike Trails tasks.

Table 3.4.

Z-scores for each of the participants with Down syndrome on the cognitive tests and composites needed to determine the cognitive profile and indications of whether they met the expected patterns across a series of binary z-score comparisons.

Participant	Mental Age	Receptive Vocabulary	Expressive Vocabulary	Grammar	Vocabulary	Motor	Expressive vocabulary < Mental age	Grammar < Mental age	Grammar < Vocabulary	Expressive Vocabulary < Receptive Vocabulary	Motor < Mental age
1	2.15	1.09	0.94	0.10	1.02	-0.90	✔	✔	✔	✔	✔
2	1.12	-0.18	-1.53	-0.74	-0.86	-7.69	✔	✔	✘	✔	✔
3	-2.24	-2.36	-1.89	-2.00	-2.13	-4.66	✘	✘	✘	✘	✔
4	-0.95	-0.54	-1.18	-2.41	-0.86	-1.51	✔	✔	✔	✔	✔
5	-1.21	-0.54	-1.53	-1.58	-1.04	-2.19	✔	✔	✔	✔	✔
6	0.60	-1.45	-1.89	-0.74	-1.67	-8.89	✔	✔	✘	✔	✔
7	1.12	-1.81	-1.89	-2.41	-1.85	-2.14	✔	✔	✔	✔	✔
8	0.08	-0.91	-1.89	-1.58	-1.40	-	✔	✔	✔	✔	
9	-3.79	-1.45	-1.18	-0.74	-1.32	-3.86	✘	✘	✘	✘	✔
10	0.86	-1.45	-1.53	0.93	-1.49	-5.00	✔	✘	✘	✔	✔
11	-1.21	-0.54	-1.18	-1.58	-0.86	-2.14	✘	✔	✔	✔	✔
12	-0.95	0.63	0.06	-0.32	-0.29	-2.60	✘	✘	✔	✘	✔
13	-0.18	0.91	-0.12	-0.32	0.40	-3.51	✘	✔	✔	✔	✔
14	-1.21	-0.91	-1.89	-2.00	-1.40	-0.43	✔	✔	✔	✔	✘
15	-0.69	-0.09	0.23	-0.32	0.07	-1.04	✘	✘	✔	✘	✔
16	-1.21	-0.91	-0.83	-1.16	-0.87	-3.80	✘	✘	✔	✘	✔
17	0.34	0.82	-0.47	-0.32	0.18	-1.48	✔	✔	✔	✔	✔
18	-0.18	-1.45	-1.53	0.10	-1.49	-1.11	✔	✘	✘	✔	✔
19	0.60	-0.27	-0.83	-1.16	-0.55	-1.69	✔	✔	✔	✔	✔
20	0.34	0.00	-0.12	-2.41	-0.06	-0.36	✔	✔	✔	✔	✔
21	-0.18	0.73	-1.89	-2.83	-0.58	-1.40	✔	✔	✔	✔	✔
22	-0.69	-0.27	-1.89	-1.58	-1.08	-7.23	✔	✔	✔	✔	✔

The z-scores for each participant with Down syndrome on the tests and composites needed for determining the cognitive profile are presented in Table 3.4. Whether or not each participant met each of the expected comparisons within the profile is indicated with either a tick or a cross. So that the criteria for meeting the profile were not overly stringent, a participant just needed to have a z-score that was lower than the comparison z-score in the appropriate direction, but there was no determination of how much lower that z-score needed to be. This allows assessment of the general pattern of strengths and weaknesses but cannot speak to significant, meaningful differences between domains. Table 3.4 shows that ten of the twenty-two children with Down syndrome (45.5%) show the expected profile at the individual level.

3.3.3 Cognitive Performance at T2

Descriptive statistics for both groups on all measures from the cognitive test battery at T2 are shown in Table 3.5. All children in both groups completed the *Leiter-R* nonverbal tasks, the *Object Assembly, ROWPVT*, *Basic Concepts* and *Expressive Vocabulary* tasks. However, four of the children with Down syndrome didn't complete the *Block Design* task. Furthermore, six of the participants with Down syndrome didn't complete the *Sentence Structure* task, due to task refusal. All of the participants with Down syndrome completed the *Nonword Repetition* task but two of the typically developing children did not. More of the participants with Down syndrome completed the *Bike Trails* task than at the first assessment but there were still four children who refused this task. One of the participants with Down syndrome was again unable to satisfactorily post the practice coin on the *Posting Coins* task and was thus excluded from the analyses for this task.

As at T1, inspection of histograms, Kolmogorov-Smirnoff tests of normality, and skewness and kurtosis statistics highlighted that the distribution of scores in both groups deviated from normality on several of the tasks. There was a negative skew in the nonverbal mental age estimates of the children with Down syndrome due to one participant with a noticeably lower age estimate. Again, the scores of the participants with Down syndrome were positively skewed on the *Object Assembly* task with the majority of children scoring at the lower end of the distribution. The distribution of scores on the *Sentence Structure* task was negatively skewed in the typically developing group due to two participants scoring substantially lower than the rest. As at T1, the distribution of scores on the *Posting Coins* task were positively skewed in both groups due to a small number of children in both groups taking a noticeably longer time to post the coins. There were

generally fewer problems with floor effects on the cognitive tests at T2 for the group of children with Down syndrome compared with T1, indicating that the tests might be more appropriate once children reach school age. However, there was still a floor effect on the *Bike Trails* task with five of the 17 participants who completed the task achieving the maximum error score. Again, where the distributions were not normal, Mann-Whitney U tests were used for group comparisons and for all other comparisons independent t-tests were used.

Table 3.5 shows that at T2 the typically developing children performed substantially better than the children with Down syndrome on the cognitive assessment battery. Indeed, the group comparisons reveal that their scores were significantly higher on all of the individual tests. As the groups were no longer matched on any of the cognitive variables, it was not possible to meaningfully examine the cognitive profile in the children with Down syndrome at T2. However, one question of interest is whether the relationships between different skills are similar in typical development and in Down syndrome, both concurrently and over time.

In order to look at the development of cognitive skills over time, it is firstly important to establish whether there has been improvement over time. Comparison of Table 3.3 and Table 3.5 indicates that the scores of both groups improved on all tests between T1 and T2. Within-subject t-tests and Willcoxon signed-rank tests shown in Table 3.5 revealed that all improvements were significant with the exception of the progress that the group with Down syndrome made on the *Basic Concepts* task. Examination of the effect sizes given in Table 3.5 suggests that the group with Down syndrome made the greatest progress on the *Expressive Vocabulary* and *Coin Posting* tasks. The typically developing children, on the other hand, made the greatest progress on the *Leiter-R* nonverbal tasks and the *Basic Concepts* task.

These results indicate that the children with Down syndrome improved significantly on the majority of the cognitive variables over the course of one year, thus enabling analysis of what factors might be important for determining progress over time.

Table 3.5.

Means, standard deviations and group differences on all measures administered at T2 and comparisons to identify significant improvement since T1.

	DS N=21	Improvement since T1 (effect size)	TD N=22	Improvement since T1 (effect size)	Group difference
Nonverbal mental age (in months)	43.29 (5.00)	*z*=-3.51, *p*<.001 (*d*=-1.72)	53.68 (6.07)	*t*=-13.62, *p*<.001 (*d*=-4.43)	*U*= 39.00, *p*<.001
Object Assembly raw score (max=37)	8.52 (7.00)	*z*=-2.24, *p*=.025 (*d*=-.87)	22.77 (6.29)	*z*=-4.02, *p*<.001 (*d*=-2.62)	*U*= 38.00, *p*<.001
Block Design raw score (max=40)	13.65 (3.35) N=17		21.14 (2.03)		*t*= -8.64, *p*<.001
Receptive Vocabulary raw score (max=170)	32.24 (13.10)	*t*=-3.46, *p*=.002 (*d*=-1.18)	54.32 (12.83)	*t*=-7.72, *p*<.001 (*d*=-2.34)	*t*= -5.58, *p*<.001
Basic Concepts raw score (max=18)	9.00 (2.07)	*t*=-1.87, *p*=.076 (*d*=-.58)	15.68 (1.70)	*t*=-10.89, *p*<.001 (*d*=-3.43)	*t*= -11.58, *p*<.001
Sentence Structure raw score (max=22)	4.60 (2.53) N=15		13.86 (3.76)		*U*= 16.50, *p*<.001
Expressive Vocabulary raw score (max=40)	7.76 (4.82)	*z*=-3.55, *p*<.001 (*d*=-1.94)	19.68 (6.83)	*t*=-8.53, *p*<.001 (*d*=-2.64)	*t*= -6.58, *p*<.001
Nonword Repetition raw score (max=18)	4.48 (2.86)	*z*=-2.88, *p*=.004 (*d*=-1.52)	12.40 (2.37) N=20	*t*=-4.28, *p*=.001 (*d*=-1.61)	*t*= -9.64, *p*<.001
Coin Posting with preferred hand (s)	21.15 (6.77)	*z*=-3.46, *p*=.001 (*d*=2.01)	11.45 (2.43)	*z*=-3.64, *p*<.001 (*d*=1.48)	*U*= 9.50, *p*<.001
Bike Trails number of errors (max = 26)	18.71 (5.80) N=17	*z*=-2.82, *p*=.005 (*d*=1.68)	10.14 (5.95)	*t*=7.48, *p*<.001 (*d*=2.51)	*U*= 57.50, *p*<.001

3.3.4 Relationships Between Cognitive Skills at T1

Correlations were computed between age and all of the cognitive tests administered at T1, in both groups, and are displayed in Table 3.6. Chronological age correlated with the language measures in the typically developing group but did not correlate with any of the cognitive variables in the group of children with Down syndrome. In the typically developing group there were moderate to strong intercorrelations between all of the language tasks. In the group with Down syndrome there were moderate correlations between the language tasks with the exception of the *Basic Concepts* task, which did not correlate significantly with any other language task. The nonverbal *Object Assembly* task was significantly correlated with both measures of vocabulary in the group with Down syndrome. In both groups the *Coin Posting* task was moderately correlated with expressive vocabulary. However, the two nonverbal measures (mental age and *Object Assembly*) were not significantly correlated in either group and neither were the two motor measures (*Coin Posting* and *Bike Trails*). This may be because the individual tests are assessing different components of the skill domain or it may be due to the nature of the demands for the different tests. For example, the bike trails task required proficient pencil skills, which was rare in both groups and at this age and ability level may not be a good indicator of overall motor skill.

As this study is concerned with the overall relationships between different skill domains, composite measures were created. A child's score on the various composite measures was their average z-score across the relevant individual tests, based on the mean performance and standard deviation in their group. There was a general language composite, which consisted of *Receptive Vocabulary*, *Expressive Vocabulary*, *Nonword Repetition* and *Basic Concepts*. Given the uneven language profile in Down syndrome, more specifically the disparity between vocabulary and grammar skill, vocabulary and grammar measures were also calculated. The vocabulary composite was the average z-score from the *Receptive Vocabulary* and *Expressive Vocabulary* tests and the grammar composite was the z-score on the *Basic Concepts* task. As there were pronounced floor effects on the *Bike Trails* task the motor measure was simply the z-score on the *Coin Posting* task. The nonverbal composite was an average of the mental age and *Object Assembly* z-scores. Although these two nonverbal measures were not well correlated they are theoretically measuring aspects of the same construct and there was a range of scores on both measures so they were both included in the composite. The correlations between the composite measures are given in Table 3.7.

Table 3.7 shows that nonverbal ability is correlated with vocabulary in both groups, but to a greater extent amongst the participants with Down syndrome. There is also a significant correlation between the broader language composite and nonverbal ability in the group with Down syndrome. Of particular note in light of the research questions, the vocabulary and grammar measures are strongly correlated in the typically developing group but are only weakly correlated in the group with Down syndrome. Finally, the motor measure is correlated with both the overall language composite and the grammar measure in the typically developing group. The same relationships are not seen amongst the participants with Down syndrome, but the correlation between the motor and vocabulary composites is of moderate strength and approaches significance (p=.065). In sum, the correlations across both the individual measures and the composites show a relatively similar overall pattern across both groups with the exception of the grammar measure, which is not related to any other measure in the group with Down syndrome.

3.3.5 Relationships Between Cognitive Skills at T2

Correlations were computed between age and the raw scores on all of the cognitive tests administered at T2, in both groups, and are displayed in Table 3.8. Similarly to the findings at T1, age was significantly correlated with several of the cognitive measures in the typically developing group but was only correlated with the *Block Design* task in the group with Down syndrome, although this was in the opposite direction than expected. While *Object Assembly* was once again not significantly correlated with *Mental Age* in either group, there were significant correlations between *Object Assembly* and *Block Design* in both groups. Furthermore, *Block Design* was correlated with *Mental Age* in the typically developing group. Thus, there were greater intercorrelations between the nonverbal measures administered at T2 than there were at T1. Although the correlations between the two motor measures were higher at T2 than at T1 they still did not reach significance in either group.

The language tests were, in general, less well correlated with each other than they were at T1. In the group with Down syndrome, the two vocabulary measures were correlated with each other, as were the two grammar measures (*Basic Concepts* and *Sentence Structure*) but there were only weak to moderate correlations across these domains. Nonword repetition was significantly correlated with *Expressive Vocabulary* and *Basic Concepts* but was only weakly correlated with the other language tests.

Table 3.6.

Correlations between age and the cognitive measures at T1. Correlations in the group with Down syndrome are above the diagonal and in the typically developing group are below the diagonal.

	Child's age	Mental age	Object Assembly	Receptive Vocab	Basic Concepts	Expressive Vocab	Nonword repetition	Coin posting	Bike trails
Child's age	1	.019	-.086	-.044	-.199	.110	.320	.195	-.160
Mental age	.228	1	.224	.387	.231	.214	.485	.016	-.069
Object Assembly	.303	.177	1	.600**	.004	.598**	.110	-.324	-.271
Receptive Vocab	.414	.395	.297	1	.090	.607**	.548*	-.366	-.003
Basic Concepts	.638**	.337	.127	.723**	1	.422	.411	.174	-.231
Expressive Vocab	.553**	.134	.402	.707**	.811**	1	.779**	-.415	-.287
Nonword repetition	.710**	.576*	.159	.509*	.790**	.641**	1	-.267	-.147
Coin posting	-.303	-.214	.102	-.296	-.451*	-.418	-.340	1	.028
Bike trails	-.276	-.040	-.095	-.494*	-.363	-.457*	-.402	-.158	1

Table 3.7.

Correlations between the cognitive composite measures at T1. Correlations in the group with Down syndrome are above the diagonal and in the typically developing group are below the diagonal.

	Nonverbal	Language	Vocabulary	Grammar	Motor
Nonverbal	1	.529*	.614**	.154	-.178
Language	.422	1	.901**	.634**	-.229
Vocabulary	.433*	.945**	1	.286	-.420
Grammar	.302	.943**	.830**	1	.174
Motor	-.073	-.425*	-.387	-.451*	1

Table 3.8.

Correlations between chronological age and the cognitive measures administered at T2. Correlations amongst the children with Down syndrome are above the diagonal and those for the typically developing group are below the diagonal.

	Child's Age	Mental Age	Object Assembly	Block Design	Receptive Vocabulary	Basic Concepts	Sentence Structure	Expressive Vocabulary	Nonword Repetition	Coin posting	Bike trails
Child's Age	1	.131	.143	.485*	-.152	-.175	-.361	-.388	-.129	.300	-.139
Mental Age	.110	1	.376	.322	.168	-.096	-.359	-.120	-.199	.132	-.568*
Object Assembly	.526*	.158	1	.599*	.586**	.162	-.240	.321	-.056	-.181	-.498*
Block Design	.152	.675**	.424*	1	.630**	.482*	.061	.536*	.144	-.332	-.571*
Receptive Vocabulary	.223	.216	-.078	-.071	1	.324	.243	.615**	.247	.000	-.164
Basic Concepts	.473*	.400	.318	.413	.478*	1	.644**	.491*	.498*	-.133	-.358
Sentence Structure	.367	.184	-.036	.171	.309	.432*	1	.169	.301	-.285	.136
Expressive Vocabulary	.469*	.360	.299	.281	.410[a]	.372	.380	1	.583**	-.138	-.206
Nonword Repetition	.400	.103	.120	-.145	.336	.187	-.024	.560*	1	-.023	-.055
Coin Posting	-.468*	-.387	-.162	-.352	-.032	-.102	-.144	-.204	.200	1	.190
Bike Trails	-.413	-.233	-.395	-.211	.128	-.141	-.165	-.195	-.248	.359	1

[a] p=.058

Table 3.9.

Correlations between the cognitive domains at T2. Correlations in the group with Down syndrome are above the diagonal and those in the typically developing group are below the diagonal.

	Nonverbal	Language	Vocabulary	Grammar	Motor
Nonverbal	1	.245	.473*	.070	-.456*
Language	.303	1	.833**	.815**	-.201
Vocabulary	.255	.905**	1	.448*	-.177
Grammar	.365	.792**	.542**	1	-.200
Motor	-.449*	-.157	-.109	-.198	1

In the typically developing group, in contrast to T1, the correlations between the language measures were generally less strong than amongst the participants with Down syndrome. The correlation between the two grammar measures was significant and between the two vocabulary measures was marginally significant. However, the only significant correlation across these domains was between *Receptive Vocabulary* and *Basic Concepts*.

At T2 there were few relationships across cognitive domains in either group. However, in the group with Down syndrome there was a consistent pattern of relationships between the nonverbal ability tests and the *Bike Trails* motor measure. The *Receptive Vocabulary* test was also related to two of the nonverbal ability measures (*Block Design* and *Object Assembly*) in this group.

As at T1, the correlations between composite measures of the different cognitive domains were calculated and are presented in Table 3.9. At this time point, the *Bike Trails* task was included in the motor composite as more children were able to perform the task at this time point and the correlation with *Coin Posting* was greater than at T1. The average z-score from the *Sentence Structure* and *Basic Concepts* tasks constituted the grammar composite at this time point and scores on the *Block Design* task contributed to the nonverbal composite. The language and vocabulary composites were composed in the same way as at T1.

Table 3.9 shows that neither nonverbal nor motor skill is significantly correlated with any type of language composite although they are significantly correlated with each other in both groups. Unlike at T1, the vocabulary and grammar composites are

significantly correlated in the group with Down syndrome as well as in the typically developing group.

3.3.6 Relationships Between T1 and T2 Individual Tests

The correlations between the cognitive tests administered at T1 and T2 are given in Table 3.10 for the children with Down syndrome and in Table 3.12 for the typically developing children. The correlations between the composite measures at T1 and T2 are given in Table 3.11 for the children with Down syndrome and in Table 3.13 for the typically developing children.

In terms of stability, Table 3.10 shows that the correlations between the T1 and T2 scores on the same task ranged from r=.260 to r=.864 in the group with Down syndrome. All tasks were significantly correlated between T1 and T2 with the exception of *Mental Age* and *Basic Concepts*. It is perhaps surprising that there was poor stability on the *Basic Concepts* task given that this was the only task not to show significant improvements over time. In general, stability on the measures was poorer in the typically developing group, which could be due to the young age of the sample and the greater gains that were made between the time points. The correlations ranged from r=.308 to r=.701, with significant correlations between T1 and T2 for all tests except the *Object Assembly* and *Coin Posting* tasks.

In terms of the relationships between individual tests over time, which gives an indication of how different cognitive and linguistic domains relate to each other in the different groups, there were significant correlations between the *Receptive* and *Expressive Vocabulary* tests in both groups. There was a consistent pattern of relationships between some of the nonverbal and vocabulary tests in the group with Down syndrome. The *Object Assembly* task was related to later *Expressive* and *Receptive Vocabulary* and the reverse relationships were also significant. Furthermore, there were moderate correlations between the T1 vocabulary measures and later *Block Design*, although the reverse relationship cannot be examined as this test was only administered at T2. In contrast, while there is a relationship in the typically developing group between T1 *Object Assembly* and T2 *Expressive Vocabulary,* no other relationship between the nonverbal and vocabulary measures is significant.

Table 3.10.

Correlations between T1 and T2 cognitive tests for the children with Down syndrome

	T2 age	T2 Mental Age	T2 Object Assembly	T2 Block Design	T2 Receptive Vocab	T2 Basic Concepts	T2 Sentence Structure	T2 Expressive Vocabulary	T2 Nonword Repetition	T2 Posting Coins	T2 BikeTrails
T1 Age	.955**	.239	.198	-.401	-.088	-.113	-.361	-.277	-.076	.309	-.147
T1 Mental Age	-.109	.397	.158	.421	.315	.311	.276	.199	.321	.216	-.473
T1 Object Assembly	-.186	.386	.864**	.689**	.754**	.371	.108	.561*	-.057	-.094	-.410
T1 Receptive Vocab	-.239	.327	.452*	.703**	.779**	.079	.041	.448*	-.031	.016	-.067
T1 Basic Concepts	-.420	-.140	-.123	-.042	.070	.260	-.013	.418	.346	.014	.329
T1 Expressive Vocabulary	-.224	-.026	.525*	.450	.625**	.417	.206	.806**	.347	-.188	.094
T1 Nonword Repetition	-.052	.008	.275	.228	.545*	.152	-.049	.674**	.647**	.173	-.094
T1 Posting Coins	.266	.114	-.301	-.525*	-.339	-.292	-.344	-.291	-.229	.674**	.181

Table 3.11.

Correlations between T1 and T2 cognitive composites for the children with Down syndrome.

	T2 Nonverbal	T2 Language	T2 Vocabulary	T2 Grammar	T2 Motor
T1 Nonverbal	.762**	.500*	.603**	.356	-.297
T1 Language	.353	.664**	.820**	.338	.012
T1 Grammar	-.169	.312	.272	.188	.115
T1 Vocabulary	.575**	.606**	.849**	.310	-.115
T1 Motor	-.281	-.406	-.338	-.339	.554*

Table 3.12.

Correlations between the T1 and T2 cognitive measures for the typically developing group.

	T2 Age	T2 Mental Age	T2 Object Assembly	T2 Block Design	T2 Receptive Vocabulary	T2 Basic Concepts	T2 Sentence Structure	T2 Expressive Vocabulary	T2 Nonword Repetition	T2 Posting Coins	T2 Bike Trails
T1 Age	.963**	.101	.419	.085	.188	.407	.270	.426*	.428	-.439*	-.420
T1 Mental Age	.259	.536*	.075	.097	.486*	.382	.282	.315	.101	-.324	-.339
T1 Object Assembly	.327	.489*	.308	.463*	.130	.208	.460*	.458*	.153	-.088	.002
T1 Receptive Vocabulary	.386	.310	.236	.155	.418[a]	.315	.219	.700**	.420	-.235	-.273
T1 Basic Concepts	.621**	.313	.161	.183	.465*	.509*	.251	.608**	.582**	-.433**	-.383
T1 Expressive Vocabulary	.540**	.302	.233	.166	.490*	.395	.172	.701**	.778**	-.138	-.122
T1 Nonword Repetition	.685**	.331	.185	-.008	.385	.486*	.014	.428	.626**	-.391	-.374
T1 Posting Coins	-.334	-.138	.064	-.060	-.569**	-.404	-.022	-.322	-.097	.377	-.171

[a] p=.053

Table 3.13.

Correlations between T1 and T2 cognitive composites for the typically developing children

	T2 Nonverbal	T2 Language	T2 Vocabulary	T2 Grammar	T2 Motor
T1 Nonverbal	.547**	.565**	.539**	.513*	-.296
T1 Language	.308	.735**	.713**	.396	-.410
T1 Grammar	.280	.695**	.639**	.449*	-.495*
T1 Vocabulary	.323	.718**	.744**	.352	-.252
T1 Motor	-.057	-.471*	-.531*	-.369	.125

As in the T1 concurrent correlations, there were no significant correlations between the vocabulary and grammar measures over time in the group with Down syndrome. In the typically developing group there was a unidirectional relationship, with T1 *Basic Concepts* significantly correlating with the T2 vocabulary measures but not vice versa.

3.3.7 Relationships Between T1 and T2 Composite Measures

There were three cross-domain relationships that were of particular interest for addressing the aims of this study: grammar-vocabulary, nonverbal-language and motor-language. The research questions concern whether performance in one of these domains predicts the other over time. To address these questions the cross-lagged correlations between the relevant composite measures were examined. This approach involves comparing the strength of the relationship between one variable (e.g. vocabulary) at T1 and the other (e.g. grammar) at T2 with the relationship in the reverse direction (Kenny, 1975). The presumption is that if vocabulary is a significantly stronger correlate of T2 grammar than T1 grammar with T2 vocabulary then vocabulary is more likely to be implicated in the development of grammar than the reverse. This method has been criticised as it fails to take account of a variable's stability over time (the autoregressor), which makes it difficult to interpret causality (Farrell, 1994). Thus, path analysis and structural equation modelling tend to be preferred methods of analysis for longitudinal data. However, the small sample size and non-normal distributions of several of the variables in the current study preclude the use of these analyses. Furthermore, recent longitudinal studies addressing similar questions have employed carefully interpreted cross-lagged correlations (Dionne et al., 2003; Moyle et al., 2007). The correlations between the composite measures are given in Table 3.11 and Table 3.13.

3.3.7.1 Vocabulary and grammar

In the group with Down syndrome, there were no significant correlations between the vocabulary and grammar composites over time and both correlations were a similar magnitude, at approximately r=.300. This suggests that these skills are somewhat dissociated during this period of development in Down syndrome. In the typically developing group, however, there was a moderate, significant relationship between T1 grammar and later vocabulary (r=.639) but a smaller correlation between T1 vocabulary and T2 grammar (r=.352). The difference between these correlations was calculated using Raghunathan, Rosenthal and Rubin's (1996) test, which takes into account the intercorrelations between all the variables. The difference was marginally significant

(z=1.48, p=.061). This indicates that grammar may have more influence on vocabulary over this developmental period than vocabulary has on grammar in the typically developing group.

3.3.7.2 Nonverbal ability and language

In the group with Down syndrome, there was a moderate and significant correlation between T1 nonverbal ability and T2 language (r=.500) and a weaker, non-significant correlation between T1 language and T2 nonverbal ability (r=.353). However, the difference between these correlations was not significant (z=0.72, p=.200). The pattern was similar in the typically developing group, with a significant correlation between T1 nonverbal ability and T2 language (r=.565) but not in the reverse direction (r=.308). Again, the difference between these correlations was nonsignificant (z=1.24, p=.094). Thus, while the pattern of correlations suggests that nonverbal ability has a greater influence on language than language has on nonverbal ability, in both groups, it cannot reliably be stated that this difference is meaningful within a sample of this size.

3.3.7.3 Motor and language

There were moderate correlations between the T1 motor measure and T2 language composite in both groups, although this was not significant in the group with Down syndrome (DS r=-.406, TD r=-.471). However, while there was a moderate, non-significant relationship between T1 language and T2 motor ability in the typically developing group (r=-.410) this was not the case in the group with Down syndrome (r=.012). The difference between the correlations over time was significant in the group with Down syndrome (z=-1.58, p=.041) but non-significant in the typically developing group (z=-0.24, p=.400). This suggests that in the group with Down syndrome motor ability has a stronger influence on language development than language has on motor development over this time period.

3.4 Discussion

The aim of this study was to examine the cognitive profile in a group of four- to five-year-old children with Down syndrome and its development over the course of approximately one year. It was expected that, in line with results from studies with older children and adults, language and motor skills would generally be weaker than nonverbal ability. Furthermore, within the language domain it was predicted that grammatical skill would be more impaired than vocabulary and receptive vocabulary would be a relative strength. The results from T1 supported these predictions in that the children with Down

syndrome showed significant weaknesses on all of the language and motor tasks, with the exception of the receptive vocabulary task, in comparison to a typically developing group matched for nonverbal mental age. Furthermore, z-score analyses indicated that grammatical skill was more impaired than vocabulary.

A further aim of the study was to examine variability in the cognitive profile. It was expected that there would be more variability in performance on the standardised tests in the group with Down syndrome compared to the typically developing group and that there would be a degree of individual variability in the expression of the cognitive profile. Contrary to expectations, variability, as indexed by standard deviations, was similar in both groups on all tests except the *Coin Posting* task on which the group with Down syndrome did show more variable performance. In line with predictions, however, there was individual variability in the cognitive profile with just under half of the sample (45.5%) showing the full, expected profile across all tests.

Lastly, this study aimed to look at how cognitive skills developed over time with a particular emphasis on looking at how vocabulary and grammar, nonverbal ability and language, and motor and language skills related to each other between T1 and T2. It was expected that vocabulary and grammar would be less strongly related in individuals with Down syndrome than those with typical development due to their disproportionate difficulties with grammar. This hypothesis was partially supported by the results, which showed that at T1 vocabulary and grammar were not significantly correlated and furthermore, there were no significant longitudinal relationships across the two domains in the group with Down syndrome. However, at T2, vocabulary and grammar were significantly correlated.

In terms of the nonverbal-language and motor-language relationships, it was predicted that children with Down syndrome would show stronger correlations across these domain pairs than typically developing children. The results lend little support to these hypotheses. The patterns of correlations were very similar across both groups for the nonverbal-language relationship. In both groups there were moderate correlations between earlier nonverbal ability and later language ability although these were not significantly stronger than the reverse relationship. Similarly, the T1 *Coin Posting* motor task was moderately correlated with later performance on the language measures in both groups. However, this relationship was significantly stronger than the influence of language on the motor task in the group with Down syndrome only, suggesting that the relative

influence of these tasks over time may differ between groups although the overall pattern of relationships looks similar.

3.4.1 Cognitive Profile

The results from this study are in line with the majority of studies that have examined the cognitive profile in older children and adolescents with Down syndrome (Silverman, 2007). In four- to five-year-old children with Down syndrome, language and motor skills were generally impaired relative to nonverbal ability. However, it should be noted that this impairment was relative to nonverbal mental age, as assessed by two subtests from the *Leiter-R* battery and, in fact, the group with Down syndrome were impaired on the additional *Object Assembly* nonverbal task. This suggests that not all nonverbal skills are equally affected in Down syndrome highlighting the importance of test selection. The *Object Assembly* task requires a degree of fine motor control in assembling the jigsaws and a degree of vocabulary knowledge to know how the finished jigsaw should look, both of which could have selectively disadvantaged the children with Down syndrome.

This study also replicated findings from older children and adults concerning the language profile in Down syndrome. In line with previous studies, such as Vicari et al. (2000) grammatical ability was more impaired than vocabulary. It should be noted that the task used to assess grammar at T1 in the present study was different from many of the tasks used in other studies as, given the young age of the participants, it did not tap complex syntax. Instead it assessed knowledge of abstract and conceptual single words in a similar way to a receptive vocabulary test. However, the results clearly show that the children with Down syndrome were weaker on the *Basic Concepts* test, compared to the standard receptive vocabulary test, suggesting that *Basic Concepts* may indeed be tapping a precursor to more complex syntactic ability in this sample. There are mixed findings in the literature with regards to whether receptive vocabulary is in line with nonverbal ability or slightly weaker (Caselli, Monaco, Trasciani, & Vicari, 2008 vs. Laws & Bishop, 2004). In the current study the difference between the groups was only marginally significant (p=.061) suggesting that while receptive vocabulary may not be entirely in line with nonverbal ability it is the strongest language skill within the cognitive profile in this age group.

In sum, these results extend Fidler et al.'s (2006) findings that two- to three-year old children with Down syndrome show the characteristic pattern of cognitive strengths and weaknesses, but only in an emerging fashion. This study supports the view that the

profile has fully emerged by four- to five-years-old, at the group level, in children with Down syndrome based on comparisons with nonverbal mental-age matched typically developing controls.

3.4.2 Variability in the Cognitive Profile

Previous review studies have highlighted that there is evidence of wide variability in cognitive ability amongst individuals with Down syndrome (Patterson et al., 2013; Silverman, 2007). However, there is little empirical evidence directly assessing whether this variability is greater than would be expected in the typically developing populations. In the current study, the standard deviations of the scores on the cognitive tests were generally similar across both the typically developing group and the group with Down syndrome. This is similar to findings from previous studies of cognitive performance in Down syndrome (Byrne et al., 2002; Chapman et al., 2002). While this suggests that interindividual variability is no greater in Down syndrome than in the typical population this would benefit from examination with larger samples using more rigorous statistical techniques. In particular, it is important to note that in the current study the typically developing group encompassed a wider chronological age range than the group with Down syndrome and thus comparisons of the group standard deviations should be interpreted with caution.

A further question regarded whether the nature of the cognitive profile was variable between individuals with Down syndrome. Tsao and Kindelberger (2009) suggest that this may be the case as almost half of their sample did not show the characteristic weakness in verbal ability compared to nonverbal ability. The present study supported these observations. Just under half of the children with Down syndrome (45.5%) showed the characteristic cognitive profile. However, it should be noted that some individual comparisons within the profile were more consistent than others. For example, whereas 95% of the sample had motor skills that were weaker than their nonverbal ability, only 68% had weaker expressive vocabulary than nonverbal ability. In sum, when taken together, these findings suggest that the cognitive profile that emerges at the group level does not characterise all individuals with Down syndrome. Understanding the source of this variability will be important for developing accurate causal models of cognitive difficulties in Down syndrome. For practitioners it will also be useful to take this individual variability account when planning educational interventions.

3.4.3 Relationships Between Skill Domains

This study utilised a longitudinal design in order to look at how skills develop over time and how they relate to each other during the developmental period of interest. In line with findings from previous longitudinal studies, the children with Down syndrome showed improvement in their raw scores on all cognitive tests between T1 and T2, with the exception of the *Basic Concepts* task. It is unclear why this task would be the only one not to improve, particularly as there were neither ceiling nor floor effects that could have masked improvement but it could be indicative of the well documented grammar deficit in Down syndrome. As the cognitive tests come from different batteries and are measured on different scales, it is difficult to establish whether one skill showed a greater rate of improvement than another over the course of the study. However, the effect sizes for the change in scores between T1 and T2 suggest that fine motor ability and expressive vocabulary may have undergone the greatest improvement although this would benefit from replication with alternative motor and vocabulary measures in a larger sample.

3.4.3.1 Relationship between grammar and vocabulary

While the relative deficit in grammatical abilities compared to vocabulary has been well established in individuals with Down syndrome (Vicari et al., 2000) there has been little research looking at how these domains covary over time. It was speculatively hypothesised that the dissociation between these domains may be an indicator that they are less closely related than in typical development. The concurrent data at T1 and across time support this hypothesis. There were no significant relationships between the grammar and vocabulary composites between T1 and T2 or at T1 alone. However, they were significantly correlated at T2 (r=.45), indicating that there is not a full dissociation of these skills across development.

There are several possible interpretations of these findings. The addition of the *Sentence Structure* task at T2, which is a more direct test of syntactic understanding, may have altered the relationships with vocabulary. However, it is not clear why this test should be more closely linked with vocabulary than *Basic Concepts*, which is much more analogous to receptive vocabulary tasks. Furthermore, the correlations between the individual tests show that *Sentence Structure* relates more weakly to vocabulary than *Basic Concepts*. This also would not explain why vocabulary at T1 does not relate to the T2 grammar composite. Instead it is possible that the group with Down syndrome are delayed in showing the typical relationships between grammar and vocabulary. Bates and Goodman (2001)

suggest that children with Down syndrome require a larger amount of vocabulary than typical children before rapid syntactic development can begin. Thus, is it possible that this critical mass of vocabulary was reached for much of the sample between T1 and T2 of the current study. This interpretation is further supported by the findings of Moyle et al. (2007), who showed that lexical bootstrapping and concurrent relationships between grammar and vocabulary emerged later in development for late talkers than for typically developing children. To explore this interpretation an additional time point would be required in the longitudinal study in order to investigate whether lexical bootstrapping of syntactic development occurs in children with Down syndrome after the age of five- to six-years-old.

It should be noted that the patterns in the typically developing group differed from that expected given the existing literature. Previous studies have found evidence of bidirectional syntactic and lexical bootstrapping across time in samples of a similar age (Dionne et al., 2003). In the present study the cross-lagged correlations indicated that grammar had more influence on vocabulary (syntactic bootstrapping) than the reverse pattern (lexical bootstrapping). However, this is likely to be due to the selection of *Basic Concepts* as the grammar measure at T1. Although not the case in the group with Down syndrome, *Basic Concepts* has a close relationship with vocabulary in the typically developing children at both time points, probably due to its similarity to a receptive vocabulary task. In fact, at T1 it correlated with the vocabulary composite at r=.83, which is higher than grammar and vocabulary would be expected to correlate at this age (r=.68 in Dionne et al., 2003). Furthermore the lexical bootstrapping correlation (T1 vocabulary and T2 grammar, r=.35) is intermediary between that found in Dionne et al. (2003; r=.47) and in Moyle et al. (2007; r=.31). Thus, it appears that the syntactic bootstrapping effect may have been inflated due to test selection rather than an unexpected lack of lexical bootstrapping.

3.4.3.2 Relationship between nonverbal and language ability

It was hypothesised, based on findings from studies of children with a broad spectrum of intellectual disabilities, that nonverbal and language ability may be more closely related in the children with Down syndrome than typically developing children. However, this hypothesis was not supported by the data. In both the typically developing group and the group with Down syndrome there were moderate relationships between nonverbal ability and language at T1 but only weak relationships at T2. Furthermore, T1 nonverbal ability was significantly correlated with T2 language skill in both groups, and not

more so in the group with Down syndrome. The cross-lagged correlation analysis revealed that, although the correlations were stronger in this direction than between T1 language and T2 nonverbal ability, this difference was not great enough in either group to conclude that nonverbal ability has more influence on language development than the reverse.

These results are in line with findings from typical development that report a relationship between nonverbal and language development in two- to four-year-old children (Price et al., 2004). However, it does not support the findings of van der Schuit et al. (2011) that nonverbal ability was a significant predictor of later phonological memory, vocabulary and syntactic skill in four-year-olds with intellectual disability but not age-matched typically developing controls. This difference is most likely due to sample characteristics. First, the typically developing sample were older and so the relationships between nonverbal and language ability could be a different strength. Second, they used a heterogeneous sample of children with mixed intellectual disabilities who performed at a higher level on the cognitive tasks than the children with Down syndrome in the current study. In sum, the data from the present study does not support the view that nonverbal ability plays a greater role in the language development of children with Down syndrome between the ages of four- and five-years-old.

3.4.3.3 Relationship between motor and language ability

It was tentatively predicted that there would be a stronger relationship between motor and language ability in children with Down syndrome than in typically developing children, largely due to findings that this is the case for children with specific language impairment (Hill, 2001). However, the patterns of correlations seen between the motor and language measures in the current study were generally similar across both groups. At T1 there were moderate relationships between the motor measure and language composite, and in fact, these were slightly higher in the typically developing group. At T2 there were weak relationships between the domains in both groups. Over time, the T1 motor measure was moderately correlated with the T2 language composite in both groups but there was only a weak correlation in the reverse direction. The only group difference emerged when the cross-lagged correlations were examined as, in the group with Down syndrome, motor ability had a significantly stronger influence on later language than language had on later motor ability. However, this result should be interpreted with caution as the T1 motor measure was the *Posting Coins* task, the scores on which were highly variable and positively skewed in the group with Down syndrome. Thus, it is important to see if this

result can be replicated with a more reliable measure. If so, then it may be possible to say that language development relies more on motor ability in children with Down syndrome. However, the weight of evidence from the current study better supports the interpretation that the relationship between these two domains is similar in both typical children and those with Down syndrome.

3.4.4 Study Limitations

The data on the cognitive profile at four-to five-years-old in the current study fit neatly with the cognitive profile described in the existing literature. However, it is important to gain a detailed understanding of the profile at all stages of development. Unfortunately, due to the more rapid development of the typically developing group, it was not possible to look at the cognitive profile at T2 of this longitudinal study as the groups were no longer matched. Future studies should consider recruiting additional, matched comparison groups at later time points, where feasible, so that the cognitive profile can be assessed at multiple time-points as well as examining relationships between skills over time.

Within the motor domain this study focussed on fine rather than gross motor skills. This was because fine motor abilities were more practical to assess in a session conducted in a school environment where there was often limited space. Furthermore, previous studies looking at the links between language and motor ability more commonly use fine motor tasks such as peg moving and finger tapping (Hill, 2001). However, given that the poor performance of the group with Down syndrome on the fine motor measures complicated interpretation of motor development over this period, it may be useful to future studies to include measures of gross motor function that may not suffer from similar floor effects.

One factor that could have potentially widened the differences between the two groups is the way in which the typically developing children were recruited. Families who don't use childcare settings are more difficult to access and invite to participate in research and so all of the typically developing children were recruited from nurseries. Around 40% of children under the age of three were enrolled in childcare settings, such as nurseries, in the UK in 2010 (OECD, 2010). Thus, recruiting children of this age solely from nurseries does not result in a fully representative sample. It is possible that children in these settings are more familiar with activities that resemble the cognitive tests administered which could

inflate their performance. However, where it was possible to calculate them, the mean standard scores on all cognitive tests were within the normal range.

Finally, it should be noted that the distributions on several of the cognitive tests were skewed and, on occasion, there were floor effects in performance, particularly at T1 in the group of children with Down syndrome. This complicated the statistical analyses and interpretation of the data and tempered the conclusions that could be drawn. It is rare that studies on Down syndrome, particularly with this young age group, use objective cognitive tests, and parent-report measures are often favoured instead (Berglund et al., 2001; Zampini & D'Odorico, 2013). Objective cognitive tests confer a major advantage as they are a more direct assessment of a child's abilities. However, in situations where a child's age and ability makes objective testing difficult and potentially unreliable, it would be interesting to investigate whether parent-report measures at a younger age can predict the more reliable performance on objective cognitive tests given at an older age. Data that addresses this question could provide evidence about the most reliable and effective way to assess the cognitive ability of children with Down syndrome at different ages, which will be explored in Chapter 4.

3.5 Conclusions

This study suggests that, at the group level, the cognitive profile typically associated with individuals with Down syndrome has fully emerged by the age of four- to five-years-old. There were significant weaknesses in language and motor skills in comparison to nonverbal ability, with the exception of receptive vocabulary. Furthermore, within the language profile, there was evidence that grammar is impaired to a greater extent than vocabulary. The data did not support the view that there is more interindividual variability in children with Down syndrome compared to typically developing children. However, there was clear variability in the consistency of the group level cognitive profile across individuals with Down syndrome. This variability has implications both for the design of interventions and for the development of accurate causal models of cognitive deficits in Down syndrome.

In terms of how skills covaried over time, the findings were mixed. Vocabulary and grammar were less related at the start of the study and between time points in the group with Down syndrome but their stronger correlation at the end of the study suggested that this may represent a delay in typical developmental patterns rather than a complete dissociation between these skills. Nonverbal and language skill seemed to relate in similar

ways concurrently and longitudinally in both groups which suggests that the language development of children with Down syndrome does not rely more heavily on nonverbal ability, at least at this age. Finally, the relationship between language and motor skill was more difficult to interpret due to the skewed distributions and floor effects on the motor tasks. However, there was no strong evidence to support the view that the relationships between motor and language skill differed between the typically developing group and the children with Down syndrome. In sum, the correlational data strengthens findings that there is difference and delay in the language skills of children with Down syndrome but does not find evidence that this can be attributed to differences in how language relates to nonverbal or motor skills. Given the difficulties with cognitive assessment of such young children, there is a valuable comparison to be made between parent-report and objective measures in predicting cognitive development.

4 Parent-Report Measures of Language and Adaptive Behaviour in Children with Down Syndrome and Their Utility in Predicting Cognitive Outcomes

4.1 Introduction

4.1.1 Overview

Chapter 3 replicated the characteristic group-level profile of cognitive strengths and weaknesses in Down syndrome. However, given the young age of the children in the study, there were problems with the distributions of scores on the cognitive measures, limiting statistical analyses. Parent-report measures are often used with children of this age instead but have their own limitations including subjectivity. They also confer advantages, such as the ability to assess the child's wider day-to-day functioning as opposed to performance on a narrow cognitive assessment. However, there has been little research examining whether parent-report measures can predict objectively measured cognitive outcomes in young children with Down syndrome. If this were the case then it may be possible to use such measures as a supplement or substitute for cognitive tests where there are concerns about performance reliability on the objective tests.

This chapter will review the use of parent-report measures with young children with Down syndrome with a particular focus on the Vineland scales (Sparrow et al., 2005), which measure adaptive behaviour, and the MacArthur Communicative Development Inventories (CDI; Fenson et al., 1993) which assess vocabulary. There is a specific profile of adaptive skills associated with Down syndrome, as with cognitive skills. This study aims to replicate this profile of adaptive skills in children with Down syndrome, according to the Vineland-II. Furthermore, this study aims to investigate whether the Vineland-II and CDI can be validated concurrently against the objective cognitive measures administered in Chapter 3 and, if so, whether they can be used to predict cognitive outcomes over time.

4.1.2 Adaptive Behaviour in Down Syndrome

Adaptive behaviour refers to how an individual uses their skills in the context of day-to-day situations. Assessing adaptive behaviour can provide additional complementary information to that gained from cognitive assessments because it is a good marker of an individual's functional capacity. Indeed, Msall and Tremont (1999) highlight the importance of assessing the functional status of individuals with genetic disorders as part of their

medical care. One of the most common tools for examining adaptive behaviour is the Vineland Adaptive Behaviour Scales (Sparrow et al., 2005), assessing four domains: communication, daily living skills, social skills and motor ability. There is evidence that the Vineland Scales are a reliable and valid measure of adaptive behaviour in individuals with developmental disorders (Balboni, Pedrabissi, Molteni, & Villa, 2001; de Bildt, Kraijer, Sytema, & Minderaa, 2005) and they have commonly been used to look at adaptive behaviour in Down syndrome (e.g. Dressler, Perelli, Feucht, & Bargagna, 2010; Dykens, Hodapp, & Evans, 2006).

Several studies have investigated the adaptive behaviour profile in Down syndrome, using the Vineland scales. Most of these studies converge to suggest that social skills in Down syndrome are a strength (Dykens et al., 2006; Fidler et al., 2006; Rodrigue et al., 1991). The majority of studies demonstrate a weakness in the Communication domain, particularly in the expressive compared to the receptive subdomain scores, not only in later childhood (Dykens et al., 2006), but also in the early years (Fidler et al., 2006). This mirrors findings on objective tests of receptive versus expressive vocabulary in Down syndrome (Chapman & Hesketh, 2000). In the Fidler et al. (2006) study, two- to three-year-old children with Down syndrome did not differ from the younger mental-age matched typically developing controls on any of the Vineland domains, including Communication. However, the within-group analyses revealed that the scores on the Communication and Motor domains were significantly weaker than the Socialisation domain. A general pattern of weaknesses in the Motor domain is also seen in older children with Down syndrome (van Duijn, Dijkxhoorn, Scholte & van Berckelaer-Onnes, 2010). Scores on the Daily Living domain tend to be higher than on the Communication and Motor domains but lower than the Socialisation domain (Fidler et al., 2006).

Notwithstanding this, the findings are not entirely consistent across studies investigating the adaptive profile in Down syndrome. For example, Dressler et al. (2010) found that between the ages of 0 and 20, individuals with Down syndrome had higher age equivalent scores in the Communication than the Daily Living or Motor domains, and Di Nuovo & Buono (2011) found a relatively flat profile of scores across all four domains although the general pattern was for social skills to be slightly in advance of communication and daily living skills, which fits with previous research. In sum, the balance of evidence suggests that, even in young children with Down syndrome, the adaptive

profile is likely to present as strengths in socialisation alongside weaknesses in communication and motor skills.

Very few studies have investigated whether Vineland scores correlate with objectively measured cognitive performance in Down syndrome. Of the studies that have addressed this question, the most common method has been to examine the correlations between a generic IQ measure and scores on the Vineland composites but the findings are somewhat mixed. Rihtman et al. (2010) found moderate correlations between all of the separate Vineland domains and the Stanford-Binet test composite (ranging from *r*=.32 to *r*=.77). However, Di Nuovo and Buono (2011) found weak, although significant, relationships between the Communication and Socialization domains and the Wechsler IQ composite (*r*=.20 and *r*=.19 respectively). It is difficult to interpret current findings because of the wide age range (4 to 39 years) in the study by Di Nuovo and Buono (2011) particularly because cognitive performance can decline in adulthood in Down syndrome (Oliver, Crayton, Holland, Hall, & Bradbury, 1998). Only Rihtman et al. (2010) looked at how the Vineland scales relate to objective domain-specific performance, in this case visuo-motor integration. They found a significant correlation between the overall Vineland composite and scores on this task, indicating that the Vineland is related to certain aspects of cognitive and motor ability in Down syndrome.

4.1.3 Parent-Report Measures of Vocabulary in Down Syndrome

The most commonly used parent-report measure of vocabulary in early childhood is the MacArthur-Bates Communicative Development Inventory (CDI; Fenson et al., 1993). The CDI is a checklist of common words, divided into different semantic categories, for which parents indicate whether their child understands and says each word. This yields a comprehension score, which can be used as a measure of receptive vocabulary, and a production score, which can be used as a measure of expressive vocabulary. Versions of the CDI have been used extensively with typically developing children (Dionne et al., 2003; Fenson et al., 1993) but also with children who have developmental disorders and delays (Moyle et al., 2007; Singer Harris, Bellugi, Bates, Jones, & Rossen, 1997; Vandereet, Maes, Lembrechts, & Zink, 2011).

The CDI has been widely used in studies of language development in Down syndrome. Miller, Sedey and Miolo (1995) showed that the CDI is highly correlated with objective vocabulary tests in young children with Down syndrome, validating its use as a vocabulary assessment in this population. Patterns of CDI-assessed vocabulary

performance and development appear to vary slightly. Both Miller (1999) and Zampini and D'Odorico (2013) find that children with Down syndrome have a significantly smaller productive vocabulary than typically developing children matched for developmental age, in line with most studies that use objective tests. However, when matched for vocabulary comprehension as opposed to nonverbal ability, Caselli et al. (1998) found that the productive vocabulary size of children with Down syndrome did not differ from that of the controls. Furthermore, Galeote, Sebastián, Checa, Rey and Soto (2011) found that Spanish children with Down syndrome had equivalent productive vocabularies to typically developing controls matched for mental age and significantly higher comprehension and gesture scores, suggesting a specific advantage for these skills. Vicari, Caselli and Tonucci (2000) also failed to find differences between children with Down syndrome and typically developing controls in the size of CDI-assessed productive vocabulary. However, the mental age assessment in the latter two studies involved a substantial motor component and, given the established motor difficulties in Down syndrome, this may have resulted in a younger, and therefore less linguistically able, control group than if a more pure nonverbal measure had been utilised.

In summary, as in studies using objective vocabulary measures, it appears that the findings depend on the way in which the two experimental groups are matched but the evidence suggests that children with Down syndrome show a deficit in productive vocabulary on the CDI when the groups are matched on purely nonverbal measures. However, it should be noted that none of the studies reviewed previously included a measure of signed vocabulary and many young children with Down syndrome use a form of sign language as their primary mode of communication (Clibbens, 2001). Thus, the weaknesses in productive vocabulary seen in children with Down syndrome may be due to speech-specific production difficulties rather than an overall deficit in lexical expression. Including children's signed vocabularies in estimates of their expressive vocabulary before comparing with typically developing controls would distinguish between these interpretations.

The CDI has been highlighted as a good predictor of typically developing children's later objectively measured vocabulary (Can, Ginsburg-Block, Golinkoff, & Hirsh-Pasek, 2013; Feldman et al., 2005). However, only one study addresses this question for children with Down syndrome. Miller et al. (1995) found that the productive vocabulary of children with Down syndrome who had a mental age of approximately 20 months, as assessed by

the CDI, was significantly correlated with objective expressive vocabulary at a mental age of 28 months. This suggests that the parent-report CDI could be used to predict later objective vocabulary measures in children with Down syndrome.

4.1.4 Aims of the Study

Previous studies, particularly those looking at the correlations between the Vineland-II Scales and objective cognitive assessments, have typically utilised small samples that span a wide age range. This often precluded statistical treatment of results and complicated the interpretation of the data. To address these limitations, this study aims to investigate the adaptive behaviour and vocabulary profiles of 22 four- to five-year-old children with Down syndrome using parent-report measures. It is predicted that, in line with previous literature, children will show strengths in social skills and deficits in communication and motor domains when assessed on the Vineland scales.

Further, it is predicted that the children with Down syndrome will have significantly weaker productive vocabularies than the typically developing controls according to the CDI. There is less research examining the comprehension scores on the CDI but research utilising objective tests of receptive vocabulary, such as the studies reviewed in section 1.3.2, would suggest that there may be no group differences on the comprehension measure. In a novel extension of previous studies, the CDI was adapted to include a measure of signing vocabulary in order to see if this addition mitigates the significant expressive vocabulary weaknesses typically reported for children with Down syndrome.

Finally, the main aim of this study is to examine the concurrent and predictive validity of these parent-report measures in order to assess whether they can be used to predict later objectively measured cognitive outcomes in children with Down syndrome. Findings regarding the relationship between the Vineland scales and cognitive tests in individuals with Down syndrome are mixed but the findings of Rihtman et al. (2010) suggest that there are significant relationships between adaptive behaviour and both IQ and more domain-specific motor tests. The present study will extend these findings by looking at the predictive value of the Vineland scales longitudinally and by examining whether specific domains of the Vineland scales predict scores on highly related cognitive tests rather than focussing on an overall adaptive behaviour composite and IQ measures. There is more evidence to support a hypothesis that the CDI can predict later scores on objective vocabulary measures in both typically developing children and two-year-old

children with Down syndrome (Miller et al., 1995). It is expected that the present study will replicate these findings in an older group of children over a longer period of development.

4.2 Method

This study formed part of the longitudinal study described in Chapter 3. Full details about the study design and participants are given in sections 3.2.1 and 3.2.2. At both time points adaptive behaviour was assessed using a face-to-face parental interview measure and vocabulary was assessed using a parent-report questionnaire.

4.2.1 Measures

4.2.1.1 Adaptive behaviour: parental report

Parents completed the Survey Form of the Vineland-II Adaptive Behaviour Scales (Vineland-II; Sparrow, Cicchetti, & Balla, 2005). This is a semi-structured standardised interview that asks parents about four domains of their child's everyday functioning: Communication, Daily Living Skills, Socialisation and Motor Skills. This assessment aims to measure how a child functions on a day-to-day basis and how they use their skills in more general contexts. Table 4.1 outlines the structure and content of the Vineland-II Scales and gives examples of items that belong in each category.

Table 4.1.

Content of the Vineland-II Scales showing the domains and sub-domains assessed with example items for each sub-domain.

Domain	Sub-domain	Example item
Communication	Receptive	"Points to common objects…as they are named"
	Expressive	"Says at least 50 recognisable words"
	Written	"Recognises own name in printed form"
Daily Living	Personal	"Sucks from a straw"
	Domestic	"Is careful around hot objects"
	Community	"Uses TV without help"
Socialisation	Interpersonal	"Shows desire to please others"
	Play and Leisure	"Plays with others with minimal supervision"
	Coping	"Says "please" when asking for something"
Motor	Gross	"Throws ball"
	Fine	"Uses twisting hand-wrist motion"

The interviewer asked open questions within each of these domains in order to score up to 433 specific items based on how often the child performed particular

behaviours and prompted for more information when necessary. The items were scored on a scale of frequency: 0 (Never), 1 (Sometimes or Partially) and 2 (Usually). A basal level for each subdomain was established by a score of 2 on four consecutive items and a ceiling was established by a score of 0 on four consecutive items. All items before the basal are automatically given a score of 2 and all items after the ceiling are given a score of 0. Thus, total scores for each subdomain, domain and for the adaptive behaviour scale as a whole can be calculated and converted into both standard scores and age equivalents (internal consistency reliability coefficient .97; test-retest reliability coefficient .90).

It should be noted that, at T1, 20 of the parents from the group of children with Down syndrome were originally interviewed using the Expanded interview forms, which contain 647 items. However, these were very lengthy interviews and often took up to two hours, which was overly long for parents. Therefore, as detailed item-level information was not required for this study, it was decided that the shorter 433-item Survey interview forms would be used for the remaining families of the children with Down syndrome and the families of the typically developing group. This form of the interview took approximately one hour to administer. As the Survey interview forms are essentially a shortened version of the Expanded forms, the majority of the questions are direct replications from the Expanded form and for the few others, the appropriate scoring criteria could be inferred from parents' responses to other questions on the Expanded form. Therefore, the 20 Expanded forms were mapped onto the Survey forms so that the same items were used in the analysis of all interviews. The Survey forms were used with all families in both groups at T2.

4.2.1.2 Vocabulary: parental report

As a measure of children's vocabulary skill, parents completed an adapted version of the Oxford Communicative Development Inventory (OCDI; Hamilton, Plunkett, & Schafer, 2000). The OCDI is a UK adaptation of the MacArthur-Bates CDI (Fenson et al., 1993), which has been validated as an early vocabulary measure and used in many language studies (e.g. Dionne, Dale, Boivin, & Plomin, 2003). The OCDI is a questionnaire listing 416 individual words across 19 semantic fields. It is targeted at children aged from 11 to 26 months. Parents' are asked to indicate separately whether their child understands each word and whether they produce it. The total number of words understood and the total number of words produced are summed to give a measure of vocabulary comprehension and a measure of production.

The OCDI was adapted, with permission, so that it was suitable for measuring the vocabularies of children with Down syndrome. As previously highlighted, children with Down syndrome often use a form of sign language to communicate productively (Clibbens, 2001). The adapted version lists 408 individual items and, for each word, in addition to asking whether the child understood and produced it, parents were also asked whether their child currently produces a sign for the word or if they used to produce a sign. This enabled estimation of the size of a child's signed vocabulary in addition to their spoken vocabulary. The adapted OCDI was completed by parents at both T1 and T2.

4.2.1.3 Cognitive assessment

Table 4.2, below, gives a summary of the tests administered at each time point. These are described in detail in Chapter 3.

Table 4.2.

The content of the cognitive assessment battery at each time point.

Cognitive Domain	T1	T2
Nonverbal	Repeated Patterns	Repeated Patterns
	Figure Ground	Figure Ground
	Object Assembly	Object Assembly
	-	Block Design
Language	ROWPVT	ROWPVT
	Expressive Vocab	Expressive Vocab
	Basic Concepts	Basic Concepts
	Language Sample	Language Sample
	Nonword Repetition	Nonword Repetition
	-	Sentence Structure
Motor	Coin Posting	Coin Posting
	Bike Trails	Bike Trails

4.2.2 Procedure

At both time points the Vineland-II interviews were conducted face-to-face with the primary caregiver or both parents, usually at the parents' home after their child had been assessed and typically lasting for around one hour. Some were completed by telephone when necessary. The adapted OCDI was given to parents during the interview visit and these were completed and returned to the experimenter by post.

4.3 Results

4.3.1 Data Preparation

Parents of all participants in both groups completed the Vineland-II scales at both time points, yielding a complete data set. The final number of OCDI questionnaires returned from each group at each time point is given in Table 4.3. The distribution of data for all variables was determined through examination of histograms, Kolmogorov-Smirnoff tests of normality, and skewness and kurtosis statistics. Distributions did not deviate from normality except where stated otherwise.

Table 4.3.

Number of OCDI questionnaires returned in both groups at each time point with the percentage of missing data given in brackets.

Group	Time 1	Time 2
Down syndrome (N (%missing))	18 (18%)	14 (33%)
Typically developing (N (% missing))	22 (0%)	18 (18%)

4.3.2 Parent-Report Measures at T1: Adaptive Profile and Vocabulary

4.3.2.1 Vineland-II results

Descriptive statistics for the children with Down syndrome and the typically developing children matched for nonverbal-mental-age on the Vineland subdomains at T1 are presented in Table 4.4. Group comparisons demonstrate that the typically developing group generally performed significantly better than the group with Down syndrome on all subdomains and subscales with the exception of the Socialization domain and the Gross and Fine Motor subscales. However, on all of the motor measures, the typically developing children attained higher scores and the difference on the overall Motor subdomain was marginally significant with a moderate effect size (p=.053, d=.60). This pattern of results suggests that the adaptive profile in Down syndrome, in this age group, was characterised by significantly weaker communication and daily living skills than expected given nonverbal ability, a trend for weaker motor skills and socialisation skills that are in line with nonverbal ability.

Table 4.4.

Mean raw scores, age equivalents, standard deviations and group differences on the Vineland-II subdomains, selected subscales and overall adaptive behaviour composite at T1

	DS (N=22) Raw scores	Age equivalent in months	TD (N=22) Raw scores	Age equivalent in months	Group difference on raw scores
Chronological age (months)	56.77 (2.41)		33.50 (4.30)		t=22.16, p<.001
Communication domain (/198)	80.27 (16.79)	32.08 (6.79)	110.41 (15.04)	40.91 (9.72)	t=-6.27, p<.001
Receptive subscale (/40)	25.82 (3.80)	31.77 (9.69)	29.64 (3.03)	44.32 (13.73)	t= -3.68, p=.001
Expressive subscale (/108)	50.73 (13.52)	28.73 (6.41)	78.36 (11.38)	47.50 (12.72)	t=-7.34, p<.001
Daily Living Skills domain (/218)	52.41 (12.36)	33.94 (6.66)	62.86 (8.88)	40.70 (4.55)	t=-3.22, p=.002
Socialisation domain (/198)	96.32 (10.91)	43.11 (7.41)	96.00 (9.93)	41.48 (6.60)	t=.101, p=.920
Motor domain (/152)	89.23 (11.24)	30.73 (4.46)	95.68 (10.27)	34.45 (6.10)	t=-1.99, p=.053
Gross motor subscale (/80)	59.00 (7.45)	29.64 (5.90)	62.45 (6.84)	33.64 (8.76)	t=-1.60, p=.117
Fine motor subscale (/72)	30.23 (5.79)	31.82 (6.69)	33.23 (5.33)	35.27 (6.07)	t=-1.79, p=.081
Adaptive behaviour composite (/766)	318.23 (41.79)	-	365.50 (36.83)	-	t=-3.98, p<.001

Table 4.5.

Mean scores, standard deviations and group differences on the adapted OCDI measures

	DS (N=18)	TD (N=22)	Group difference
Expressive vocabulary (signed and spoken)	218.89 (84.73)	369.09 (59.42)	*U*=24.50, *p*<.001
Expressive vocabulary (spoken only)	179.28 (120.13)	369.09 (59.42)	*U*=21.50, *p*<.001
Receptive vocabulary (words understood)	282.78 (76.93)	379.00 (29.48)	*U*=33.00, *p*<.001

4.3.2.2 Adapted OCDI results

The raw scores on the adapted OCDI measure are presented in Table 4.5. Two expressive vocabulary scores were calculated; one summed the number of words either signed or spoken and the other summed only the spoken words. The total number of words reported to be understood by the child was summed for a comprehension score. There were ceiling effects on all measures in the typically developing group and so non-parametric Mann-Whitney U tests were employed to investigate group differences.

Table 4.5 shows that the typically developing group knew significantly more words on the OCDI, both expressively and receptively, even when the signing vocabulary of the children with Down syndrome was taken into account.

4.3.3 Parent-Report Measures at T2: Adaptive Behaviour and Vocabulary

4.3.3.1 Vineland-II results

The raw scores and age equivalents on the subdomains and subscales of the Vineland-II at T2 are presented in Table 4.6, which shows that the typically developing group scored significantly higher on all Vineland-II measures. In order to determine whether children in both groups showed significant improvement between T1 and T2, within-subjects t-tests were calculated for each measure. Effect sizes (Cohen's *d*) were also calculated to compare the magnitude of changes on different scales. The results of these analyses are presented in Table 4.7.

Table 4.6.

Raw scores, age equivalents and group differences on the Vineland-II measures at T2

	DS (N=21) Raw Score	Age Equivalent	TD (N=22) Raw Score	Age Equivalent	Group Differences on Raw Scores
Chronological age (months)	71.52 (2.21)		46.91 (4.99)		t=20.73, p<.001
Communication domain (/198)	98.38 (17.63)	40.44 (7.01)	130.73 (9.63)	58.17 (11.64)	t=-7.51, p<.001
Receptive subscale (/40)	27.90 (2.68)	37.52 (8.74)	32.68 (2.63)	62.00 (20.51)	t=-5.90, p<.001
Expressive subscale (/108)	62.10 (13.00)	34.33 (7.33)	89.73 (5.02)	62.00 (11.12)	t=-9.28, p<.001
Daily Living Skills domain (/218)	61.24 (11.22)	40.75 (6.38)	84.82 (7.88)	52.98 (5.92)	t=-8.01, p<.001
Socialisation domain (/198)	94.14 (13.15)	40.40 (8.05)	119.41 (10.32)	58.86 (8.82)	t=-7.03, p<.001
Motor domain (/152)	93.19 (13.21)	32.88 (6.94)	119.36 (10.30)	49.80 (8.51)	t=-7.26, p<.001
Gross motor subscale (/80)	59.76 (6.32)	30.19 (6.01)	70.95 (5.42)	47.73 (12.29)	t=-6.24, p<.001
Fine motor subscale (/72)	33.43 (8.37)	35.57 (9.41)	48.41 (7.04)	51.86 (7.40)	t=-6.37, p<.001
Adaptive behaviour composite (/766)	346.95 (46.46)		454.32 (31.06)		t=-8.95, p<.001

Table 4.7.

Differences between the raw scores at T1 and T2 on the Vineland-II scales in both groups

	DS T1 (N=21)	DS T2 (N=21)	Difference over time with effect size	TD T1 (N=22)	TD T2 (N=22)	Difference over time with effect size
Communication domain (/198)	79.05 (16.16)	98.38 (17.63)	*t*=-10.77, *p*<.001 *d*=3.37	110.41 (15.04)	130.73 (9.63)	*t*=-8.97, *p*<.001 *d*=3.06
Receptive subscale (/40)	26.00 (3.80)	27.90 (2.68)	*t*=-3.01, *p*=.007 *d*=.99	29.64 (3.03)	32.68 (2.63)	*t*=-7.28, *p*<.001 *d*=2.23
Expressive subscale (/108)	49.38 (12.25)	62.10 (13.00)	*t*=-8.06, *p*<.001 *d*=2.50	78.36 (11.38)	89.73 (5.02)	*t*=-6.06, *p*<.001 *d*=2.43
Daily Living Skills domain (/218)	51.52 (11.93)	61.24 (11.22)	*t*=5.75, *p*<.001 *d*=1.78	62.86 (8.88)	84.82 (7.88)	*t*=-10.19, *p*<.001 *d*=3.08
Socialisation domain (/198)	95.29 (10.02)	94.14 (13.15)	*t*=.52, *p*=.611 *d*=.17	96.00 (9.93)	119.41 (10.32)	*t*=-10.42, *p*<.001 *d*=3.14
Motor domain (/152)	88.76 (11.30)	93.19 (13.21)	*t*=-2.54, *p*=.020 *d*=.80	95.68 (10.27)	119.36 (10.30)	*t*=-13.64, *p*<.001 *d*=4.12
Gross motor subscale (/80)	58.81 (7.57)	59.76 (6.32)	*t*=-.86, *p*=.402 *d*=.27	62.45 (6.84)	70.95 (5.42)	*t*=-7.05, *p*<.001 *d*=2.18
Fine motor subscale (/72)	29.95 (5.78)	33.43 (8.37)	*t*=-2.55, *p*=.019 *d*=.85	33.23 (5.33)	48.41 (7.04)	*t*=-14.91, *p*<.001 *d*=4.76
Adaptive behaviour composite (/766)	314.62 (39.15)	346.95 (46.46)	*t*=-7.01, *p*<.001 *d*=2.30	365.50 (36.83)	454.32 (31.06)	*t*=-15.09, *p*<.001 *d*=4.63

Table 4.7 shows that the typically developing group improved significantly on all measures. The group with Down syndrome, however, did not show significant improvement in socialisation or gross motor skills according to the Vineland-II Scales although they did show improvement in all other domains. Comparison of effect sizes suggests that the group with Down syndrome showed large improvements in Communication (particularly on the Expressive subdomain), in line with the findings from the objective vocabulary measures in Chapter 3. The effect sizes were more similar across the domains in the typically developing group but the greatest improvement was on the Motor domain, particularly on the Fine Motor scale.

Table 4.8.

Means, standard deviations and group differences on the adapted OCDI measures at T2

	DS (N=14)	TD (N=18)	Group difference
Expressive vocabulary (signed and spoken)	289.50 (91.14)	393.50 (33.98)	*U*=25.00, *p*<.001
Expressive vocabulary (spoken only)	268.86 (121.48)	393.50 (33.98)	*U*=25.00, *p*<.001
Receptive vocabulary (words understood)	341.07 (76.93)	394.22 (33.92)	*U*=36.50, *p*<.001

Table 4.9.

Improvement in mean scores on the adapted OCDI measures between T1 and T2 in both groups. Cohen's *d* effect sizes for the differences are given.

	DS T1 (N=14)	DS T2 (N=14)	Improvement over time with effect size	TD T1 (N=18)	TD T2 (N=18)	Improvement over time with effect size
Expressive vocabulary (signed and spoken)	238.79 (82.86)	289.50 (91.14)	*z*= -3.20, *p*=.001 *d*=-1.11	366.11 (64.76)	393.50 (33.98)	*z*=-2.87, *p*=.004 *d*=-0.40
Expressive vocabulary (spoken only)	209.43 (113.91)	268.86 (121.48)	*z*= -3.30, *p*=.001 *d*=-1.21	366.11 (64.76)	393.50 (33.98)	*z*=-2.87, *p*=.004 *d*= -0.40
Receptive vocabulary (words understood)	300.14 (70.26)	341.07 (76.93)	*z*= -3.11, *p*=.002 *d*=-1.02	378.61 (30.92)	394.22 (33.92)	*z*=-2.94, *p*=.003 *d*= 0.32

4.3.3.2 Adapted OCDI results

The mean scores on the adapted OCDI at T2 are given for both groups in Table 4.8. Again, there were ceiling effects on all of the OCDI measures in the typically developing group. Thus, group differences were examined using the non-parametric Mann-Whitney U test. The results of these group comparisons are given in Table 4.8 and show, unsurprisingly, that the scores in the typically developing group were significantly higher on all of the measures at T2.

To investigate the improvement between T1 and T2 for the groups, the non-parametric Wilcoxon signed ranks test was employed. Cohen's *d* effect sizes were also calculated to give an estimate of the magnitude of change. The results of these analyses are presented in Table 4.9. Both groups improved significantly on all of the adapted OCDI measures between T1 and T2. The effect sizes indicate that these changes were greater in the group with Down syndrome, although this is likely to be due to ceiling effects at T1 in the typically developing group. There was slightly greater improvement on the expressive vocabulary measures than on the receptive measure in the group with Down syndrome, according to the effect sizes.

4.3.4 Relationships Between the Parent-Report and Objective Measures

Intercorrelations between the different Vineland scales at T1 and T2 are presented in Appendix 1. Generally, the different domains were moderately to highly correlated with each other in both groups. The intercorrelations were slightly lower but generally similar to those stated in the Vineland-II manual for the appropriate age groups (Sparrow et al., 2005). There were also moderate to strong correlations between the OCDI measures in both groups and, at T1, the OCDI measures were significantly correlated with the Communication domain of the Vineland-II. At T2 the correlations between the Vineland-II Communication scale and the OCDI remained in the group with Down syndrome but not in the typically developing group, perhaps due to ceiling effects on the OCDI measure in this group.

One primary aim of this study was to examine how parent-report measures relate to, and predict, objective cognitive measures. This question is more pertinent to the group with Down syndrome, for whom early assessment of abilities is important for determining intervention strategies. Thus, the relationships in the group with Down syndrome will be the focus of the present analyses. However, the analogous data for the typically developing

group are presented in Appendix 2 and will be commented on in the main text only where there were notable differences on key measures between the two groups.

The correlations between the parent-report measures and the cognitive tests detailed in Chapter 3 were calculated and are presented in Table 4.10 for T1 and in Table 4.12 for T2. There were moderate correlations between the Communication scale of the Vineland-II and the objective language tests, which were stronger at T2. The Expressive scale of the Vineland-II, in particular, related significantly to all of the objective language tests at T1 and all but one at T2. At both T1 and T2, the expressive scale of the OCDI correlated with the objective vocabulary composite. The Motor subdomain on the Vineland-II was the only other which mapped directly onto aspects of the cognitive assessment. At T1 the Motor subdomain did not correlate significantly with the motor composite from the cognitive assessment or either of the individual motor tests. However, at T2 the Motor subdomain did correlate with the Bike Trails motor task. It is possible that the lack of a relationship between the parent-report and objective motor measures at T1 was due to the non-normal distributions of data on the objective motor measures at this time point. The patterns in the typically developing group were generally similar although it is interesting to note that at T1, in the group with Down syndrome, nonverbal ability was the most consistent cognitive correlate of the different Vineland-II scales whereas in the typically developing group, the most consistent correlate was language ability. At T2 there was no clear, consistent cognitive domain that related to all Vineland-II scales in either group.

The results show that at both time points there were consistent relationships between the parent-report and objective measures indicating that both could potentially be used to measure the same underlying cognitive constructs. To investigate this further, the relationships between the measures across time points were examined.

4.3.5 Relationships Between the Parent-Report Measures at T1 and Objective Measures at T2.

The correlations between the parent-report measures (Vineland-II and OCDI) administered at T1 and the objective tests and composites administered at T2 are presented in Table 4.11. Significant relationships between the relevant domains of the parent-report measures at T1 and the objective tests at T2 would suggest that parent-report measures could potentially be used to predict children's cognitive development. This will be explored further using regression analyses in the next section.

Table 4.10.

Correlations between the parent-report measures and objective cognitive tests and composites at T1 in the group with Down syndrome.

	V-II Communication	V-II Receptive	V-II Expressive	**V-II Daily Living**	**V-II Social**	**V-II Motor**	V-II Gross	V-II Fine	OCDI words + signs	OCDI words	OCDI receptive
Mental age	.611**	.454*	.563**	.404	.552**	.212	-.030	.450*	.359	.311	.551*
Object Assembly	.402	.235	.357	.333	.237	.416	.359	.360	.560*	.586*	.479*
Receptive Vocabulary	.477*	.114	.479*	.075	.337	.240	.186	.225	.531*	.467	.530*
Basic Concepts	.382	-.084	.447*	-.223	-.051	-.404	-.566**	-.057	-.297	-.028	-.423
Expressive Vocabulary	.513*	-.145	.598**	.166	.245	.138	.093	.148	.516*	.666**	.275
Nonword Repetition	.472	-.427	.661**	.078	.181	.064	.110	-.009	.319	.567*	.030
Coin Posting	-.359	-.037	-.398	-.186	-.186	-.234	-.208	-.197	-.477	-.507*	-.451
Bike trails	-.245	-.310	-.224	-.250	-.296	-.297	-.242	-.290	-.677*	-.649*	-.535
Nonverbal composite	.636**	.429*	.576**	.453*	.498*	.390	.194	.507*	.578*	.566*	.643**
Language composite	.583**	-.126	.676**	.027	.236	-.003	-.095	.116	.357	.534*	.146
Vocabulary composite	.552**	-.017	.601**	.135	.325	.210	.156	.208	.569*	.609**	.445
Grammar composite	.382	-.084	.447*	-.223	-.051	-.404	-.566**	-.057	-.297	-.028	-.423
Motor composite	-.359	-.037	-.398	-.186	-.186	-.234	-.208	-.197	-.477	-.507*	-.451

Table 4.11.

Correlations between the parent-report measures administered at T1 and the objective cognitive tests and composites administered at T2 in the group with Down syndrome

	V-II Communication	V-II Receptive	V-II Expressive	**V-II Daily Living**	**V-II Social**	**V-II Motor**	V-II Gross	V-II Fine	OCDI: words + signs	OCDI: words	OCDI: receptive
Mental Age	.305	.324	.252	.066	.291	.150	.079	.189	.404	.133	.548*
Object Assembly	.268	.083	.247	.395	.133	.405	.438*	.217	.559*	.541*	.423
Block Design	.623**	.497*	.585*	.308	.347	.510*	.302	.554*	.675**	.612*	.685**
Receptive Vocabulary	.427	.108	.430	.039	.131	.208	.181	.170	.731**	.774**	.515*
Basic Concepts	.606**	.400	.594**	.457*	.544*	.463*	.267	.555**	.438	.636**	.387
Sentence Structure	.275	.294	.188	.448	.464	.424	.202	.608*	.555*	.547	.583*
Expressive Vocabulary	.495*	.123	.553**	-.019	.074	-.113	-.173	.005	.401	.557*	.227
Nonword Repetition	.505*	.037	.635**	-.012	-.064	-.185	-.164	-.147	.292	.562*	.154
Coin Posting	-.098	-.132	-.015	-.217	-.042	-.029	.154	-.243	-.246	-.161	-.188
Bike Trails	-.468	-.527*	-.409	-.677**	-.570*	-.538*	-.421	-.500*	-.387	-.260	-.582*
Nonverbal Composite	.459*	.355	.401	.322	.331	.436*	.359	.381	.675**	.551*	.661**
Language Composite	.631**	.217	.677**	.207	.246	.196	.091	.263	.629**	.825**	.461
Vocabulary Composite	.513*	.128	.547*	.011	.114	.053	.005	.097	.602**	.707**	.395
Grammar Composite	.553**	.372	.522*	.463*	.518*	.505*	.299	.595**	.503*	.668**	.472*
Motor Composite	-.345	-.421	-.250	-.524*	-.347	-.248	-.012	-.453*	-.380	-.266	-.419

Table 4.12.

Correlations between the parent-report measures and objective cognitive tests and composites at T2 in the group with Down syndrome.

	V-II Communication	V-II Receptive	V-II Expressive	**V-II Daily Living**	**V-II Social**	**V-II Motor**	V-II Gross	V-II Fine	OCDI: words + signs	OCDI: words	OCDI: receptive
Mental Age	.266	.349	.178	.138	.216	.207	-.009	.334	.445	.259	.467
Object Assembly	.427	.267	.406	.319	.164	.347	.096	.476*	.456	.482	.324
Block Design	.675**	.549*	.677**	.269	.391	.439	.225	.502*	.660*	.652*	.538
Receptive Vocab	.511*	.274	.434*	-.087	-.015	.111	-.113	.260	.598*	.627*	.431
Basic Concepts	.714**	.324	.696**	.572**	.455*	.597**	.458*	.596**	.575*	.649*	.463
Sentence Structure	.329	.037	.315	.161	.237	.286	.249	.265	.486	.474	.622
Expressive Vocab	.501*	.138	.529*	.068	-.005	-.013	-.091	.047	.421	.547*	.178
Nonword repetition	.574**	.293	.625**	.113	.081	.191	.109	.219	.462	.587*	.178
Posting Coins	-.314	-.260	-.348	.001	.000	-.170	-.035	-.235	-.363	-.380	-.410
Bike Trails	-.583*	-.680**	-.535*	-.585*	-.371	-.665**	-.459	-.648**	-.346	-.315	-.285
Nonverbal composite	.548*	.489*	.478*	.306	.305	.410	.132	.547*	.614*	.554*	.523
Language composite	.729**	.313	.725**	.229	.183	.324	.162	.388	.685**	.799**	.447
Vocabulary composite	.563**	.229	.536*	-.011	-.011	.054	-.113	.171	.536*	.618*	.320
Grammar composite	.629**	.246	.616**	.478*	.406	.547*	.453*	.521*	.586*	.671**	.467
Motor composite	-.540*	-.526*	-.540*	-.325	-.206	-.435	-.221	-.506*	-.464	-.455	-.456

Table 4.11 shows that the Communication scale of the Vineland-II was significantly correlated with the later objectively measured language, vocabulary and grammar composites. The expressive scales of the OCDI were also well correlated with all of the later objective language composites. However, the Motor scale of the Vineland-II was not significantly correlated with the later objective Motor measure, although it was well correlated with one of the individual tests (*Bike Trails*). It should be noted that the Fine motor scale of the Vineland-II did correlate with the motor composite, which would be predicted given that the objective tests assessed fine motor skills. However, given the problems with the score distributions on the objective motor tests, analyses looking at prediction of these outcomes would be of questionable reliability. Thus, on balance, the decision was made to primarily investigate how well the Communication scale of the Vineland-II and the OCDI can predict the objective language measures, and motor outcomes were omitted from these analyses.

4.3.5.1 Prediction of T2 Cognitive Outcomes from T1 Parent-Report Measures

The question of whether the Vineland-II and adapted OCDI measures could be used to predict cognitive outcomes in the children with Down syndrome was addressed with a series of linear regression analyses. The T2 language, vocabulary and grammar cognitive composites were used as the outcome measures as they were found to consistently correlate with the relevant T1 parent-report measures and were less affected by skewed score distributions than the motor composite. The appropriate Vineland scales, a composite OCDI measure and the T1 versions of the language, vocabulary and grammar composites were entered as predictors. The composite OCDI measure was formed by calculating a z-score for each child on the three scales (expressive vocabulary, both verbal alone and including signing, and receptive vocabulary) and then calculating the average of these z-scores. The amount of variance in the outcome measure accounted for by the relevant objective and parent-report predictors were compared to establish the predictive validity of the parent-report measures. The results of the regression analyses are presented in Table 4.13.

4.3.5.1.1 Predicting the overall language composite

As shown in Table 4.13, both the Vineland Communication scale at T1 and the T1 objective language composite were significant predictors of the T2 objective language composite. The Vineland Communication scale accounted for 40% of the variance in language outcomes at T2. This is a similar amount of variance to that accounted for by the

earlier T1 objective language composite (44%) suggesting that the Vineland Communication scale can be used as a substitute, or complementary measure, to earlier objective testing when general language skill is the outcome of interest.

4.3.5.1.2 Predicting the vocabulary composite

Table 4.13 shows that the T1 objective vocabulary composite, the Vineland Communication scale at T1 and the adapted OCDI at T1 were all significant predictors of the T2 vocabulary composite. However, in this case, the T1 objective vocabulary composite predicted much more variance (72%) than either of the parent-report measures, most likely due to the fact that the objective measures were the same across the time points and therefore were assessing knowledge of the exact same items over time, hence the high level of stability. However, out of the two parent-report measures the OCDI, which is a more targeted measure of vocabulary predicted more variance (39%) in objectively measured vocabulary at T2 than the Vineland Communication scale (26%).

4.3.5.1.3 Predicting the grammar composite

The Vineland Communication scale was a significant predictor of the T2 grammar composite but the T1 grammar measure (*Basic Concepts*) was not a significant predictor. As shown in Table 4.13, the T1 grammar measure only accounted for 3% of the variance in the T2 composite whereas the Vineland Communication scale accounted for 31%. This suggests that of these two measures, the parent-report Vineland Communication scale was a better predictor of children's later grammar ability.

Table 4.13.

Linear regression analyses showing the prediction of the T2 objective outcomes from the T1 objective and parent-report measures.

Outcome	Predictor	R^2	F	β	*p*
T2 language composite	T1 language composite	.44	15.02	.66	.001
	T1 Vineland Communication	.40	12.58	.63	.002
T2 vocabulary composite	T1 vocabulary composite	.72	49.06	.85	<.001
	T1 Vineland Communication	.26	6.78	.51	.017
	T1 OCDI composite	.39	10.40	.63	.005
T2 grammar composite	T1 grammar composite	.04	.70	.19	.415
	T1 Vineland Communication	.31	8.35	.55	.009

4.3.5.1.4 Summary of regression analyses

For children with Down syndrome the Vineland Communication scale significantly predicted language, vocabulary and grammar at T2 and the adapted OCDI significantly predicted vocabulary at T2. When general language ability or grammar skills were the outcome measures of interest, the parent-report Vineland Communication scale was an equivalent or better predictor than earlier objective testing. However, perhaps unsurprisingly, although both of the parent-report measures predicted objective vocabulary scores, neither was a better predictor than the earlier version of the same objective vocabulary test. In the typically developing group, the objective composites at T1 were always stronger predictors of T2 outcomes than the parent-report measures (for full results see Appendix 3).

4.4 Discussion

The aim of this study was to investigate, longitudinally, the adaptive behaviour and vocabulary profiles of a group of young children with Down syndrome and to examine the utility of parent-report measures in predicting cognitive outcomes. It was predicted that on the Vineland scales, children with Down syndrome would show significant weaknesses in communication and motor skills but would not differ from the typically developing group in socialisation scores. Children with Down syndrome showed the expected pattern of results for the communication and socialisation domains and the difference in the overall motor domain was marginally significant. In line with the predictions, the group with Down syndrome had smaller spoken vocabularies as measured by the CDI, even when signed vocabulary was taken into account.

The study also explored whether parent-report measures could predict objective cognitive outcomes. This was primarily investigated for the group with Down syndrome for whom accurate early assessment is important for planning intervention. As predicted, the CDI was a significant predictor of objectively assessed vocabulary one year later, although earlier performance on the same objective vocabulary tests was a stronger predictor. For the Vineland scales the Communication scale was a significant predictor of overall objective language scores and predicted a similar amount of variance to an earlier version of the same objective language composite. The Communication scale also predicted grammar skills and, in fact, was a stronger predictor than one of the earlier T1 grammar measures. However, while the Communication scale was a significant predictor of vocabulary scores, it did not predict as much variance in the outcome as the same vocabulary tests at T1.

4.4.1 Adaptive Behaviour and its Development

The results from T1 of this study indicate that the four- to five-year-old children with Down syndrome had significantly weaker communication and daily living skills than nonverbal-age matched typically developing controls, as measured by the Vineland scales. Socialisation skills, however, were in-line in both groups. While it was expected that there would be a significant difference between the groups in motor skills, in favour of the typically developing children, this difference was only marginally significant in the current study. One possible explanation for this is the young age of the typically developing control group. Motor development is at its most rapid during the early years and physically there is a large difference between a two- and a four-year-old, which is the age difference between the two experimental groups. While individuals with Down syndrome show clear motor delays, even in the early years (Pereira et al., 2013; Tudella et al., 2011), these are likely to become more pronounced over development as typically developing children advance more quickly.

With the exception of the findings for the motor domain, the results for the adaptive profile are broadly consistent with previous research in older children and adults with Down syndrome (Dykens et al., 2006; van Duijn et al., 2010). There are also similarities with the results of Fidler et al. (2006), who studied adaptive behaviour in younger children. Fidler et al. (2006) found that two- to three-year-olds with Down syndrome showed weaknesses in communication and motor skills relative to socialisation skills and the daily living domain did not differ statistically from the others. However, they did not find any group differences in comparison to a nonverbal mental-age matched typically developing group. The results of the present study suggest that by 4 to 5 years-old, the deficit in communication has become more pronounced and a deficit in daily living skills has emerged. The motor weaknesses also appear to have become more pronounced although the group difference is only marginally significant. However, social skills remained a strength at T1, which was reflected by the lack of significant difference between the typically developing group and the children with Down syndrome.

The typically developing group showed significant improvements in all domains between T1 and T2. The group with Down syndrome improved significantly in most of the domains, with the exception of the gross motor and socialisation domains. In particular, the lack of improvement in the socialisation domain is unexpected given the social strengths consistently reported for individuals with Down syndrome. Speculatively, this might be

linked to the fact that most of the children with Down syndrome started formal schooling between the two study time points and social weaknesses may become more apparent in such settings. However, it would be important to replicate these findings before making strong interpretations. The lack of improvement in the gross motor domain is less unexpected as gross motor milestones in the middle childhood years often require a large improvement in skill, for example riding a bicycle without stabilisers and catching a tennis ball, which may not be achievable for most of the group with Down syndrome over this time period.

In terms of relative gains in scores on the different domains, there is one interesting observation to make. Differences in effect sizes on different measures should be interpreted cautiously but it should be noted that the greatest improvement was in the communication domain for the children with Down syndrome, particularly in the expressive subdomain. This is in line with the findings from the objective measures administered in Chapter 3, which showed a similar pattern on the objective expressive language tests. Taken together, these findings could suggest that the period of development under investigation in these studies is a key time for expressive language growth.

4.4.2 Parentally Reported Vocabulary Development

In terms of vocabulary, parents of the children with Down syndrome reported smaller expressive and receptive vocabularies than parents of the typically developing children at both time points. This finding is in line with the results on the objective expressive vocabulary test in Chapter 3. However, this study also showed that the expressive weakness remained even when children's signing vocabulary was taken into account suggesting that it is not simply due to speech difficulties but a more fundamental deficit in word knowledge. It was more unexpected that the group with Down syndrome also showed significant weaknesses in receptive vocabulary, according to parental report. In Chapter 3, while the group differences on the objective receptive vocabulary measure did not quite reach significance there was certainly a trend for higher scores amongst the typically developing group, in line with the results from the CDI.

In terms of improvement, the group with Down syndrome showed substantial gains in their scores on both the expressive and receptive scales over the course of a year. There was no significant improvement in the typically developing group, likely due to ceiling effects. While the differences between the improvement effect sizes on the different scales for the group with Down syndrome were small, there was a slightly greater improvement

on the expressive than the receptive scale. This is in line with findings from the Vineland scales and the objective cognitive tests, further strengthening the interpretation that children with Down syndrome undergo measurable growth in expressive language over the time period of this longitudinal study.

4.4.3 Can Parental Report Measures Predict Cognitive Outcomes?

The key research question for this study was whether the Vineland-II and adapted CDI measures could predict objective cognitive outcomes for the children with Down syndrome. The results of the study showed far fewer problems with the distributions of the data from these parent-report measures in comparison to the T1 objective measures in Chapter 3. Thus, in terms of instrument reliability, there would be advantages in using parent-report measures with this age group of children with Down syndrome, if their predictive validity can be established.

In line with Rihtman et al. (2010), who found concurrent relationships between overall IQ and composite Vineland scores, there were moderate correlations between the Vineland Communication scales and the objective language tests. However, whereas Rihtman et al. (2010) found relationships with objective motor tasks, this was not the case in the current study at T1 although there were some significant relationships between the Vineland Motor scale and the objective motor tasks at T2. The discrepancy in these results is most likely due to the skewed distributions on the motor tasks at T1, masking potential relationships. There were also significant, moderate concurrent correlations between the adapted CDI measure and the objective language tests at both time points, in line with previous studies (Miller et al., 1995).

In terms of predicting cognitive outcomes, there were consistent relationships between the Communication scale of the Vineland at T1, the CDI at T1 and the objective language tests at T2. Thus, these variables were the focus of the longitudinal analyses. The Vineland Communication scale was a significant predictor of the objective language, vocabulary and grammar composites at T2. The adapted CDI was also a significant predictor of the vocabulary composite. In the cases where general language and grammar were the objective outcomes of interest, the parent-report measure (Vineland-II Communication scale) was an equivalent or better predictor than the earlier T1 objective measures. When the outcome of interest was objectively measured vocabulary, neither of the parent-report measures were equivalent or stronger predictors than earlier scores on the same objective vocabulary tests. However, this is unsurprising as the same precise vocabulary items were

being assessed at both time points on the objective tests, whereas different items were assessed by the parent-report measures. Indeed, both parent-report measures predicted a substantial amount of variance in T2 objective vocabulary scores (39% and 26%). Out of the two parent-report measures it was the CDI that was the stronger predictor. The relationship found between the CDI and later objective vocabulary in the current study is in line with the findings of Miller et al. (1995). They calculated simple correlations between the CDI at T1 and the objective vocabulary measures at T2, finding a significant moderate correlation (p=.65) which is similar in size to the analogous simple correlation in the current study (p=.56). Thus, for researchers and practitioners interested in vocabulary growth, the CDI may be a more appropriate parent-report measure than the Vineland-II.

In sum, these results suggest that the Vineland-II Communication scale can be used to predict general language and grammatical outcomes in young children with Down syndrome. While repeated testing using the same objective measures might prove more informative with regards to vocabulary outcomes, the CDI can also be used as a valid predictor of objective vocabulary, as can the Vineland Communication scale to a more limited extent.

While the focus of the current study is particularly on predicting language outcomes in Down syndrome, it does raise the question of whether the Vineland scales could be used to predict other cognitive skills over time. Given the concurrent relationships sometimes seen between overall IQ and the Vineland scales (Rihtman et al., 2010), it would be worth investigating this relationship longitudinally, particularly as the Vineland scales are a quicker and easier measure to administer than a full IQ battery. Furthermore, although it was not possible in the current study, it would also be interesting to examine whether the Motor scale from the Vineland could predict objectively measured motor abilities.

4.5 Conclusions

This study investigated the adaptive behaviour and vocabulary profiles in young children with Down syndrome using parent-report measures. It was found that four- to five-year-old children with Down syndrome had weaknesses in Communication and Daily Living skills but relative strengths in Socialisation. The group differences in Motor skills did not reach significance but there was a trend for the group with Down syndrome to show weaker performance in this domain also. The results from the CDI suggest that children with Down syndrome have weaker expressive and receptive vocabulary than typically

developing controls matched for nonverbal ability, even when signing is taken into account. These findings are largely in line with the findings from the objective tests in Chapter 3. The findings from the current study also tentatively support the interpretation that expressive language skills undergo noticeable improvement over the course of the year studied, in the group with Down syndrome.

The novel research question concerned whether these parent-report measures predict objectively measured cognitive skills one year later for children with Down syndrome. There were significant relationships between the Vineland Communication scale and all language outcomes and there was a relationship between the CDI and vocabulary outcomes. In fact the Vineland Communication scale was a better predictor than earlier objective testing for grammatical skill, and an equivalent predictor of overall language skill. These results suggest that the CDI and Vineland scales can provide useful information about the cognitive development of children with Down syndrome and thus could be used as an informative substitute or addition to early cognitive testing, particularly in situations where early cognitive testing could prove difficult.

5 Relationship Between Health Indices and Cognitive Outcomes in Children with Down Syndrome

5.1 Introduction

5.1.1 Overview

Influential models of cognitive development highlight reciprocal relationships between cognitive, biological and environmental factors (Morton, 2004). It has been well documented that children with Down syndrome have increased risks for a number of health related conditions and illnesses. Health could influence development at both the biological and environmental levels. However, despite evidence of both cognitive difficulties and health problems in Down syndrome, very few studies have attempted to examine the relationship between the two domains. The current study attempts to bridge this gap by investigating whether parentally reported health variables are related to the cognitive and adaptive outcomes measured in Chapters 3 and 4 in young children with Down syndrome.

5.1.2 Health Problems in Down Syndrome and their Relationship to Cognition

Chapter 2 provides a comprehensive overview of research on the prevalence and nature of health problems in Down syndrome. Individuals with Down syndrome are often born with, or develop, serious health conditions, most notably congenital heart defects (Roizen et al., 2014; Schieve et al., 2009). Compared to unaffected individuals they also spend more time in hospital over their lifespan (Zhu et al., 2013). However, there has been very little research examining how such health indices may relate to cognitive impairments in Down syndrome. One retrospective cohort study tried to address this question at the broadest level by examining the medical records of 129 individuals with Down syndrome (Määttä et al., 2006). Using the weight of an individual's medical records as a proxy for general health they found that this was negatively correlated with IQ. However, this leaves many open questions concerning which aspects of poor health could underlie this relationship. The current study will focus on specific health factors that have been suggested to relate to cognition, as detailed in Chapter 2, to see which aspects of health may have particularly important implications for cognition.

5.1.2.1 Congenital heart defects

Around half of all children with Down syndrome are born with some form of congenital heart defect (Freeman et al., 1998; Roizen et al., 2014). Only two studies have examined the relationship between heart defects and cognition in Down syndrome, focussing on the very early stages of development. Visootsak et al. (2011) and Visootsak, Hess, Bakeman and Adamson (2013) found that children with Down syndrome had lower scores on tests of motor, language and nonverbal ability. At the age of one, these differences only reached significance in the motor domain (Visootsak et al., 2011) and, in a different group of children, at the age of three these differences only reached significance in the language domain (Visootsak et al., 2013). The present study aims to examine this relationship during the next stage of development in Down syndrome (ages four- to six-years-old) to see how the impact of heart defects may change over time.

It should be noted that the two studies by Visootsak classify heart defects in different ways. In the earlier paper, children were recruited after surgery to repair an atrioventricular septal defect (AVSD), a specific type of heart defect, meaning that they were a homogeneous group ascertained through a medical clinic. In the later paper however, a wider range of heart defects was included and ascertainment was through parent-report of heart defects. As both studies showed some evidence of cognitive differences between the groups of children with and without heart defects, it appears that parent-report can be used as a way of determining heart status. Since the current study had no access to medical records, parent-report was used to ascertain the presence of heart defects, in line with Visootsak et al. (2013).

5.1.2.2 Sleep problems

There is mounting evidence to suggest that children with Down syndrome suffer from sleep difficulties, primarily in the form of frequent night-time arousals and awakenings (Levanon et al., 1999), perhaps in part due to an increased incidence of obstructive sleep apnoea (Shott et al., 2006). In otherwise typically developing children, sleep difficulties can be associated with subtle impairments in cognitive functioning, particularly in the domains of memory and attention (Blunden & Beebe, 2006; Blunden et al., 2000; Gottlieb et al., 2004). In Down syndrome specifically, parent-report and objective measures of sleep apnea frequency have been linked to greater impairments in visuoperceptual skills and executive functioning (Andreou et al., 2002; Chen et al., 2013). This suggests that poor sleep in individuals with Down syndrome could be related to

aspects of cognitive dysfunction. However, the few studies that have been conducted have focussed on older children, adolescents or adults with Down syndrome. The present study aims to extend this research in order to investigate whether sleep problems in early childhood are also related to cognitive abilities using parent-report measures of sleep quality.

5.1.2.3 Hearing problems

As reviewed more fully in section 2.3.2.3, hearing losses are common amongst children and adolescents with Down syndrome (Marcell & Cohen, 1992; Shott, Joseph, & Heithaus, 2001). The evidence surrounding the extent to which hearing difficulties are related to cognitive and linguistic outcomes in Down syndrome is somewhat mixed. While some studies find that hearing levels are associated with language performance, others do not (e.g. Abbeduto et al., 2003 vs. Chapman, Schwartz, & Bird, 1991). A recent study has suggested that examination of childhood hearing history might show a closer relationship with language outcomes than concurrent hearing levels (Laws & Hall, 2014). This study found that 4- to 11-year-old children with Down syndrome who had hearing difficulties between the ages of 2 and 4 years old also had weaker language skills than those without a history of hearing difficulties. The present study aims to look at hearing status during early childhood in relation to cognitive outcomes between 4 and 6 years old to see if a similar pattern of results is seen when examining children within a narrower age band.

5.1.2.4 Hospitalisations and perinatal factors

Individuals with Down syndrome are around twice as likely to be admitted to hospital and tend to undergo longer hospital stays than children from the general population (Hung et al., 2011; Zhu et al., 2013). The risk of hospitalisation is even more substantial in the early years, with almost half of children with Down syndrome hospitalised before the age of three (So et al., 2007). No research thus far has examined whether the increased frequency of hospitalisation in Down syndrome is related to subsequent cognitive impairment and little has done so in relation to typical development. Notwithstanding this, there are well established findings that low birth weight and prematurity, two highly interrelated measures, are both associated with an increased risk of cognitive disability (Anders et al., 2011; Boulet, Schieve, & Boyle, 2011; MacKay, Smith, Dobbie, & Pell, 2010). Children who are born prematurely with low birth weight are also likely to experience increased hospitalisations throughout their lives (Gäddlin, Finnström, Hellgren, & Leijon, 2007) and it is unclear to what extent cognitive outcomes are mediated

by these frequent hospital visits. Hospitalisation is an indirect measure of illness, which may account for the lack of research around its impact on cognition. However, for a population such as those with Down syndrome where individuals are at risk of a range of medical problems, it may provide a useful index of overall general health. Thus, the present study will examine whether measures of hospitalisation, as well as measures of birth weight and gestational age, are related to cognitive outcomes in children with Down syndrome.

5.1.3 Aims of the Current Study

The current study aimed to investigate the relationship between health problems and cognitive development in four- to six-year-old children with Down syndrome. A general picture of the child's health, from birth to the present day, was determined through parental interviews. While some would argue that the most reliable way to determine health history is directly through medical records, this is often not possible and health records may contain important omissions. Indeed, previous studies have successfully used parent-report questionnaires or interviews as a measure of medical history (McGrath, Stransky, Cooley, & Moeschler, 2011; Visootsak et al., 2013) although using both interviews and medical records in conjunction would most likely be optimal. Information about health was related to measures of cognitive ability administered at four and five years of age.

The first aim of the study is to replicate findings that, on average, children with Down syndrome have a greater incidence of health problems and are more frequently hospitalised for longer periods of time than typically developing children. The second aim is to look in detail at whether selected health variables are related to later cognitive ability. Based on previous literature it is expected that children born with heart defects, or who have a history of hearing problems, will show weaker language skills than those without (Laws & Hall, 2014; Visootsak et al., 2013). Given research showing that sleep problems are linked with aspects of cognitive ability in adolescents and adults with Down syndrome (Andreou et al., 2002; Chen et al., 2013), it is expected that this may also be true for younger children although this will be the first study to investigate such links. It is also expected, in line with studies of typically developing children, that birth weight and gestational age will correlate with cognitive ability (Boulet et al., 2011; MacKay et al., 2010). As there are no studies looking at the impact of hospitalisation on cognitive development in Down syndrome, hypotheses of a relationship are more tentative. Theoretically, measures of hospitalisation can be used as an indicator of overall health and,

for the reasons previously discussed, poor health could impact negatively on cognition. Furthermore, the time a child spends in hospital is time they are spending away from an enriched educational or home environment, and this may accentuate cognitive impairments. Thus, it is expected that measures of frequency and length of hospital stays will be related to cognitive ability.

5.2 Method

5.2.1 Design

This study formed part of the longitudinal study described fully in Chapter 3. Data are from the same participants collected at two points in time (T1 and T2), one year apart. Children underwent an objective cognitive assessment (see Chapter 3) and parent-report assessment of adaptive behaviour (see Chapter 4). For the purposes of the current study, parents also answered questions about their child's past and present health in a semi-structured interview format and through questionnaires.

5.2.2 Participants

A full description of participant characteristics and recruitment can be found in Chapter 3.

5.2.2.1 Children with Down syndrome

Twenty-four children with Down syndrome and their families consented to participate and cognitive measures were only collected from 22 of these children (see Chapter 3). Accordingly, as the primary aim is to look at relationships between the two domains, health data are reported from the same 22 participants. The 22 children had a mean age of 4 years, 9 months at the start of the study, but one participant was lost to follow-up meaning that only 21 families took part at T2.

5.2.2.2 Typically developing children

Twenty-two typically developing children were individually matched to the children with Down syndrome on nonverbal mental age. They had a mean chronological age of 2 years, 10 months at the start of the study. All 22 children and their families participated at both T1 and T2.

5.2.3 Materials

5.2.3.1 Health interview with parents at T1

At T1, parents were administered a bespoke semi-structured interview measure that covered their child's past and present health, and family background. This interview took approximately one hour to complete. It covered a wide range of developmental and background factors, but for the purpose of this study the most relevant questions focussed on the areas of health outlined above: serious discrete health conditions (such as heart defects), perinatal factors, length and frequency of hospitalizations, hearing difficulties and sleep problems. The questions from the interview that are of interest to the current study are listed in Table 5.1. Parents were prompted to give as much detail as possible to accompany their responses and the researcher recorded what was said in note form.

5.2.3.1.1 Response coding and scoring

5.2.3.1.1.1 Health conditions

The questions about whether children had childhood or current health problems were coded as a binary yes or no response. If a parent considered their child's health issue(s) to have been disruptive and 'problematic' then a 'yes' response was recorded, otherwise a 'no' response was recorded. Thus, according to parental report in the group with Down syndrome, illnesses such as heart defects, serious respiratory infections and thyroid abnormalities were considered to be health problems whereas conditions such as croup, jaundice and asthma were not. In the typically developing group persistent or serious respiratory infections, which required medical intervention, and the genetic condition Marfan's syndrome were considered by parents as health problems whereas jaundice, ongoing childhood allergies and eczema were not. Details of children's past and present medical conditions were noted and then coded according to where they fitted within certain symptom categories. These categories were based on those used by Yam et al. (2008) in their survey of medical issues in teenagers with Down syndrome. The *cardiovascular, endocrine, gastrointestinal, haematological, neurological* and *skeletal* category labels were retained but the *sleep, visual and hearing* categories were removed as they were being assessed elsewhere within the interview. A category for *respiratory* conditions was added as it was deemed necessary based on the parentally reported prevalence of these, particularly among the children with Down syndrome.

5.2.3.1.1.2 Perinatal factors

A child's birth was classified as full term if they were born at more than 37 weeks gestation, in line with common medical guidelines. The child's weight, according to parental report, was recorded in pounds (lb) and ounces (oz) and then converted to kilograms (kg).

5.2.3.1.1.3 Hospitalisation

A hospitalisation was defined as admittance to a hospital as an inpatient, whether for injury or illness. Reasons for each hospitalisation were recorded alongside the length of each stay. The total length of each individual stay was summed to give a total number of days in hospital for each participant. The mean number of days per hospital visit was also calculated by dividing the total number of days in hospital by the number of hospital visits. This was calculated because a longer stay per visit is likely to indicate greater illness severity.

5.2.3.1.1.4 Vision and hearing problems

All vision and hearing questions required binary 'yes' or 'no' responses. Parents were asked whether their child's vision or hearing was within normal limits at their most recent test, which was always within the past year for the children with Down syndrome. From this response, the child was coded as either having a difficulty with hearing or vision, or not having a difficulty. The typically developing children had rarely had recent official hearing and vision tests so parents instead reported whether they had any concerns. However, only one parent of a typically developing child reported concerns with their child's vision and this was supported by an official test.

5.2.3.1.1.5 Sleep problems

The average length of a child's night-time sleep was recorded in hours. All questions about the frequency of sleep behaviours ("How often does…") were scored on a 5-point scale of frequency (*never, occasionally, sometimes, frequently, almost always*) by parents. The frequency scores across all five questions were then summed to give an overall sleep disturbance score, out of 25. Questions concerning whether parents had discussed their child's sleep with their doctor or whether the child had taken part in a sleep study (an overnight sleep recording) were scored in a binary "yes" or "no" fashion.

Table 5.1.

Questions that parents were asked about their child's health during the semi-structured interview.

Category	Question
Health Conditions	Did your child have any health problems at birth or in childhood?
	Does your child have any current health problems?
Perinatal Factors	Was your child born full term?
	How much did your child weigh when they were born?
Hospitalisation	Has your child ever been hospitalised? Details about frequency, duration of stays and reasons for hospitalisation.
Vision/Hearing	Does your child have hearing difficulties?
	Does your child wear a hearing aid?
	Has your child ever had grommets?
	Does your child have any problems with their eyesight?
	Does your child wear glasses?
Sleep Problems	How long, on average, does your child sleep during the night?
	How often does your child have difficulty falling asleep?
	How often does your child have difficulty staying asleep?
	How often does your child appear to be excessively sleepy during the day?
	How often do you hear pauses in your child's breathing during sleep?
	How often have you noticed that your child sounds like they're gasping or choking during sleep?
	Have you ever discussed your child's sleep with their doctor?
	Has your child ever taken part in a sleep study?

5.2.3.2 Health interview with parents and sleep questionnaire at T2

A shorter interview was administered at T2 in order to obtain up-to-date information about the child's health status and development over the course of the 12 to 15 months between T1 and T2. This included an update on vision and hearing status, newly diagnosed medical conditions and recent hospitalisations. The questions were structured in a broadly similar way to the analogous questions at T1 but with the caveat "In the past 12-15 months…". Parents were also asked how many days of school their children missed due

to illness during the previous academic year. This interview took approximately half an hour.

At T2, instead of assessing sleep problems through a series of questions in the semi-structured interview, a well-established questionnaire measure of child sleep was completed by parents. The Children's Sleep Habits Questionnaire (CSHQ; Owens, Spirito, & McGuinn, 2000) is a 45-item questionnaire assessing children's sleep within eight sub-scales (bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night waking, parasomnias, sleep disordered breathing and daytime sleepiness) as well as yielding a total score. All items are rated on a three-point scale indicating the frequency with which the behaviour occurs in a typical week, with some items reverse scored such that a higher score always reflects a greater difficulty with the sleep behaviour.

5.2.3.3 Outcome measures: Cognitive skill and adaptive behaviour

To investigate how health indices relate to cognitive and adaptive outcomes, the participants completed a battery of cognitive tests and parents completed a standardised interview measure of adaptive behaviour, at T1 and T2. Full details of the cognitive assessment can be found in Chapter 3 but a summary list of tests that the children were given at each time point is presented in Table 5.2.

Table 5.2.

The content of the cognitive assessment battery at each time point.

Cognitive Domain	T1	T2
Nonverbal	Repeated Patterns	Repeated Patterns
	Figure Ground	Figure Ground
	Object Assembly	Object Assembly
	-	Block Design
Language	ROWPVT	ROWPVT
	Expressive Vocab	Expressive Vocab
	Basic Concepts	Basic Concepts
	Language Sample	Language Sample
	Nonword Repetition	Nonword Repetition
	-	Sentence Structure
Motor	Coin Posting	Coin Posting
	Bike Trails	Bike Trails

The Vineland-II Adaptive Behaviour Scales (Sparrow et al., 2005) were used to assess adaptive skills. Full details of the administration and content of this semi-structured parental interview are presented in Chapter 4. The measure yields scores on four subdomains (communication, daily living, socialisation and motor), as well as an overall adaptive behaviour score.

5.2.4 Procedure

The overall procedure for the longitudinal study and the administration of the cognitive battery is detailed in Section 3.2.4 and details of the procedures for administering the Vineland-II are given in Section 4.2.2. At both time points the health and development interviews were conducted face-to-face with the primary caregiver or both parents, usually at the parents' home after their child had been assessed. In cases where parents were not available for a face-to-face interview, they were completed by telephone. The CSHQ was given to parents during the interview visit, or sent by post, and these were completed and returned to the researcher by post.

5.3 Results

5.3.1 Summary of Health Indices

In order to summarise the general health status of the children with Down syndrome and assess whether this was significantly different from the typically developing group, the responses to the most relevant health questions in the semi-structured interview are summarised in Table 5.3. For each group, the mean value is presented for variables that are measured on continuous scales and the percentage of children that fall into a given category is presented for categorical or binary variables. All participants responded to all health questions and measures with the exception of the CSHQ at T2, which was a parent-report questionnaire as opposed to interview measure. Fourteen questionnaires were returned by parents of children with Down syndrome and nineteen by parents of the typically developing children.

The data distributions of continuous variables were initially examined by visual inspection of histograms and consideration of statistical tests of normality, skewness and kurtosis. Mean birth weight was negatively skewed in the group with Down syndrome, with most children at the higher end of the birth weight scale but with a few notable exceptions. The mean number of hospitalisations and days spent in hospital were positively skewed in both groups, with the majority of children experiencing little time in hospital. The average

length of night-time sleep was negatively skewed in the typically developing group with the majority of the group sleeping for longer lengths of time. The frequencies of difficulties falling asleep, unusual breathing during sleep and pauses in breathing were positively skewed in both groups, with most children showing these features infrequently. Frequency of difficulties staying asleep was again positively skewed in the typically developing group and the group with Down syndrome had a very flat distribution with children evenly spread across the different frequency values. The average frequency of daytime sleepiness was positively skewed in the typically developing group but the distribution was normal in the group with Down syndrome. Finally, the CSHQ scores in the typically developing group were positively skewed, with most children scoring at the lower end of the distribution. As the distributions of all of the continuous health variables deviated from normality in either one or both groups, group differences were assessed with the Mann-Whitney U test. Group differences on the categorical variables were assessed using the Chi squared test. When the expected value was less than 5 in any cell for the Chi-squared test, Fisher's exact test was computed to determine the *p*-value.

5.3.1.1 Perinatal factors

Table 5.3 shows that significantly more of the children with Down syndrome were born prematurely (<37 weeks gestation) and had, on average, a significantly lower birth weight. According to the ICD-10, a child is classed as having a 'low birth weight' if they weigh less than 2.5kg (World Health Organisation, 1992). According to this definition, five of the children with Down syndrome (22.7%) had a low birth weight whereas none of the typically developing children did.

5.3.1.2 Health conditions

Table 5.3 shows that significantly more of the children with Down syndrome were classified as having health problems in early childhood, at the time of the T1 assessment and between the T1 and T2 assessment points. A breakdown of the specific health conditions experienced by the children by the T1 assessment in each group is given in Table 5.4.

Table 5.3.

Descriptive statistics summarising the status of the children with Down syndrome and the typically developing children on all health indices, with tests of group differences.

	Down Syndrome	Typically Developing	Group Difference
Perinatal Factors			
Proportion born prematurely (%) [1]	27.3	4.5	$\chi^2(1) = 4.25$, $p = .047$
Mean birth weight (kg)	2.94	3.68	$U = 96.50$, $p = .001$
Health Problems [2]			
Proportion with health problems in early childhood (%)	68.2	22.7	$\chi^2(1) = 9.17$, $p = .002$
Proportion with current health problems at T1 (%)	45.5	9.1	$\chi^2(1) = 7.33$, $p = .007$
Hospitalisation			
Proportion of children hospitalised in childhood (%)	86.4	27.3	$\chi^2(1) = 15.66$, $p < .001$
Mean number of hospitalisations	3.50	0.50	$U = 69.00$, $p < .001$
Mean number of days spent in hospital over childhood	31.09	0.73	$U = 52.00$, $p < .001$
Mean number of days spent in hospital per visit	11.82	1.43	$U = 9.50$, $p = .002$
Vision/Hearing			
Proportion with hearing difficulties, according to parental report (%)	31.8	0.0	$\chi^2(1) = 8.32$, $p = .004$
Proportion that wear hearing aids (%)	4.5	0.0	$\chi^2(1) = 1.02$, $p = .500$
Proportion that have had grommets inserted (%)	18.2	4.5	$\chi^2(1) = 2.03$, $p = .172$
Proportion with visual difficulties, according to parental report (%)	77.3	4.5	$\chi^2(1) = 24.07$, $p < .001$
Proportion that wear glasses (%)	59.1	0.0	$\chi^2(1) = 18.45$, $p < .001$
Sleep			
Average length of sleep each night (hours)	9.98	10.86	$U = 127.50$, $p = .018$
Average frequency of difficulties falling asleep	0.86	0.76	$U = 209.50$, $p = .561$
Average frequency of difficulties staying asleep	2.23	1.77	$U = 198.50$, $p = .292$
Average frequency of daytime sleepiness	1.95	1.45	$U = 188.50$, $p = .193$
Average frequency of pauses in breathing	0.82	0.05	$U = 140.50$, $p = .002$
Average frequency of unusual breathing	1.14	0.55	$U = 149.00$, $p = .016$
Total sleep disturbance score	7.00	4.48	$U = 111.50$, $p = .003$
Proportion who have consulted doctor about sleep (%)	45.5	4.5	$\chi^2(1) = 9.82$, $p = .002$
Proportion who have participated in a sleep study (%)	50.0	0.0	$\chi^2(1) = 14.67$, $p < .001$
Mean CSHQ total score at T2	51.64	40.95	$U = 37.50$, $p < .001$

[1] In line with standard medical guidelines, prematurity was defined as <37 weeks gestation

[2] For current purposes, presence of health problems was scored according to parental response to a binary yes/no question. Further details about the nature of health problems were recorded and are reported in section 5.3.1.2.

Table 5.4.

Number and proportion of children with Down syndrome and typically developing children who were reported to have suffered from various medical conditions, grouped according to type of problem.

	Down syndrome		Typically developing	
	No. of children	%	No. of children	%
Cardiovascular	**11**	**50.0**	**0**	**0.0**
Ventricular septal defect	3	13.6	0	**0.0**
Atrial septal defect	3	13.6	0	**0.0**
Atrioventricular septal defect	2	9.1	0	**0.0**
Patent ductus arteriosus	1	4.5	0	**0.0**
Tetralogy of Fallot	2	9.1	0	**0.0**
Not specified	2	9.1	0	**0.0**
Respiratory	**9**	**40.9**	**3**	**13.6**
Pneumonia	5	22.7	2	**9.1**
Recurrent chest infections	8	36.4	0	**0.0**
Other	0	0.0	1	**4.5**
Endocrine	**3**	**13.6**	**0**	**0.0**
Thyroid problems	2	9.1	0	**0.0**
Diabetes	1	4.5	0	**0.0**
Gastrointestinal	**3**	**13.6**	**1**	**4.5**
Duodenal stenosis	1	4.5	0	**0.0**
Gastric infection requiring hospitalisation	2	9.1	1	**4.5**
Haematological problems	**2**	**9.1**	**0**	**0.0**
Acute leukemia	1	4.5	0	**0.0**
Polycythemia	1	4.5	0	**0.0**
Neurological problems	**1**	**4.5**	**0**	**0.0**
Not specified	1	4.5	0	**0.0**
Skeletal problems	**0**	**0.0**	**1**	**4.5**
Talipes foot	0	0.0	1	**4.5**
Genetic disorders other than Down syndrome	**0**	**0.0**	**1**	**4.5**
Marfan syndrome	0	0.0	1	**4.5**

It should be noted that each child contributes only once to prevalence estimates of an overall category but may contribute to more than one of the sub-conditions for that category. For example, a single child with an atrial septal heart defect and a tetralogy of fallot would be counted in each subcategory but would only contribute once to the overall estimate of children with *cardiovascular* problems. In this way, all percentages represent the proportion of affected children, from the group of 22, but within a category the sum of the affected children in all individual sub-categories will not necessarily be equivalent to the category-level estimate.

In line with parent's ratings of whether their child had suffered health problems, Table 5.4 shows that very few typically developing children had documented health conditions in comparison to the group with Down syndrome, although acute respiratory infections, such as pneumonia, were the most common reported conditions. In the group with Down syndrome there was a wide variety of health complaints, many of which were serious. Half of the children were born with a congenital heart defect and the next most prevalent concern was respiratory infections including mild, chronic and acute infections that required medical intervention. A small number of children also suffered from endocrine, haematological or neurological conditions.

5.3.1.3 Hospitalisations

Table 5.3 shows that children with Down syndrome spent significantly more time in hospital, according to all indices. The vast majority (86.4%) of children with Down syndrome had been hospitalised during their early childhood and the average number of hospitalisations was 3.50. In comparison, around one quarter of typically developing children had been hospitalised and the average number of hospitalisations was less than one (0.50). The average length of hospital stay was also significantly greater in the group with Down syndrome.

5.3.1.4 Vision and hearing problems

Table 5.3 shows that significantly more of the children with Down syndrome had parentally reported vision and hearing difficulties. Indeed, three quarters of the children with Down syndrome had problems with vision and one third had hearing difficulties. As such, significantly more of the children with Down syndrome wore glasses. Although, numerically, more children with Down syndrome had hearing aids and grommets, the group difference on these variables was not significant due to the small number of children with Down syndrome who had received interventions for their reported hearing difficulties.

5.3.1.5 Sleep problems

As shown in Table 5.3, the typically developing children slept, on average, for significantly longer at night (11 hours vs. 10 hours). It is possible that this difference could be due to their younger age. On the measures of sleep behaviours, parents of children with Down syndrome reported a higher frequency of all types of problem. However, the group differences only reached significance on the measures concerning the frequency of unusual breathing problems during sleep, including pauses in breathing that could be an indicator of sleep apnoea. Furthermore, the participants with Down syndrome had a significantly higher overall sleep disturbance score. Significantly more of the parents of children with Down syndrome had consulted their doctor about their child's sleep and half of the children with Down syndrome had participated in a sleep study. Also, at T2, the group with Down syndrome scored significantly higher on the parent-report questionnaire measure of sleep difficulties (CSHQ).

5.3.2 Relationships Between Health Predictors and Cognitive Outcomes

The relationships between the key indices from each health category with cognitive and adaptive skills were explored. It is clear from Table 5.3 that there was a very low frequency of health problems in the typically developing group. Therefore, the relationships between the health indices and cognitive outcomes were explored in the group with Down syndrome alone. This question was primarily addressed using bivariate and point biserial correlational analyses. However, the specific issue of the impact of congenital heart problems was also explored in separate analyses. The rationale and methods for determining the cognitive and adaptive outcomes are set out below.

5.3.2.1 Cognitive and adaptive outcomes measures

In line with the approach taken in this thesis, cognitive outcomes were split into three domains: language, motor and nonverbal abilities. These are also the domains assessed by the two studies that examine the impact of congenital heart problems on cognitive outcomes in Down syndrome (Visootsak et al., 2013; Visootsak et al., 2011). The findings of Chapter 4 showed that, with respect to measuring language ability, the Communication scale of the Vineland-II was highly correlated with the objective language tests at both time points and the scores were distributed more normally than on the objective measures. Therefore scores on the Communication subdomain of the Vineland-II scale were used as the measure of language outcomes for the present study. Although the correlations between the Motor scale of the Vineland-II and the objective motor tests were

not as high, the Motor scale from the Vineland-II was selected as the motor outcome, primarily because there were serious problems with the score distributions on the objective motor tests (see section 3.3.1). Mental age, as assessed by the Leiter-R, was used as the measure of nonverbal ability and the scores were well distributed on this test.

Two further outcome measures were selected. The Vineland-II composite score was included as an overall measure of adaptive behaviour outcomes because health could feasibly have a greater impact on day-to-day skills than on cognitive measures, but both outcomes are of importance to an individual. Finally, as vocabulary is a specific variable that is of particular interest to this thesis, the objective vocabulary composite was also included as an outcome measure. In summary, the outcome measures selected were: Vineland Communication subdomain score, Vineland Motor subdomain score, nonverbal mental age, overall Vineland adaptive behaviour composite and the vocabulary composite from the objective assessment. The same outcome measures were used at both T1 and T2.

5.3.2.2 Correlations between key health indicators and cognitive and adaptive outcomes

As premature birth and birth weight tend to be closely linked, birth weight was selected as the perinatal predictor as it is a continuous variable, and thus potentially a more sensitive measure. The proportion of children with health problems in early childhood was selected as the primary 'health problem' indicator as this encompasses a wider critical period for development compared to the current health problems question. The total number of days spent in hospital and average length of hospitalisation were entered as the hospitalisation variables. Total time in hospital gives an indication of illness frequency whereas average length of hospitalisation is an indirect measure of illness severity. One child was an outlier on both of these measures, as due to a particularly serious illness they had spent over 200 days in hospital. In order to avoid this child's data artificially inflating any correlations, they were ascribed a length of time in hospital that was two standard deviations above the mean (140 days total; 70 days per visit) ensuring that they were still at the extreme end of the distribution but less likely to bias the analysis. The dichotomous variables asking about the presence of vision and hearing problems were also entered. In terms of sleep problems, average length of night-time sleep, overall sleep disturbance score on interview measures at T1 and CSHQ score at T2 were selected as

Table 5.5.

Correlations between health variables and T1 cognitive and adaptive outcomes

	T1 mental age	T1 Vineland communication	T1 Vineland motor	T1 Vineland adaptive behaviour composite	T1 objective vocabulary composite
Birth weight	.407	.481*	.226	.437*	.340
Early health problems	-.140	-.400	-.130	-.230	-.340
Total days in hospital	.048	-.092	-.347	-.211	.034
Average days in hospital per visit	-.109	-.118	-.143	-.114	-.155
Hearing problems	.350	.590*	-.130	.220	.130
Vision problems	.150	.140	-.475	-.195	-.150
Hours sleep per night	.348	.188	.281	.320	.049
Total sleep disturbance	-.117	-.369	.027	-.228	.126

Table 5.6.

Correlations between health variables and T2 cognitive and adaptive outcomes

	T2 mental age	T2 Vineland communication	T2 Vineland motor	T2 Vineland adaptive behaviour composite	T2 objective vocabulary composite
Birth weight	.476*	.433	.288	.389	.177
Early health problems	-.560*	-.480	-.310	-.400	-.400
Total days in hospital	-.563**	-.173	-.485*	-.373	.158
Average days in hospital per visit	-.711**	-.123	-.189	-.131	.071
Hearing problems	.520	.870**	.290	.600*	.560*
Vision problems	-.140	-.140	-.475	-.290	.014
Hours sleep per night	-.044	.053	.184	.277	-.009
Total sleep disturbance	-.129	-.129	-.156	-.262	.195
T2 CSHQ total	-.022	-.060	-.007	-.190	.299

correlates. The CSHQ scores at T2 were only entered into the correlation matrix for the T2, and not T1, outcomes. All other variables were entered into the matrix for both T1 and T2. Biserial correlations were calculated where the predictors were dichotomous (early health problems, vision and hearing problems) and Pearson's *r* was calculated for the remaining, continuous, predictors. The correlations between these health indicators and the cognitive and adaptive outcome measures are shown in Table 5.5 for T1 outcome measures and in Table 5.6 for T2 outcome measures. Correlations less than *r*=.40 were considered weak, those greater than *r*=.70 were considered strong and those in between were considered moderate.

Table 5.5 and Table 5.6 show that birth weight was a reasonably stable predictor of mental age, communication skills and adaptive behaviour at both T1 and T2. While these correlations did not always reach significance, due to the small sample size, the correlations between those outcomes and birth weight were consistently above *r*=.35. The presence of hearing problems was a significant correlate of communication abilities at both time points, although this correlation was particularly strong at T2. At T2 hearing problems were also significantly correlated with adaptive behaviour and objective vocabulary scores and moderately related to mental age, although the correlation was only marginally significant. The presence of early health problems was moderately correlated with all T2 outcome measures, with the exception of motor skill, but was only moderately correlated with communication skills at T1. These patterns suggest that hearing problems and early health problems are related to developmental outcomes and that these relationships become more apparent and stronger between the ages of four and six-years-old.

Vision problems, on the other hand, did not significantly correlate with any of the outcome measures, although the correlation with motor skills was of moderate strength at both T1 and T2. The hospitalisation and sleep measures also did not correlate with T1 cognitive and adaptive outcomes. At T2, however, the hospitalisation variables correlated significantly with mental age and the total time in hospital was also a significant correlate of communication skills. This suggests that hospitalisations in early life relate to later developmental outcomes in the language and nonverbal domains.

5.3.2.3 Relationship between congenital heart problems and cognitive and adaptive outcomes

An approach analogous to that of Visootsak et al. (2013) and Visootsak et al. (2011) was adopted to enable comparisons with these studies. The children with Down syndrome were separated into two groups consisting of those that had been born with a congenital heart defect (N=11) and those that had not (N=11). The group with congenital heart defects was heterogeneous, consisting of all children whose parents reported the presence of a heart defect at some time during their life whether this was minor or major, and whether it required surgery, was ongoing or resolved on its own. The numbers of children that fell into these severity and treatment categories could not be reliably calculated as parents were not asked closed questions about their child's heart defects and the level of detail provided to the open-ended questions was often insufficient. The various types of heart defect are detailed in Table 5.4.

The average age of the group with congenital heart defects did not differ from that of the group without heart defects (57.60 vs 55.83 months U= 43.00, p= .270). They did, however, spend longer in hospital both in terms of total days (49.20 vs 5.67 days; U= 13.00, p= .001) and average number of days per visit (20.00 vs 2.92 days; U= 9.50, p= .003). The group with congenital heart defects also tended to have lower birth weight (2.57 vs 3.45kg; U = 32.50, p=.065) although this difference was only marginally significant.

The two groups were compared on the cognitive and adaptive outcomes at both T1 and T2. Cohen's *d* effect sizes are also reported for group comparisons, in line with Visootsak et al. (2013). Table 5.7 shows that the group with congenital heart defects performed more poorly on all of the T1 cognitive and adaptive outcome measures, though only the difference on the vocabulary composite reached significance, with a large effect size. Furthermore there were moderate effect sizes for the group differences on both the Vineland communication and overall adaptive composite. This suggests that the presence of a congenital heart defect was related to greater impairments in language and adaptive skills than nonverbal and motor abilities at age four to five.

Table 5.8 shows that while there are no significant group differences on the T2 outcome measures, the group with congenital heart defects still show weaker performance on all variables. Unlike at T1, the effect sizes are small to moderate on all measures and there is no apparent difference across the outcome domains.

Table 5.7.

Mean scores of children with Down syndrome with or without a congenital heart defect on the T1 outcome measures with tests of group differences and effect sizes.

	Without congenital heart defect (N=11)	With congenital heart defect (N=11)	Group differences and effect sizes
T1 mental age (months)	37.91 (4.35)	36.82 (5.65)	*U*=59.50, *p*=.949, *d*=.22
T1 Vineland communication	85.27 (17.05)	75.27 (15.69)	*U*=41.00, *p*=.217, *d*=.61
T1 Vineland motor	90.82 (8.95)	87.64 (13.40)	*U*=49.00, *p*=.478, *d*=.28
T1 Vineland adaptive composite	326.73 (44.27)	309.73 (39.35)	*U*=42.00, *p*=.243, *d*=.41
T1 vocabulary composite (z-score)	.38 (.84)	-.38 (.81)	*U*=28.00, *p*=.034, *d*=.92

Table 5.8.

Mean scores of children with Down syndrome with or without a congenital heart defect on the T2 outcome measures with tests of group differences and effect sizes.

	Without congenital heart defect (N=10)	With congenital heart defect (N=11)	Group differences and effect sizes
T2 mental age	44.10 (4.15)	42.55 (5.77)	*U*= 50.50, *p*=.756, *d*=.31
T2 Vineland communication	101.70 (15.03)	95.36 (19.93)	*U*=45.00, *p*=.512, *d*=.36
T2 Vineland motor	95.70 (10.17)	90.91 (15.62)	*U*=38.00, *p*=.251, *d*=.36
T2 Vineland adaptive composite	357.00 (42.85)	337.82 (49.72)	*U*=40.00, *p*=.314, *d*=.41
T2 vocabulary composite	.15 (.72)	-.14 (1.05)	*U*=42.50, *p*=.387, *d*=.32

5.4 Discussion

This study aimed to describe the health history of a group of young children with Down syndrome and examine to what extent health problems were related to cognitive ability. As predicted, children with Down syndrome showed a greater number and variety of early health problems and were more frequently hospitalised for long periods of time. In line with the hypotheses there was some evidence that congenital heart defects and a history of hearing problems were related to poorer language abilities. There were also associations between birth weight and most outcome measures. However, contrary to expectations, there was no evidence of a relationship between sleep problems and cognitive outcomes, and only limited evidence of a relationship between hospitalisation and nonverbal ability.

5.4.1 Overview of the Health Status of Children with Down Syndrome

In line with previous research, this study showed that children with Down syndrome suffered poorer health than typically developing children. They were more likely to be born prematurely at a lower birth weight and were more likely to have sleep difficulties. Around two-thirds of the children with Down syndrome were classified as having health problems during early childhood and 86% had been hospitalised at least once. In comparison, only one-quarter of the typically developing children had health problems and approximately one-quarter had been hospitalised at least once. So et al. (2007) reported that only around 50% of children with Down syndrome are hospitalised at least once before the age of three. In the present study hospitalisation before the age of five was assessed which may explain the substantially larger estimate. However, there are also differences in the health services between the US and the UK with the lower costs of healthcare in the UK perhaps leading to a greater number of admissions. Future large-scale studies in the UK would be required to distinguish between these possibilities. In addition, it should be noted that the control group in the present study may not be the most appropriate for health comparisons, due to the disparity in chronological age, and general population comparisons with, for example, Hospital Episode Statistics (HES) are needed.

In line with prevalence estimates from larger samples (Freeman et al., 1998), 50% of the children with Down syndrome in the present study were born with a congenital heart defect. In line with So et al. (2007), the most common health problems after congenital heart defects were respiratory disorders such as pneumonia. The prevalence estimates for a childhood history of hearing difficulties in Down syndrome in the current

study are also broadly in line with those found by Laws and Hall (2014; 32% and 39% respectively). These estimates suggest that, although small, the sample in this study is broadly representative of the wider population of children with Down syndrome in terms of their health.

5.4.2 Relationship Between Measures of Health and Cognition in Down Syndrome

The evidence from the present study about the links between health and cognition was mixed with respect to the initial hypotheses. Broadly in line with Visootsak et al. (2011) and Visootsak et al. (2013), there was evidence that children with Down syndrome who were also born with a congenital heart defect exhibited some cognitive and linguistic weaknesses in comparison to those born without a heart defect. Consistent with the earlier studies, while the general pattern was that children with heart defects achieved lower scores on all cognitive and adaptive outcome measures, very few of the group comparisons reached statistical significance, most likely because of a lack of statistical power associated with small group sizes and, thus, effect sizes were examined as a more appropriate measure of group difference.

At T1, when the children were between four- and five-years-old, those with heart defects had significantly poorer vocabulary than those without, with a large effect size. At this age, there were also moderate effect sizes for differences in more general language and adaptive skills, as assessed by the Vineland-II. However, there were only small effect sizes for the differences in nonverbal and motor ability. This suggests that, in line with the findings of Visootsak et al. (2013) with two- to three-year-old children with Down syndrome, language is still disproportionately impaired in children born with a congenital heart defect compared to motor and nonverbal skills when children are between four- and five-years-old. The findings from the current study also suggest that more general adaptive behaviour is weaker in children with a heart defect.

At T2, when the children were between five- and six-years-old, the results look somewhat different. While the children with heart defects still exhibited lower scores in all domains, the differences were small, and of a similar size (around d=.30) across all language, motor and nonverbal outcomes. The only moderate effect size was for adaptive behaviour, where the difference between the groups was similar to that at T1. This suggests that the clear differences in language ability have diminished somewhat by the age of six. However, the impact of heart defects on adaptive behaviour remained constant

across this developmental period. Without further research it is impossible to say why the language weaknesses seemed to become less pronounced, although it is worth noting that between T1 and T2 the vast majority of the sample began formal schooling. It is possible that the formal language interventions introduced at school compensated for the early difficulties of the children with heart defects. Longer-term follow-up studies are required to investigate whether the group differences then remain stable across childhood. Furthermore, the only research to look at the impact of heart defects on cognition in Down syndrome has used very small samples which make it very difficult to assess how meaningful the group differences really are. A large-scale longitudinal study tracing development across childhood and relating this to heart status would provide stronger evidence of any association between heart defects and cognitive impairments.

Hearing difficulties were also found to be a significant correlate of language ability. At T1 the only significant correlation was with the Vineland communication scale, but by T2 hearing problems were also related to objective measures of vocabulary and overall adaptive behaviour. Furthermore the relationship with general communication skill had become stronger so that at T2 the two constructs were highly related (r=.87). This is in line with Laws and Hall (2014), who found that children with Down syndrome who had a history of hearing impairment had significantly weaker speech and language at age six than those without such impairment.

In the current study it was not possible to split the children with Down syndrome into two groups based on hearing status in a similar way to Laws and Hall (2014) and in the way that heart defects were examined. This is because only seven children in the present study had a history of hearing problems and such small, uneven group sizes would render even non-parametric group comparisons potentially unreliable. Thus, biserial correlations were utilised instead and should be interpreted with caution. However, it is clear that despite using a different method of analysis, the results are consistent with the only previous study to address the same research question, suggesting that a childhood history of hearing difficulties has a negative impact on language development in Down syndrome.

Also in line with predictions, birth weight was a consistent correlate of nonverbal ability, communication skills and overall adaptive behaviours at both T1 and T2. However, contrary to expectations, there were no significant correlations between any sleep variables and the cognitive and adaptive outcome measures at either time-point. This was unexpected given that both Andreou et al. (2002) and Chen et al. (2013) found a

relationship between measures of sleep apnoea and cognitive skills. However, the discrepancy with the current results may be due to the fact that none of the present outcome measures specifically tap visuoperceptual and executive skills, which were the focus of the earlier studies; but instead primarily examined performance on language measures, which have not explicitly been linked to sleep difficulties in Down syndrome in previous research. Furthermore, recent evidence suggests that performance on neuropsychological tests in individuals with Down syndrome is more closely linked to the length of time spent in slow-wave sleep than to the frequency of apnea events (Brooks et al., 2014), something which needs to be assessed through polysomnography as opposed to parent report measures. In terms of the relationships between sleep and language in typically developing children, the most striking and consistent links are between sleep and the consolidation of newly learned words as opposed to performance on standardised language tests (Brown, Weighall, Henderson, & Gaskell, 2012; Henderson et al., 2012). Thus, future studies could investigate the role that sleep difficulties in Down syndrome may play in language development through the use of experimental tasks assessing the consolidation of new vocabulary instead of the standardised tests employed in the current study.

The present study also failed to find convincing evidence that hospitalisations are related to cognitive outcomes in Down syndrome. At T1, there were no significant correlations between outcomes and the total number of days spent in hospital or between outcomes and the average length of hospital stays. At T2 there were moderate to strong relationships between both of these hospitalisation measures and nonverbal ability, and a moderate correlation between the total number of days in hospital and motor outcomes. However, inspection of the relevant scatter plots suggest that these T2 correlations are largely driven by one participant who spent an unusually long time in hospital due to a particularly serious illness. Thus, it is not possible to have confidence in these findings without replication, particularly since frequency and length of hospitalisation may be subject to local policy variations creating a lot of unrelated noise on these variables. As such, a much larger study sample would be required to detect a true effect.

Taken together, the findings from the current study suggest that there is value in considering health and medical history when examining the cognitive development of children with Down syndrome. The reasons for variability in cognitive outcomes in Down syndrome are poorly understood, but if research converges to suggest that health could be

a contributing factor then it is possible that children at risk of greater cognitive difficulties could be identified at an early stage. This study suggests that congenital heart defects and a history of hearing difficulties may confer particular risks in the language domain. Larger studies are required to determine if more general, indirect measures, such as time in hospital are also related to cognitive outcomes.

5.4.3 Conclusion

This study is one of the first to look in detail at the possible impact of health problems on cognitive development in children with Down syndrome. Findings of an increased prevalence of serious health conditions, primarily heart defects, and a greater frequency and length of hospitalisations in Down syndrome were replicated. In line with the hypotheses, congenital heart defects and a history of hearing difficulties were found to negatively impact on language development although the strength of the relationship with heart defects seemed to get weaker over time while the relationship with hearing history became stronger. However, this study failed to find support for the hypotheses that sleep problems and time in hospital would also be linked to poorer cognitive and adaptive outcomes. Taken together, these results suggest that health problems have a role to play in understanding variability in cognitive outcomes in Down syndrome. Of all cognitive skills, language abilities appear to be the most vulnerable to health problems in this population. More research is needed to clarify these links so that children with Down syndrome at risk of the poorest cognitive and language outcomes could potentially be identified at an early stage in development enabling timely interventions to be put in place.

6 Investigating Sleep and the Consolidation of New Vocabulary in Individuals with Down Syndrome

6.1 Introduction

6.1.1 Overview

Chapter 5 explored the impact of sleep problems on cognitive skills in Down syndrome but failed to find a relationship between parent-report measures of sleep and standardised measures of cognitive and adaptive behaviour in young children. However, recent research has shown that sleep plays a particularly important role in the consolidation of new vocabulary, in both adults (Dumay & Gaskell, 2007) and children (Henderson et al., 2012). Given the language difficulties associated with Down syndrome and the emerging evidence for a high prevalence of sleep difficulties amongst individuals with the disorder, investigation into vocabulary consolidation and maintenance could provide greater insights into the relationship between sleep and language learning in Down syndrome. The current study used a dynamic vocabulary training paradigm with multiple follow-up assessments to establish whether individuals with Down syndrome show a deficit in the consolidation of new vocabulary and whether performance on the learning task is related to sleep quality.

6.1.2 Memory Consolidation and the Role of Sleep

In order for a new word to be learnt and remembered it must first be accurately encoded in verbal short-term memory. Over time this newly learnt information undergoes a period of consolidation (McGaugh, 1966) in which the representation of the new word stabilises and integrates with existing word knowledge in long-term memory. Thus, successful consolidation will aid long-term retention of a vocabulary item. The process of consolidating information, linguistic or otherwise, can have two behavioural outcomes. It can lead to maintenance of the learnt information and it can lead to discernible memory enhancement for the new information over time (Robertson & Cohen, 2006). Enhancement effects, most often seen after a period of sleep, are currently attracting much research interest regarding the role of sleep in memory consolidation. Explicit vocabulary knowledge is considered to be part of the declarative memory system, which subserves the learning of facts and episodes (Squire, 1992a). Thus, the research that will be reviewed presently will focus primarily on the role of sleep in declarative memory consolidation.

Jenkins and Dallenbach (1924) presented one of the earliest demonstrations of a memory enhancement for newly learnt information after sleep. They systematically presented participants with strings of nonsense syllables and found that participants' free recall of the strings was better after an interval of sleep than after an equivalent waking interval. Many studies since have replicated the beneficial effects of sleep on recall using a variety of declarative learning material including verbal paired-associates (e.g. Plihal & Born, 1997), short stories (e.g. Tilley & Empson, 1978), word lists (e.g. Lahl, Wispel, Willigens, & Pietrowsky, 2008), speech sounds (e.g. Fenn, Nusbaum, & Margoliash, 2003) and novel words (e.g. Dumay & Gaskell, 2007).

The mechanisms by which sleep produces these enhancing effects are still debated. Ellenbogen, Payne and Stickgold (2006) suggest that sleep does more than simply protect memories from interference. Rather, they argue that sleep plays an active role in stabilising and integrating newly learnt information in memory. The focus of the current study is vocabulary learning. When material to be learnt consists of novel words, there is evidence that sleep is important for establishing a novel word as a new vocabulary item in the mental lexicon (Davis, Di Betta, Macdonald, & Gaskell, 2009; Dumay & Gaskell, 2007). Dumay and Gaskell (2007) exposed participants to novel words that were derived from bi-syllabic English words but with a final consonant cluster added (e.g. "shadowks"). If lexicalised, each novel word would establish a representation that would compete with its close, existing neighbour (e.g. "shadow"). They found that the novel words only showed competition effects with their existing neighbour after a period of sleep, suggesting that sleep played a critical role in establishing the novel words as new lexical items. Dumay and Gaskell (2007) also found that the magnitude of the lexical competition effect was positively correlated with free recall performance, supporting the idea that lexicalisation is an important part of the memory process for new words. Overall, this study suggests that sleep aids the integration of new vocabulary words into the mental lexicon, which is an essential step for successful word learning.

If sleep plays an active role in consolidation then it is important to determine what is happening at the biological level. Findings from neuropsychological patients, brain imaging studies and animal studies converge to suggest that the hippocampus plays an important role in the encoding and consolidation of declarative information (Squire, 1992b). McClelland, McNaughton and O'Reilly (1995) propose that this is via a process of

covertly reactivating memories, something which recent studies indicate may be happening during slow wave sleep (Gais & Born, 2004; Plihal & Born, 1997).

Another way of exploring the role of sleep in consolidation is to investigate whether individuals with sleep difficulties exhibit any difficulties with consolidation. A meta-analysis conducted by Beebe, Groesz, Wells, Nichols and Mcgee (2003) found that individuals who suffer from obstructive sleep apnoea, a condition which results in disruptive pauses in breathing during sleep, show poorer cognitive skills in certain domains, particularly executive functioning and vigilance. Although implying that sleep may be important for many aspects of cognition, the analysis did not look at the effects on declarative memory consolidation specifically. However, Kloepfer et al. (2009) found that, indeed, patients with sleep apnoea showed significantly less improvement on a declarative memory task overnight than healthy controls. Similarly, patients with primary insomnia, who show a significant reduction in slow wave sleep but not REM sleep, remember significantly fewer word pairs after a period of sleep than healthy controls (Backhaus et al., 2006). Although the conclusions of these studies are tempered by small sample sizes, they provide further support for the importance of sleep in declarative memory consolidation.

In sum, sleep appears to play an important role in the consolidation of new declarative information, including new vocabulary. The role of sleep goes beyond passive protection from interference to facilitating active integration of new memories with existing knowledge and aiding the lexicalisation of new vocabulary items. For declarative information, the hippocampus is central to the learning process and consolidation is particularly aided by slow-wave sleep. Evidence from patients with sleep difficulties further supports these findings. However, the majority of the evidence has come from adult studies. The current study focuses on consolidation in children and, thus, it is important to consider whether these processes operate in the same way across development.

6.1.3 Word Learning and Retention in Typically Developing Children

There is a plethora of research surrounding infant word learning and the conditions through which learning is facilitated. However, much of this research considers only the immediate acquisition of new words and not the pattern of retention. It is consistently found that young children are able to rapidly acquire a novel verbal label for a new object, in a process known as ‘fast mapping’, a term coined in Carey and Bartlett's (1978) seminal study. These associations are often introduced in the context of a different task, such as a game or a story, and children can be assessed for their recognition of the

novel object when given the verbal label or their production of the correct label when shown the novel object. There is debate in the literature as to whether such a brief, incidental exposure to a word creates a lasting consolidated representation. For very young children tested on their recognition of the referent of a novel word, it appears that there is retention over a period of 24-hours (Woodward, Markman, & Fitzsimmons, 1994) or even a week (Childers & Tomasello, 2002) if the new items are explicitly named multiple times. However, when children are exposed just once to a novel item, in an incidental context two-year-old children are unable to retain the new association over a ten minute delay despite good immediate learning (Horst & Samuelson, 2008). Thus, retention of new words may critically depend on the learning procedure and quality of initial encoding in young children, which is enhanced by explicit naming and multiple repetitions of an item.

However, the way in which children learn and remember new words in the later stages of childhood may be quite different to that of infants (Dockrell, Braisby, & Best, 2007). Storkel (2001) tested the effects of phonotactic probability on word learning in three- to six-year-old children and included a retention test after one week. Children were taught eight novel words in the context of a storybook, four with a common sound structure and four with a rare structure. The results showed that when words had a common structure, children's expressive recall was significantly better after one week than it was at the end of training. This enhancement was also seen on a task of form identification, where children had to select the correct label for a pictured item, but not on a referent recognition task similar to those used in infant studies. Retention of new words has also been shown over longer periods of four (Norbury, Griffiths, & Nation, 2010) and sixteen weeks (Dockrell et al., 2007) in children of a similar age. Thus, similarly to adult findings, there is evidence of maintenance, and even improvement, in memory of new words over time in three- to six-year-old children, at least when explicit recall is the outcome measure.

Thus, it appears that children do consolidate vocabulary information over time. However, the patterns of consolidation and the role played by sleep may be quite different between adults and children. Sleep characteristics do not remain stable over the lifespan. Children spend a longer time asleep and a greater proportion of time in slow-wave sleep (Ohayon, Carskadon, Guilleminault, & Vitiello, 2004; Wilhelm, Diekelmann, & Born, 2008). It is possible that these differences in sleep architecture may result in differences in vocabulary consolidation.

6.1.4 The Relationship Between Sleep and Consolidation in Children

The first investigation of sleep and declarative consolidation in children was conducted by Backhaus, Hoeckesfeld, Born, Hohagen and Junghanns (2008). They presented nine- to twelve-year-old children with forty word pairs until they could correctly remember at least 50% of the pairs. Recall of the word pairs was significantly better after a night's sleep when compared to an equivalent waking period suggesting that sleep plays a key role in declarative consolidation in children as well as adults. Furthermore, in this study, the amount of time that children spent in non-REM sleep was correlated with recall performance, in line with adult studies. A study by Wilhelm et al. (2008) replicated the importance of sleep for the consolidation of declarative information in children.

The present study examined the consolidation of new vocabulary words in children and to date very few studies have attempted to examine whether sleep plays a role in children's learning of vocabulary. Brown, Weighall, Henderson and Gaskell (2012) familiarised seven- and twelve-year-old children with novel words that were based on real words but with the endings changed. After 24 hours, recall performance was significantly improved in both age groups. In contrast, there was no change over time in recognition though ceiling effects among the twelve-year-olds may have masked any potential for improvement. Although the design of this study cannot discern between the effects of sleep and the effects of time, it does provide evidence to suggest that children consolidate new vocabulary over a period of 24 hours, similarly to adults. In order to examine whether sleep is essential to this process Henderson et al. (2012) conducted a further study utilising an a.m.-p.m. design. In this study, they familiarised two groups of children (7- to 12-years-old) with novel words, one group being trained in the morning and one in the evening. Both groups were then reassessed after 12 and 24 hours; for the morning group, the 24 hour interval contained sleep but the 12 hour interval did not whereas for the evening group sleep occurred during the first 12 hours. Both recall and recognition of the new words was significantly improved for both groups, but only after periods that contained sleep. Together these findings provide stronger evidence that sleep is important for vocabulary consolidation in children as well as adults.

However, although both vocabulary consolidation studies showed consolidation on free recall tasks, their findings about lexicalisation of the new words were divergent. Brown et al. (2012) found that neither seven- nor twelve-year-old children showed reliable lexical competition effects for the new words in lexical decision despite improvements in free

recall. Thus, this study did not find evidence that sleep aided the integration of new words into the lexicon. In contrast, Henderson et al. (2012) used a different type of task and did find the expected lexical competition effects for novel words after periods of sleep. Hence, further investigations are needed before it can be concluded that sleep boosts consolidation of vocabulary in children in exactly the same way that it does in adults.

In sum, the balance of evidence suggests that sleep is important for the consolidation of declarative information in children and the consolidation of new words in particular. However, whereas it has been proposed that lexicalisation supports this effect in adults, there is not yet conclusive evidence that this same mechanism operates in children. Thus, while sleep is evidently important for vocabulary consolidation in children, there is still much to learn about precisely how sleep and memory interact in children.

6.1.5 Why Examine Vocabulary Consolidation in Children with Down Syndrome?

Given the association between sleep and successful consolidation of new vocabulary in children, it is logical to hypothesise that children who have sleep problems may also have problems with certain types of memory consolidation. There is evidence that children with sleep disordered breathing, ranging from mild snoring to more severe sleep apnoea, do generally show impairments in cognitive skills such as attention and memory compared to controls, although their scores are often still within the normal range (Blunden & Beebe, 2006; Blunden et al., 2000; Gottlieb et al., 2004). However, very few studies have looked specifically at whether these problems with sleep affect consolidation in a dynamic learning task. Kheirandish-Gozal, De Jong, Spruyt, Chamuleau and Gozal (2010) investigated whether children with obstructive sleep apnoea (OSA) showed impaired consolidation in a pictorial declarative memory task. When children were asked to recall the names of the pictures they had learnt on the previous evening, children with OSA remembered significantly fewer than controls and in fact demonstrated significant forgetting overnight. However, the children with OSA also performed worse in the initial learning task and therefore, their lack of consolidation could be due to poor encoding rather than specific difficulties with consolidation. Furthermore, it is not clear if the groups were equated in general cognitive ability. Despite these limitations, the findings of this study do indicate that there is merit in investigating consolidation difficulties in children with sleep problems and it paves the way for similar, more tightly controlled work.

Many developmental disorders put children at increased risk for sleep difficulties (Krakowiak, Goodlin-Jones, Hertz-Picciotto, Croen, & Hansen, 2008), including Down

syndrome. Both objective measures and parental report indicate that individuals with Down syndrome show increased night-time waking and restlessness (Ashworth, Hill, Karmiloff-Smith, & Dimitriou, 2013; Breslin, Edgin, Bootzin, Goodwin, & Nadel, 2011; Carter et al., 2009). Furthermore, individuals with Down syndrome are at increased risk of sleep apnoea (Levanon et al., 1999; Shott et al., 2006), particularly if they already have a history of snoring (Fitzgerald, Paul, & Richmond, 2007). Some preliminary studies of sleep architecture in Down syndrome suggest that there are differences in comparison to typically developing controls, primarily shorter Stage 2 non-REM sleep latencies (Levanon et al., 1999; Miano et al., 2008) and an increased number of shifts between sleep stages (Levanon et al., 1999). However, whereas Miano et al. (2008) found that individuals with Down syndrome spent proportionally less time in REM sleep than controls, Levanon et al. (1999) found no difference, possibly due to their use of a control group with primary snoring. Furthermore, of interest to the question of declarative consolidation, neither study found a difference in the proportion of time spent in slow-wave sleep between the individuals with Down syndrome and controls. Thus, although it is reasonable to hypothesise that, given their sleep difficulties, individuals with Down syndrome may show consolidation impairments, it is also possible that their preserved slow-wave sleep would protect against these impairments. Although previous research has linked sleep problems in Down syndrome to individual differences in visuoperceptual and executive skills (Andreou et al., 2002; Chen et al., 2013), no known studies to date have examined whether individuals with Down syndrome show sleep-related consolidation difficulties.

Certain characteristics of individuals with Down syndrome also provide indirect evidence of potential difficulties with memory consolidation. At the biological level, several studies converge to suggest that individuals with Down syndrome show some hippocampal abnormalities. Both adults (Aylward et al., 1999) and children (Pinter et al., 2001b) with Down syndrome have disproportionately reduced hippocampal volumes and display altered synaptic inhibition and functional connectivity within the hippocampus (for review see Contestabile, Benfenati, & Gasparini, 2010). Furthermore, on neuropsychological tests, individuals with Down syndrome perform particularly poorly on tasks intended to draw on hippocampus-dependent long-term memory, suggestive of specific hippocampal dysfunction as opposed to more generalised brain dysfunction (Pennington et al., 2003). Given the proposed role of the hippocampus in the consolidation of declarative information, as reviewed in section 6.1.2, it seems logical to predict consolidation difficulties in individuals with Down syndrome.

Further indirect evidence to support the hypothesis that individuals with Down syndrome will have deficits in vocabulary consolidation comes from research looking at their performance on language and long-term memory tests. Language is a known weakness in the cognitive profile associated with Down syndrome, with particular weaknesses in expressive language, including expressive vocabulary (see section 1.3.2). It is possible that poor consolidation could be a contributory factor to this overall language deficit. Several studies have also documented a long-term memory deficit in Down syndrome, often in both the verbal and the nonverbal domains (Carlesimo, Marotta, & Vicari, 1997; Pennington et al., 2003; Vicari, Bellucci, & Carlesimo, 2000). However, it should be noted that the difficulties with verbal long-term memory seem to be in line with general level of verbal ability rather than presenting as a specific difficulty (Jarrold, Baddeley, & Phillips, 2007). Although it is possible that generally poor long-term memory is a consequence of deficient encoding or problems with retrieval, it is equally possible that consolidation difficulties may play a part. Research that looks at these individual aspects of the memory process separately will be necessary to elucidate what underlies long-term memory difficulties in Down syndrome.

In sum, although no known studies have directly assessed the consolidation of new vocabulary in Down syndrome, there is much indirect evidence to support the proposal that it could be a problem in this population. The first part of this review highlighted the importance of sleep for declarative consolidation in general and vocabulary consolidation more specifically. Down syndrome is associated with sleep difficulties and furthermore, individuals with Down syndrome have well-documented impairments in language and long-term memory and at the biological level often display hippocampal abnormalities, all of which could be consistent with vocabulary consolidation difficulties. Clearly, however, it is important to assess vocabulary consolidation in an experimental paradigm in order to see if this hypothesis is supported by direct evidence.

6.1.6 Fast Mapping in Down Syndrome

Although consolidation of new vocabulary has not been directly assessed, it is important to understand precisely what is already known about the word learning process in Down syndrome, so that findings about consolidation can be more accurately interpreted. The majority of research to date focuses on the immediate acquisition of verbal labels through fast mapping paradigms.

The first of these fast mapping studies was conducted by Chapman, Kay-Raining Bird and Schwartz (1990). They presented 48 individuals with Down syndrome (aged 5 to 20 years), and 48 typically developing children (aged 2 to 6 years) with a novel verbal label that was associated with a novel item in the context of a 'hiding' game. The groups were matched on nonverbal ability but also scored similarly on a measure of receptive vocabulary. After just one exposure to the item and its name, approximately 75% of the children in both groups were able to recognise the item (as demonstrated by selecting it from an array that included a known object and an unlabelled novel object alongside the target). Furthermore there were no group differences on a production task where participants were asked to name the target novel item, although performance was far weaker than on the recognition test in both groups. Similarly, there were no group differences when these tests were repeated one hour after the original exposure. The findings of this study suggest that individuals with Down syndrome are able to immediately acquire novel words at a level consistent with their nonverbal ability and understanding of existing vocabulary items.

Building on this early work, several studies have investigated fast mapping in Down syndrome using larger and more varied item sets. For example, Chapman, Sindberg, Bridge, Gigstead and Hesketh (2006) found no difference between individuals with Down syndrome and controls on either comprehension or production tests when participants were required to fast map eight novel words. Kay-Raining Bird, Chapman and Schwartz (2004) found that individuals with Down syndrome are able to remember and produce novel words as well as controls matched for nonverbal ability when the new words were presented in a story context but they had more trouble defining the words. There is also evidence that individuals with Down syndrome are equally proficient as controls at fast mapping novel items that are verbs, as well as nouns, even when comprehension depends on utilising pragmatic and syntactic cues (McDuffie, Sindberg, Hesketh, & Chapman, 2007).

Thus, generally speaking, findings converge to suggest individuals with Down syndrome are able to immediately acquire novel verbal labels in line with their nonverbal ability and receptive language ability. This is somewhat surprising given that individuals with Down syndrome show a well-replicated deficit in verbal short-term memory (Jarrold, Baddeley, & Phillips, 1999). However, it is worth noting that several of the studies detailed above utilise the same small group of individuals with Down syndrome, bringing into question the generalizability of these fast mapping findings.

6.1.7 Word Learning in Down Syndrome

Recent investigations of word learning in Down syndrome have used more explicit and intensive paired-associate learning to investigate whether there are differences in the quality of the phonological representations of new words. If there were then this may reconcile findings of generally in-tact fast mapping, at least in older children and adolescents with Down syndrome, in the presence of verbal short-term memory deficits. One criticism of several of the above fast mapping studies is that the criteria used for scoring correct productions of newly learnt words are relatively lax, allowing a response to be scored correct if just two out of the three phonemes are said in the correct order and allowing for minor additions in the word. While this makes it less likely that the participants with Down syndrome would be disadvantaged by their articulation difficulties, it is possible that this masks subtle differences in the quality of phonological learning between individuals with Down syndrome and typically developing children.

Jarrold, Thorn and Stephens (2009) assessed the quality of the phonological representations of new words in participants with Down syndrome, avoiding the need for a verbal response. They taught 22 individuals with Down syndrome (aged 14 -29 years), and 64 typically developing children with equivalent receptive vocabulary levels (aged 5-8 years), the names of cartoon aliens, presented in groups of three. They were tested on their knowledge of the phonological form or referent of the names until they knew all three on two consecutive trials up to a maximum of 10 trials per item set. In the form knowledge condition, participants were shown each alien sequentially and heard three attempts at naming each, one of which was correct alongside two foils, each of which differed from the target by a single phoneme. The task was to select the correct name, thus assessing the specificity of their phonological representations without necessitating a verbal response. This can also be referred to as a mispronunciation task. In the referent knowledge condition, participants had to point to the alien that matched the verbal label they heard. Jarrold et al. (2009) found that the participants with Down syndrome took significantly more trials to learn the form of the words but were unimpaired compared to controls at learning referents. In both groups, form learning was related to verbal short-term memory whereas referent learning was not. This indicated that individuals with Down syndrome have difficulty forming the precise phonological representations essential for effective word learning and this is, perhaps in part, to do with their verbal short-term memory deficit.

However, a follow up study by Mosse and Jarrold (2011) challenged this interpretation. Using a similar learning procedure to Jarrold et al. (2009), but assessing learning using an expressive naming task as opposed to a mispronunciation task, they found that individuals with Down syndrome were just as proficient in the word learning tasks as controls matched on receptive vocabulary whether the stimuli were real names, wordlike novel names or non-wordlike novel names. This was surprising as they used stringent criteria to determine correct responses, which would rely on well-specified phonological representations. Participants were asked to repeat the names during training and then their responses to the expressive naming tasks had to match this repetition with no phoneme substitutions, additions or omissions. Furthermore, they also found that the group with Down syndrome were unimpaired on a mispronunciation task. They suggest that the discrepancy between these findings and those of Jarrold et al. (2009) is due to the nature of the recognition task. In Jarrold et al. (2009) the correct target was presented on more occasions than any of the individual foils, which were rotated across trials, whereas this was controlled in the Mosse and Jarrold (2011) study. Thus, it is possible that group differences did not reflect differences in the quality of the phonological representations of the words but, rather, the typically developing children may have been able to better utilize the added familiarity of the target items, boosting performance. Thus, the authors conclude that individuals with Down syndrome are unimpaired, relative to their level of vocabulary, at learning new words and can do so at a level beyond their verbal short-term memory skills, which suggests that they may acquire new vocabulary through a different route.

In a related study, Mengoni, Nash, & Hulme (2013) investigated spoken word learning in Down syndrome. They used an enriched and detailed paired-associate (novel word and novel picture) training protocol involving several item repetitions, segmentation of the phonemes within the novel words and corrective feedback of responses during training. This intensity, while different from previous studies, ensured that children in this age range could achieve a score above floor level on the test tasks that were administered after a delay. The advantage of this type of procedure is that it allows assessment of how well the learnt information has been retained over time and allows for an increased number of items to be learnt together. They found that children with Down syndrome were able to learn new words as well as typically developing children, even when tested after a short delay, and their learning was boosted by seeing the written form of the word to the same extent as typically developing children matched for reading ability. Reading is usually

considered a strength in the cognitive profile associated with Down syndrome in relation to oral language, including vocabulary (Byrne et al., 2002). This makes the levels of learning in the Mengoni et al. (2013) study all the more impressive amongst the group with Down syndrome as it is possible, although this cannot be confirmed given the background tests administered, that the children with Down syndrome had inferior receptive vocabulary to the typically developing group.

In summary, individuals with Down syndrome appear to be able to learn the phonological form of new words as well as might be expected given their existing vocabulary or reading skill. This is surprising given their poor verbal short-term memory skill but also the generally slow vocabulary acquisition and growth seen in this population. Therefore, when the sleep problems and long-term memory deficits in Down syndrome are also considered, it is possible the reduced vocabulary growth is due to problems with consolidation over time rather than difficulties with initial encoding of new words.

6.1.8 Introduction to the Current Study

This study aimed to investigate whether individuals with Down syndrome demonstrate difficulties with the consolidation of new words over time. Given the sleep difficulties associated with Down syndrome and the role that sleep typically plays in consolidation, examining the relationship between sleep and the vocabulary consolidation tasks was also of interest. However, practical constraints prohibited the use of an a.m.-p.m. design (such as that used by Henderson et al., 2012), which is the gold standard for investigating the role of sleep in consolidation processes. Thus, for the purposes of this study, a parent-report questionnaire measure of sleep quality was collected. Although such a measure cannot speak to the causal role of sleep in the consolidation tasks they can highlight any potential relationships of interest for future investigations.

Using a vocabulary training design, a group of nine- to eighteen-year-old participants with Down syndrome and a typically developing control group with similar levels of existing vocabulary (5-6 years old) were taught the associations between six novel words and their corresponding novel picture. They were subsequently assessed on their immediate memory for these new words and their referents. As this study aimed to look specifically at consolidation, the initial encoding process was controlled by training participants to a learning criterion. Similarly to Backhaus et al. (2008), this study used a criterion of 50% correct on an expressive naming test of the trained items. In support of this criterion level, Wilhelm, Metzkow-Mészàros, Knapp and Born (2012) highlight that

there is a 'sweet spot' for initial learning, in order to see expected consolidation effects, which is sufficiently above floor but below ceiling on the learning tasks.

However, since previous studies of vocabulary learning in Down syndrome and in young children have found very low levels of expressive production after training procedures (typically around 1 or 2 items correct e.g. Storkel, 2001), the effectiveness of the initial training was of paramount importance. Thus, this study utilised an enriched novel word training procedure similar to that in Mengoni et al., (2013). Pilot work demonstrated that it was necessary to use a very explicit procedure, in order to produce acceptable levels of learning. Although the intensity of the procedure is a departure from the way that new vocabulary is acquired in the real world, it enables a detailed look at consolidation processes after sufficient initial encoding has occurred.

In order to assess consolidation, participants were tested on their knowledge of the novel items at three time-points: immediately after learning, 24-hours after learning and 1-week after learning. The 24-hour post-test was included to assess any overnight changes and the 1-week follow-up was to assess longer term maintenance of learning and is an interval that has been included in other studies of vocabulary learning (Henderson et al., 2012). Knowledge of the new items was assessed in three ways: expressive recall of the new words when shown the associated picture, pointing to the correct referent in response to one of the novel verbal labels and, following on from Mosse and Jarrold (2011), a test of phonological knowledge in the form of a mispronunciation task.

It was expected that, in line with Henderson et al. (2012) the typically developing children would show an overnight improvement on all tasks that would be sustained at the 1-week post-test. However, it should be noted that the findings for the younger age range in question have been somewhat mixed and the nature of the training, stimuli and post-tests are different in the current study, for example pairing the novel words with pictures and assessing knowledge of this picture referent.

Given the pervasive language learning difficulties in Down syndrome and the prevalence of sleep disturbances, it was expected that this group would have difficulties with consolidation and thus would be unlikely to show the same degree of improvement. Two possible outcomes were hypothesised with regards to the specific pattern of consolidation and maintenance for the group with Down syndrome:

a) A relatively flat function where performance on the post-tests neither improves nor declines over time, indicating a lack of consolidation but no forgetting of information.
b) A decline in performance over time that indicates not only a lack of consolidation but also forgetting over time.

In addition, it was expected that the sleep measure would relate to performance on the learning tasks in both groups. However, the studies reviewed above that find a relationship between sleep and consolidation all link overnight polysomnographic measures to memory for the new information and, thus, it is possible that the parent-report measure of sleep will relate in a different way to the learning tasks.

6.2 Method

6.2.1 Participants

Two groups of participants were recruited for this study. Thirteen children and adolescents with Down syndrome (aged 9 – 18 years; mean = 13 years, 1 month) took part. All individuals had participated in previous research projects at the University of York and their families had consented to be contacted about future projects. Eight of the participants also took part in the Mengoni et al., (2013) study. Information about the current study was sent to parents from this database and the children of those who provided written consent were included. Four participants attended mainstream primary schools, one attended a special primary school, five attended mainstream secondary schools, two attended special secondary schools and one child split their education between mainstream and special secondary schools.

Fifteen typically developing children (aged 5 – 6 years; mean = 6 years, 0 months) were recruited from a local primary school. This age group was recruited with the expectation that the two groups of participants would have similar levels of vocabulary, based on the average scores of the group of participants with Down syndrome. Thus, the participants were matched for vocabulary at the group level but were not explicitly matched at an individual level. Children who had been identified with special educational needs were excluded. Headteacher consent for school participation was obtained alongside parental consent for the individual children who took part.

6.2.2 Assessment Battery

6.2.2.1 Nonverbal reasoning

The *Matrix Reasoning* subtest from the *Wechsler Preschool and Primary Scale of Intelligence- Third Edition (WPPSI-III;* Wechsler, 2003*)* was administered as a test of nonverbal ability. Participants were required to select the missing portion of an incomplete pattern matrix from four or five response options. One point was awarded for each correct selection with a maximum of 29 points. Testing was discontinued after either four consecutive incorrect responses or four incorrect responses in five consecutive items.

6.2.2.2 Receptive vocabulary

The *Receptive One-Word Picture Vocabulary Test – Second Edition* (*ROWPVT*; Brownell, 2000a) was administered as a test of receptive vocabulary. Participants were asked to select a picture, from a choice of four, which best matched the word said by the examiner. One point was awarded for each correct response with a maximum of 170 points. Testing was discontinued after six errors were made in eight consecutive items.

6.2.2.3 Expressive vocabulary

The *Expressive One-Word Picture Vocabulary Test – Second Edition* (*EOWPVT*; Brownell, 2000b) was administered as a test of expressive vocabulary. Participants named a series of pictures that ranged from boat to dolmen. One point was awarded for each correct response, taking into account consistent articulation errors in both groups, with a maximum score of 170. Testing was discontinued after six consecutive incorrect responses.

6.2.2.4 Short-term memory

Verbal short-term memory was assessed using the *Word List Recall* subtest from the *Working Memory Test Battery for Children* (*WMTB-C*; Pickering & Gathercole, 2001). Participants were asked to repeat lists of one syllable words in the correct order. The length of the word lists increased over the course of the test. Participants were credited with a point if they correctly remembered the whole list in the correct order, with a maximum score of 42. When participants correctly remembered four lists in a block of six at a particular list length they moved onto lists with an additional item. Testing was discontinued when participants made three errors within a block of six lists at a particular

length. The total number of correct trials was used in the analysis rather than the span score.

Visual short-term memory was assessed using the *Block Recall* subtest from the *WMTB-C* (Pickering & Gathercole, 2001). Participants saw sequences of increasing length tapped out on an array of blocks and were asked to reproduce the sequences in the same order. One point was awarded for correctly remembered sequences, with a maximum score of 54. When four sequences in a block of six at a particular length were correctly reproduced, the examiner proceeded to sequences that increased by one item. Testing was discontinued after three errors within a block of six sequences at a particular length. The total number of correct trials was used in the analysis rather than the span score.

As a test of phonological short-term memory, the *Preschool Repetition Test* (*PSRep*) from the *Early Repetition Battery* (*ERB*; Seef-Gabriel, Chiat, & Roy, 2008) was administered. Participants were asked to repeat a list of 18 words and 18 nonwords, with each list containing six one-syllable, six two-syllable and six three-syllable words. Given the age range and spectrum of ability found within the experimental group, six four-syllable extensions items were added to both lists. The two lists of words were phonologically matched with the nonwords created by changing the vowel in the one-syllable words or transposing consonants in the longer words. Participants' responses were audio recorded for later scoring. The repetition attempts on the word list were used to identify consistent articulation errors for individual children, which were taken into account when scoring the nonword lists. One point was awarded for each nonword that was repeated correctly with a maximum score of 24. There was no discontinuation rule on this task so participants attempted all items.

6.2.3 Training Materials

Participants were introduced to six novel words. All items were one-syllable, three-letter words with a consonant-vowel-consonant structure (*mav, nep, vot, zem, tus, pid*). Children with Down syndrome are known to have difficulties with articulation, particularly of later acquired phonemes (Stoel-Gammon, 1997), and thus only phonemes that typically emerge early in speech development (Dodd, Holm, Hua, & Crosbie, 2003) were included in the novel items. Each vowel sound featured at least once in the set of items.

The novel words were presented to participants as the names of "things found on an alien planet". Each word was randomly paired with a novel picture sourced from Microsoft Clip Art. These pictures represented a range of semantic categories including creatures, tools and transport. The novel words and corresponding pictures are presented in Appendix 4.

The training materials and post-tests were all presented to participants via a Toshiba Satellite Pro L300 laptop. The familiarisation phase of the training was implemented using Microsoft PowerPoint and all other tasks were designed and implemented using E-Prime Version 1 (Schneider, Eschman, & Zuccolotto, 2002).

6.2.4 Training Procedure

The current study aimed to examine consolidation effects. Thus, participants were trained to criterion on the learning task to ensure that any differences in retention of the novel items could not be attributed to initial encoding differences. Due to the demanding nature of language learning tasks, very few studies have attempted to train children to a criterion level and no known studies to date have attempted this procedure with children younger than seven years old or with individuals with learning disabilities such as Down syndrome. Thus, different versions of training were piloted extensively on a group of 19 typically developing five-year-old children from a primary school in York. Piloting indicated that the most effective procedure for enabling children to reach a criterion of three items correct out of six involved familiarising the children explicitly and extensively with the six items, presented with contextual information in two groups of three, before testing their knowledge of them. It was also found that performance typically only reached acceptable levels if participants were cued with the initial phoneme of a novel item when they provided a response that started with the wrong letter or were unsure. The final procedure is detailed below.

6.2.4.1 Familiarisation phase

Participants were told that they were going to learn about "things from an alien planet" as an introduction to the training procedure. The images of the novel items were superimposed on a red planetary background throughout the familiarisation phase in order to enrich the context of the procedure and make the task more engaging (see Appendix 5)

Participants were also introduced to the alien character 'Bob' who sat in the corner of the screen throughout the familiarisation phase. They were told that Bob had trouble remembering the names of the things on the planet and that they were going to try to remember more things than Bob in the later games in order to enhance motivation to learn and remember the words.

Each item was presented twice during the familiarisation phase. To reduce the verbal short-term memory demands of the task, the six novel items were randomly divided into two groups of three words during the initial familiarisation period. The items *mav*, *nep* and *vot* were in Group 1 and the items *zem*, *tus*, and *pid* were in Group 2. The presentation order of the two groups of items was counterbalanced across participants.

Participants were introduced to each of the three items in the group in turn. They saw the picture of the item and were told its name (e.g. "This is a pid") and were asked to repeat it three times. Corrective feedback was provided throughout the training procedure and the item name was repeated whether or not the correct answer was provided (e.g. "That's right, it's a pid" or "That's not quite right, it's a pid"). Participants were told a short fact about the novel item (e.g. "a pid likes to tickle the other aliens"; for a full list see Appendix 4) and then had to recall its name. If participants failed to provide a response or provided a response that started with the wrong phoneme, they were cued with the correct phoneme (e.g. "this one starts with a p...") and their responses were then scored and corrective feedback provided. Finally, they heard the item segmented (e.g. "p-i-d") and were asked to provide the last sound. This was to draw attention explicitly to the sounds in the new words in order to enhance learning. The picture of the item remained on the screen throughout.

Once each item in the group of three had been presented once, participants were given a receptive and an expressive test of item knowledge. The receptive task involved selecting each of the items, presented in a fixed random order, from an array of all three items. The positions of the three items within the array varied across the three trials, as did the position of the correct response. The expressive test was a picture naming task. Each picture was presented in turn in a fixed random order that was different to their introductory presentation order and participants were asked to name each one. Responses were only considered correct if all phonemes were correctly produced in the correct order.

However, individuals with Down syndrome often have articulation difficulties; and for each child consistent errors across the repetition trials, indicative of a speech output problem, were allowed for. Again, participants were cued with the correct initial phoneme of an item if they failed to provide a response or produced a word that started with an incorrect phoneme.

This familiarisation procedure was run twice with each set of items, after which participants were shown a random array of all six item pictures and were asked to name each one in turn, in a fixed random order.

6.2.4.2 Criterion trials

Participants completed the 'Beat Bob' task which acted as criterion trials. This was an expressive picture naming task, repeated until participants could correctly name three out of the six items, including correct responses that were cued with the initial sound if necessary. Participants saw a large version of each of the item pictures in turn on a plain white background and were asked to name them. The order of the items was randomised on each trial. Corrective feedback was provided throughout and during this task participants were shown a tick above the item picture if they correctly named it alongside the verbal feedback or they were shown a cross if their response after cuing was incorrect. All participants completed a practice trial after which the game continued until the participant could name at least three of the items. Thus, there was a minimum of two 'Beat Bob' trials and a maximum of six.

6.2.5 Post-tests

There were three post-tests, administered in a fixed order: the expressive vocabulary test, the receptive phonology test and then the receptive vocabulary test. The post-tests were administered in this fixed order to reduce possible priming effects in responses (for example, hearing an item name in the receptive vocabulary task boosting performance in the expressive vocabulary task). Participants completed the post-tests at three time points: firstly at the end of the initial learning session, after completing a filler task, and again 24-hours and 1-week after the initial learning session.

6.2.5.1 Expressive vocabulary

In the expressive vocabulary test participants saw the pictures of each of the six items presented alone on a white background in a random order. Participants attempted to name each item and were provided with a cue to the first sound if they did not provide a response or their response began with the wrong phoneme. No explicit feedback was provided. The number that each participant remembered correctly, both with and without cuing, was recorded, with a maximum of six.

6.2.5.2 Receptive phonology

This task was designed to assess participants' knowledge of the phonological form of the item names without requiring an expressive response. Participants heard three words, recorded by a female adult speaker, and were asked to pick which of the three was one of the novel words they had encountered during training. The three words included a target, a foil where the first phoneme differed in either voicing or place of articulation and a foil where the last phoneme differed in the same way (e.g. "pib", "pid", "tid"). Each word was associated with a colourful number and participants were asked to point to the number that went with the correct version of the word. There were two practice trials and then six experimental trials using the novel item names. The order of the trials was randomised and the correct answer appeared in each response position twice over the course of the task. Participants were not given any feedback and were awarded one point for each word that they correctly identified, with a maximum of six. The auditory items were presented either over Sennheiser HD205 headphones or over the laptop speakers in a quiet room, depending on circumstances and whether the participant used hearing aids.

6.2.5.3 Receptive vocabulary

This task assessed participants' knowledge of the mapping between the phonological form of the item and its associated picture. Participants saw an array of all six of the item pictures simultaneously on the screen and were asked to point to the picture that went with the word they heard. All words were presented as recordings by a female, adult speaker. The positioning of the six items and the positioning of the correct response was randomised for each trial and the order in which the words were presented was also randomised within the E-Prime program. Participants were awarded a point for each picture they correctly selected, with a maximum of six.

6.2.6 Overall Procedure

Participants were assessed either at home or in a quiet room within their school. This study comprised three sessions for each participant, with the two follow-up sessions taking place 24 hours and 7 days after the first session, respectively. One child from the typically developing group was unable to participate 7 days after their first session and so they were seen the following day (day 8) instead. In the first session participants were trained on the six novel items using the procedure detailed above. After participants reached the learning criterion, or attempted the maximum number of training cycles, they completed the *WPPSI-III Matrix Reasoning* task. Then, the three learning post-tests were administered in the order noted above. In the two follow-up sessions, the experimental post-tests were administered at the start of each session and the remaining standardised tests were completed over the course of the two sessions.

6.2.7 Sleep Assessment: Children's Sleep Habit's Questionnaire

Parents of the children in both groups were asked to complete the Children's Sleep Habits Questionnaire (CSHQ; Owens, Spirito, & McGuinn, 2000). This is a 45-item questionnaire that asks a range of questions about children's sleep and can yield scores for eight sub-scales (bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night waking, parasomnias, sleep disordered breathing and daytime sleepiness) and a total score. All items are rated on a three-point scale indicating the frequency with which the behaviour occurs in a typical week. Parents of the participants with Down syndrome were sent the questionnaires by post after their child had been seen for the learning tasks but for the typically developing children the questionnaire was included with the consent forms and information about the study so parents returned them at the same time as returning consent.

6.3 Results

6.3.1 Data Preparation

Raw scores were generally used in the analyses but, for the standardised measures for which they are available, age equivalents are also presented for the purposes of sample description. The data set is complete, with all participants completing all measures. The distribution of scores on each measure was examined through inspection of histograms and skewness and kurtosis values. Scores on the word span measure were positively skewed in the group with Down syndrome, with more participants scoring at the lower end

of the distribution. Conversely, the scores on the nonword repetition task were negatively skewed in the typically developing group due to ceiling effects on this task. As these two variables deviated from normality, Mann Whitney-U tests were used to assess group differences whereas independent t-tests were used for comparisons on all other variables.

6.3.2 Participant Characteristics

Table 6.1 shows that the group with Down syndrome were significantly older and performed significantly worse on the tests of nonverbal ability, verbal short-term memory (word recall) and nonword repetition. However, there were no differences between the groups on the measures of vocabulary, both receptive and expressive, nor on the visual short-term memory task (block recall). It is also worth noting that the standard deviations on the vocabulary and nonword repetition tasks are greater in the group of individuals with Down syndrome, indicating wider variability in performance within this group.

6.3.3 Performance During Training

In order to examine how the groups progressed through the training procedure, the mean score for each group on the expressive naming task between the end of familiarisation and the final criterion trial is displayed in Figure 6.1. In all analyses of both training and post-tests, the sum of cued and un-cued responses was used for the expressive task. A 2 (Group: TD vs. DS) x 2 (un-cued responses vs. total including cued) x 4 (Time: end of training, immediate, 24 hour, 1 week) repeated-measures ANOVA revealed that there was a main effect of cue, $F(1, 26)= 34.03$, $p<.001$, $\eta_p^2= .567$, with higher scores when cues were allowed. The main effect of group, $F(1, 26)= 1.09$, $p=.307$, $\eta_p^2= .040$, and the interaction between cue and group, $F(1, 26)= .87$, $p=.349$, $\eta_p^2= .032$, were not significant. This indicates that the two groups responded to cuing in a similar way.

Figure 6.1 shows that there was slow and steady improvement over time in both groups. At all stages the group of participants with Down syndrome obtained higher scores than the typically developing participants. A 2 (Group: TD, DS) x 3 (Training stage: 1, 2, 3) mixed-design ANOVA reveals that the main effect of group was not significant, $F(1, 26)= 2.46$, $p= .129$, $\eta_p^2= .086$. The main effect of time, however, was significant, $F(2, 52)= 7.15$, $p= .002$, $\eta_p^2= .216$. Repeated contrasts reveal that there was a significant improvement between scores on the practice trial of the Beat Bob game and the final trial, when the participants have reached criterion. The interaction between group and time was not significant, $F(2, 52)= .438$, $p=.447$, $\eta_p^2=.031$.

In order to examine whether there were any differences between the groups in the amount of training necessary to reach criterion, the mean number of trials on the Beat Bob task needed to reach criterion was calculated for each group. An independent samples t-test revealed that the difference between the number of trials required by the typically developing group (*M*= 3.13, *SD*= 1.69) and the group with Down syndrome (*M*= 2.62, *SD*= 1.33) was not significant, *t*(26)= .89, *p*=.380, *r*= .17. Overall, these findings suggest that the groups responded in a similar way to the training procedure and at a similar ability level.

6.3.4 Patterns of Consolidation: Post-test Scores

The mean scores on each of the post-tests at each testing occasion were calculated for each group in order to examine consolidation over time. The scores are displayed in Figure 6.2. It can be seen that neither group show much change between post-test sessions on the expressive test but both groups show improvement on the mispronunciation task and receptive post-tests. The groups perform at a similar level on the expressive and receptive task but the scores on the mispronunciation task are generally lower in the participants with Down syndrome.

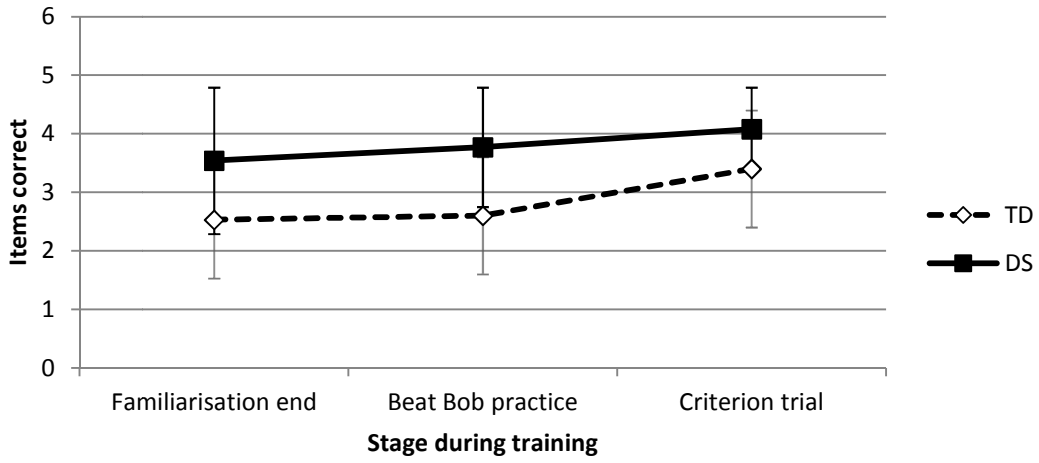


Figure 6.1. Mean expressive naming scores at different points during training. Error bars display 95% confidence intervals

Table 6.1.

Mean scores, standard deviations and group differences on background measures.

	DS N=13	TD N=15	Group difference
Age (in months)	156.69 (39.95)	72.47 (3.02)	t= -7.58, p<.001
Matrices raw score (max=29)	11.92 (5.01)	16.60 (6.16)	t= 2.18, p= .038
Matrices age equivalent (in months)	60.31 (15.05)	74.13 (16.72)	t= 2.29, p= .031
ROWPVT raw score (max=170)	67.92 (17.58)	72.87 (11.67)	t= .887, p= .383
ROWPVT age equivalent (in months)	74.00 (22.02)	79.40 (14.60)	t= .775, p=.446
EOWPVT raw score (max=170)	61.00 (17.73)	61.87 (11.47)	t= .156, p= .877
EOWPVT age equivalent (in months)	70.23 (21.44)	70.80 (13.82)	t= .085, p=.933
Word recall raw score (max=42)	14.15 (3.58)	19.07 (3.41)	U= 27.50, p= .001
Block recall raw score (max=42)	18.46 (4.39)	20.33 (5.42)	t= .994, p= .330
Nonword repetition (max=24)	14.85 (5.79)	22.00 (2.24)	U= 11.00, p<.001

ROWPVT = Receptive One Word Picture Vocabulary Test; *EOWPVT* = Expressive One Word Picture Vocabulary Test

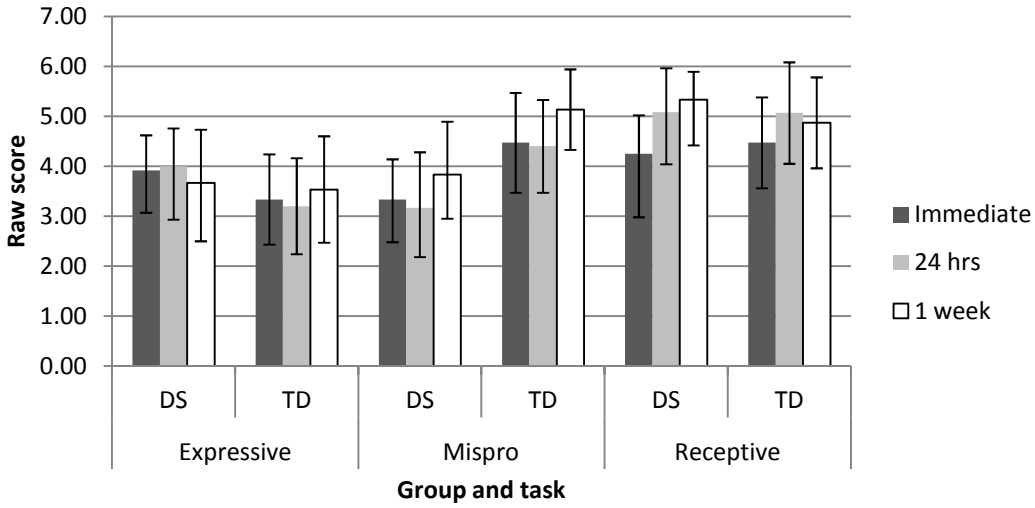


Figure 6.2. Mean raw score on the word learning post-tests for each group immediately after training, 24-hours later and 1-week later. Error bars represent 95% confidence intervals.

The accuracy data were entered into separate 2 (Group: TD, DS) x 3 (Session: immediate, 24-hours, 1-week) mixed-design ANOVAs. On the expressive task, there was no significant change in performance across sessions, $F(2, 52)= .07$, $p= .938$, $\eta_p^2= .002$. There were also no group differences, $F(1, 26)= .48$, $p= .493$, $\eta_p^2= .018$ and no significant interaction between group and session, $F(2, 52)= 1.15$, $p= .324$, $\eta_p^2= .042$.

On the mispronunciation task there was a significant improvement in performance across sessions, $F(2, 52)= 5.15$, $p= .009$, $\eta_p^2= .165$. Simple contrasts reveal that while there was no difference between the immediate and 24-hour session ($F(1, 26)= .09$, $p= .773$, $\eta_p^2= .003$) there was a significant improvement between the 24-hour and 1-week sessions ($F(1, 26)= 10.92$, $p= .003$, $\eta_p^2= .296$). Accuracy was greater in the typically developing group than the group with Down syndrome, $F(1, 26)= 4.67$, $p= .040$, $\eta_p^2= .152$. However, the interaction between group and session was not significant, $F(2, 52)= .01$, $p= .994$, $\eta_p^2< .001$.

On the receptive vocabulary task there was also a significant improvement across sessions, $F(2, 52) = 6.22$, $p= .004$, $\eta_p^2= .193$. Repeated contrasts reveal that there was significant improvement between the immediate and 24-hour sessions ($F(1, 26)= 7.29$, $p= .012$, $\eta_p^2= .219$) but no significant change between the 24-hour and 1-week sessions ($F(1, 26)= .01$, $p= .911$, $\eta_p^2< .001$). There was no significant difference between the groups, $F(1, 26)= .02$, $p= .879$, $\eta_p^2= .001$, and the interaction between group and session was not significant, $F(2, 52)= 1.07$, $p= .352$, $\eta_p^2= .039$.

The results of these analyses suggest that the only group differences were in the levels of accuracy on the mispronunciation task where, overall, the typically developing group outperformed the group with Down syndrome. There were no group differences in the patterns of consolidation over time. On the expressive vocabulary test, accuracy performance did not change across the post-test sessions. However, there was improvement over time on both other post-tests, with the greatest gains at the 24-hour post-test for the mispronunciation test and at the 1-week post-test for the receptive vocabulary test.

6.3.5 Sleep Measure: CSHQ

All parents of the 15 children in the typically developing group completed the CSHQ on behalf of their child but one parent of a child with Down syndrome returned an incomplete questionnaire meaning that 12 questionnaires were used for analysis in this group. The mean raw scores on each sub-scale of the CSHQ and the total mean score are shown for each group in Table 6.2. A higher score indicates a greater problem within that sleep domain.

Table 6.2.

Mean scores (standard deviation) on each scale of the CSHQ, and the total sleep disturbance scores, in both groups

	DS N=12	TD N=15	Group differences
Bedtime Resistance (/18)	7.17 (1.85)	6.27 (.59)	*t*= -1.62, *p*= .130
Sleep Onset Delay (/3)	1.25 (.45)	1.20 (.56)	*t*= -.25, *p*= .804
Sleep Duration (/9)	4.33 (1.67)	3.53 (1.13)	*t*= -1.42, *p*= .172
Sleep Anxiety (/12)	6.17 (1.70)	4.67 (.98)	*t*= -2.89, *p*= .008
Night Wakings (/9)	4.25 (1.42)	3.60 (.83)	*t*= -1.40, *p*=.178
Parasomnias (/21)	9.75 (1.96)	8.27 (1.53)	*t*= -2.21, *p*= .037
Sleep disordered breathing(/9)	4.33 (1.37)	3.47 (.74)	*t*= -1.97, *p*=.066
Daytime sleepiness(/24)	12.42 (3.15)	11.07 (2.25)	*t*= -1.30, *p*= .206
Total sleep disturbance (/99)	47.25 (7.05)	40.00 (5.37)	*t*=-3.04, *p*=.006

The individuals with Down syndrome score more highly on all of the sleep scales, and there is more variability among their scores. The group differences are significant on the sleep anxiety scale, the parasomnias scale and the total sleep disturbance scale. The difference on the sleep disordered breathing scale approaches significance.

The relationships between the sleep measures and the learning and consolidation tests were of particular interest. The primary question was whether the sleep measures relate to consolidation-related changes over time rather than absolute performance on the learning tasks. Thus, partial correlations were calculated examining the relationships between the CSHQ measures and the individual post-tests given at 24-hours and 1-week while controlling for performance on the same post-test at the immediate testing point. These correlations are shown for the individuals with Down syndrome in Table 6.3 and for the typically developing group in Table 6.4.

There were no significant relationships between the CSHQ scales and the learning post-tests in the typically developing group. Similarly, in the group with Down syndrome there were few significant correlations. In the expected direction, severity of bedtime resistance was negatively correlated with the receptive test at the 24-hour post-test. However, in the opposite direction to that expected, there was a positive correlation between parasomnias and the expressive post-test at 24-hours and between the total sleep disturbance score and the receptive post-test at 1-week. Inspection of the scatter plots for these correlations reveal that ceiling effects in the receptive post-test could be influencing the correlation with sleep disturbance. Furthermore, two participants who scored particularly poorly on the expressive test and also happened to have low parasomnia scores, which may be driving the relationship between these two variables.

Table 6.3.

Correlations between the CSHQ scales and the learning post-tests in the individuals with Down syndrome.

	Bedtime resistance	Sleep onset delay	Sleep duration	Sleep anxiety	Night wakings	Parasomnia	Disordered breathing	Daytime sleepiness	Total sleep disturbance
Expressive - 24 hr	-.407	.202	.336	-.347	.095	.790*	.575	.366	.491
Mispro - 24 hr	.377	-.178	-.169	.284	.418	-.434	-.197	-.538	-.267
Receptive - 24 hr	-.626*	-.442	-.446	-.195	-.064	.322	-.220	.222	-.177
Expressive - 1 wk	-.270	-.343	-.103	-.562	-.184	.470	.196	.023	-.097
Mispro - 1 wk	-.058	.023	-.097	-.059	.540	.150	-.061	-.233	-.028
Receptive - 1 wk	.151	.174	.272	.312	.362	.487	.465	.326	.707*

Table 6.4.

Correlations between the CSHQ scales and the learning post-tests in the typically developing children

	Bedtime resistance	Sleep onset delay	Sleep duration	Sleep anxiety	Night wakings	Parasomnia	Disordered breathing	Daytime sleepiness	Total sleep disturbance
Expressive - 24 hr	.424	.378	.214	.033	.108	.124	.271	.171	.293
Mispro - 24 hr	-.046	.078	.335	.113	-.313	-.148	-.089	.264	.105
Receptive - 24 hr	.191	.025	-.016	.193	.004	-.386	-.197	-.181	-.169
Expressive - 1 wk	.252	.187	.039	.013	-.222	-.159	.259	.032	.016
Mispro - 1 wk	.146	.022	-.053	-.166	.030	-.403	-.218	-.030	-.181
Receptive - 1 wk	.031	.136	.073	-.017	.268	-.022	.096	-.020	.061

6.4 Discussion

This study aimed to investigate whether individuals with Down syndrome have a deficit in consolidating new vocabulary, perhaps in part due to sleep difficulties. It was expected that the group with Down syndrome would perform more poorly than the typically developing group at the 24-hour and 1-week post-tests, indicating reduced consolidation and maintenance of learning. Contrary to the hypothesis, the patterns of learning across one week in the group with Down syndrome closely mirrored that of the typically developing children on all of the recall tasks. The only group difference lay in the poorer overall performance of the group with Down syndrome on a mispronunciation task, although the patterns of consolidation did not differ from the typically developing children. Furthermore, it was predicted that measures of sleep quality would relate to word learning performance. This hypothesis was not supported by the parent-report questionnaire measure of sleep that was collected in this study.

6.4.1 Performance on the Word Learning Tasks

This study utilized a novel training paradigm to investigate spoken word learning in Down syndrome. The results showed that the procedure led to good levels of learning in both groups. Indeed, at the end of the initial familiarisation phase of training, before the criterion trials began, children in both groups were able to expressively recall approximately three out of the six items. This is substantially better performance than is typically seen in word learning studies with children of an equivalent age and ability level, where often participants are only able to remember one or two of the items expressively (Storkel, 2001). The effectiveness of this training procedure in both groups enabled us to look reliably at vocabulary consolidation but also has potential implications for vocabulary intervention methodology. Future research could dissect aspects of the training procedure to pinpoint which features are key determinants of the rapid and robust learning effects. The patterns of vocabulary consolidation over time differed somewhat from predictions in both groups, particularly for the expressive recall test. It was expected that the typically developing group would show a consolidation-related boost in performance after 24 hours, which would be maintained 1 week later, whereas the group with Down syndrome would show no improvement and perhaps some evidence of forgetting over time. However, both groups showed equivalent performance across the three sessions with no evidence of consolidation-related improvement or forgetting over time. Although this was the expected pattern for the group with Down syndrome, the similarity to the typically developing

controls suggest that this is not due to a consolidation deficit in Down syndrome but, rather, is typical for children of this language level using this procedure.

It was somewhat surprising that the typically developing children did not show improvement on the expressive recall task over time given previous research. Both Brown et al. (2012) and Henderson et al. (2012) found a significant boost in recall performance after 24 hours in seven- to twelve-year-old children. However, the procedures used in both of these studies differed substantially from the present study. As well as using older samples, the training and tests involved only auditory stimuli with no links to pictures or other semantic information, which could lead to different patterns of consolidation. However, Storkel (2001) found a significant improvement in word recall after one week in typically developing children who were within the same age range as in the current study and using a procedure where the new words were linked to picture referents. The potential discrepancy between this finding and our own results may lay with the substantially poorer recall performance after training in the Storkel (2001) study, leaving more room for improvement over time. Wilhelm et al. (2012) found that an intermediate level of performance on a motor learning task resulted in overnight consolidation; adults with too much training and children with too little training did not improve on the task overnight. While we ensured that children's performance on our expressive recall task was at an intermediate level, this required extensive explicit training with a large number of repetitions and recall attempts. This intensity of training may have meant that, while children were performing at an intermediate level on the task we designed, they were performing at the maximum level of their learning capacity on this type of task at this age. Thus, they may exhibit similar patterns to adults who were trained to high performance levels in the Wilhelm et al. (2012) study.

On the other two learning tasks (mispronunciation and receptive vocabulary) both groups showed consolidation related improvement, although the time-course differed. On the receptive vocabulary test there was a boost in performance after 24 hours whereas on the mispronunciation task improvement was not evident until one week later. The differences between these tasks may be due to the different aspects of word-specific knowledge required for each. The complementary learning systems hypothesis suggests that memories are initially encoded in a faster, episodic fashion and full lexicalisation then occurs more slowly (McClelland et al., 1995). There is evidence that tasks involving retrieval of the links between words and pictures depend more on the faster episodic memory

system (Takashima, Bakker, van Hell, Janzen, & McQueen, 2014). The mispronunciation task, on the other hand, is the only post-test that does not feature the picture referent and therefore relies solely on well-specified phonological knowledge. This is likely to depend on slower lexicalisation processes for improvements in task performance. Thus, it is perhaps unsurprising that the mispronunciation task shows evidence of slower consolidation processes than the receptive vocabulary test. However, these two types of tasks have not been contrasted in young children in any previous studies so further research would be needed to confirm that this pattern of findings is typical.

It could be argued that the improvements on the mispronunciation and receptive vocabulary tests are due to practice effects. However, participants did not receive corrective feedback on these tests at any of the testing occasions. Although, as both tests included an auditory presentation of the correct stimulus, participants were exposed to the correct verbal labels two additional times at each assessment point but never in conjunction with the correct picture. This design is common in the consolidation literature though and previous work (Davis et al., 2009) has looked at whether consolidation-related improvements can be accounted for by repeated testing. They found that the same degree of improvement was seen with either one or multiple testing occasions, suggesting that practice effects do not account for improvements.

While there were little in the way of group differences in consolidation over time, the group with Down syndrome did perform significantly more poorly on the mispronunciation task overall. This is in contrast to the findings of Mosse and Jarrold (2011) where the group with Down syndrome performed at the equivalent level to the typically developing controls on a similar mispronunciation task. However, in a crucial difference from the Mosse and Jarrold (2011) task, the corresponding picture referents of the novel words were not presented during the mispronunciation task in the current study, making it a purely auditory phonological task. Many have suggested that individuals with Down syndrome can use visual learning strategies to boost their performance in the language domain (Boudreau, 2002; Fidler, Most, & Guiberson, 2005). Thus, presenting the picture of the visual referent alongside the auditory response options could have enhanced the performance of the participants with Down syndrome in the Mosse and Jarrold (2011) study but such cues weren't available in the current task. This interpretation could be investigated by contrasting two versions of a mispronunciation task with the same item set,

one where the corresponding pictures are presented and one where they aren't presented to examine the impact that this has on accuracy in participants with Down syndrome.

Although they did not reach significance, there were also some emerging group differences on the expressive recall task. In general, the group with Down syndrome were achieving higher scores than the typically developing group. While the small sample size and variability within the groups mean that this difference is not reliable, the pattern is noticeable. This slight advantage for the group with Down syndrome is most likely due to their increased experience with teaching and learning environments which may have meant that they responded better to the intensive and explicit training than the much younger typically developing group. Furthermore, it should be noted that individuals with Down syndrome have been shown to expressively recall new words as well as reading-matched controls, who would be at a higher level of vocabulary than the group with Down syndrome, which would be in line with the current pattern of results (Mengoni et al., 2013). It is also worth noting that there was a slight trend for the typically developing group to improve on the expressive recall task after one week whereas there was a decrease in scores in the group with Down syndrome. These differences were very small in the current study but it would be interesting to see whether, over a longer period of time, these patterns crystallise as slow consolidation effects for the typically developing group and long-term forgetting in the group with Down syndrome.

In sum, this study did not find evidence to support the hypothesis that individuals with Down syndrome have a deficit in consolidating new vocabulary, relative to their existing vocabulary level. This is puzzling given the slow vocabulary development and long-term memory difficulties in Down syndrome. However, one possible explanation is to do with the explicit nature of the training procedure. In naturalistic contexts, vocabulary acquisition typically occurs implicitly, with minimal exposures to a new word and no direct instructions to try and remember the word. Evidence suggests that individuals with Down syndrome are unimpaired on implicit Hebb learning tasks and that their performance on these tasks relates to their nonword learning performance (Mosse & Jarrold, 2010; Mosse & Jarrold, 2008). This would seem to indicate that implicit word learning may be preserved in individuals with Down syndrome alongside explicit learning. However, there have been no direct assessments of this hypothesis using experimental implicit word learning tasks. It is possible that, despite certain in-tact processing mechanisms for implicit information, there could be deficits in extracting and selecting the relevant implicit information from the

language environment, which would impact on effective vocabulary learning. Indeed, in the Hebb learning literature, while the measured outcomes are implicit, they are determined through direct and focussed exposure to the relevant stimuli in an explicit task. Future work could directly compare implicit word learning tasks such as storybook reading, where no explicit attention is drawn to the novel items, to an explicit training procedure in order to investigate whether deficits in aspects of implicit learning, rather than consolidation, may be at the heart of the language difficulties in Down syndrome.

6.4.2 Relationships Between Sleep and Word Learning

As predicted, the group with Down syndrome showed significantly more difficulty with sleep, according to the parent-report CSHQ, in line with the findings from younger children in Chapter 5. This was particularly true for the sleep anxiety and parasomnia measures, although there was also a significant difference for overall sleep disturbance. This is in line with previous research highlighting sleep problems in Down syndrome (Ashworth et al., 2013; Breslin et al., 2011). The novel aspect of the current study was assessing whether this difficulty with sleep was related to performance on the word learning task.

It was predicted that there would be a relationship between the sleep measures and performance on the word learning tasks in both groups. In general, this hypothesis was not supported by the findings. On the CSHQ there were no significant correlations with the word learning outcomes in the typically developing group. For the group with Down syndrome, there was a significant correlation between bedtime resistance and overnight consolidation on the receptive vocabulary test, such that increased bedtime resistance was associated with lower scores on the receptive test at 24 hours. However, there were two significant correlations in the opposite direction to that expected, namely between parasomnias and expressive performance at 24 hours and between total sleep disturbance scores and receptive vocabulary performance at 1 week. However, both of these correlations appear to be unduly affected by a small number of outliers and ceiling effects, respectively. This makes it clear that the current sample is likely too small to investigate questions that require a correlational analysis such as this, and a larger-scale study would be necessary to draw firm conclusions.

In the current study, strong conclusions about the relationship between sleep and word learning in Down syndrome are precluded by methodological limitations. A small sample size and ceiling effects in some of the word learning measures make correlations

difficult to interpret. While the results are in contrast to much of the literature in typically developing children (Backhaus et al., 2008; Brown et al., 2012; Henderson et al., 2012), all studies that have found a relationship between sleep and word learning thus far used either a.m.-p.m. experimental designs or polysomnography. It is possible that parent-report measures of sleep are not sensitive enough to detect a relationship. Thus, further studies would benefit from utilizing one of the more rigorous designs used in sleep research when investigating sleep and consolidation in Down syndrome.

6.4.3 Conclusions

This study aimed to investigate the consolidation of new vocabulary in Down syndrome and its relationship with sleep. The results suggest that individuals with Down syndrome are able to consolidate new words as well as typically developing children matched for existing vocabulary, when explicitly and extensively trained on the new items. Both groups showed consolidation-related improvements over time on a mispronunciation and receptive vocabulary test although neither group improved on the expressive test, perhaps due to over-training on this aspect of word learning. There was no strong evidence of a relationship between sleep and word learning in either group, probably due to the use of parent-report measures rather than sleep-sensitive experimental designs or polysomnography.

The findings from this study have practical implications for language interventions in Down syndrome. The procedure used was effective in achieving good levels of vocabulary learning in a short time, which was maintained over the course of a week. Thus, similar procedures could be applied in targeted vocabulary interventions. The implications for theories of language learning in Down syndrome are more puzzling and suggest that a consolidation deficit does not underlie vocabulary difficulties. Thus, there are outstanding questions about the origins of such language difficulties. One potential avenue for future research would be to examine differences between implicit and explicit word learning as the current literature base focuses on explicit learning and weaknesses in the implicit domain could potentially underlie word learning difficulties in naturalistic contexts.

7 General Discussion

This thesis aimed to examine the development of cognitive, language and adaptive skills in children with Down syndrome and the influence of health on these outcomes. At the heart of the thesis was a fifteen-month longitudinal study tracing the cognitive development of four- to five-year-old children with Down syndrome and a group of nonverbal age-matched typically developing controls. The sample of children were drawn from a birth cohort study and their ages fell within a narrow age range; a strength of the thesis. As part of this study, parents were interviewed about their children's health so that links between health and cognition could be examined. A separate experimental study was also conducted to look specifically at a putative link between health and cognition, namely the relationship between sleep and vocabulary consolidation.

The central aim of the thesis was addressed via three primary research aims. The first of these concerned describing the overall profile of cognitive and adaptive strengths and weaknesses in young children with Down syndrome and how this develops over time. Through comparisons with the typically developing control group, Chapter 3 identified the cognitive strengths and weakness and Chapter 4 identified the adaptive strengths and weaknesses. Chapter 3 also aimed to examine cognitive variability in Down syndrome and the relationships between cognitive domains across the developmental period studied. Comparing these indices with typical development addressed novel questions about the extent to which cognitive development is qualitatively different in Down syndrome, which is important for theoretical models of development in Down syndrome. To answer a more methodological question in the assessment of cognitive and adaptive skills in young children Down syndrome, Chapter 4 evaluated how well parent-report measures of language and adaptive skills related to objectively measured cognitive skill both concurrently and across time.

A second, related, aim was to address outstanding questions about the unusual language profile in Down syndrome, primarily through the investigation of vocabulary and grammatical abilities, which are usually discrepant in individuals with Down syndrome. The aims was to provide a detailed description of the language profile according to both parent-report and objective measures in four- to five-year-olds and specifically to investigate whether development of these two language skills follows a typical or disordered course. Chapter 6 aimed to extend research on experimental word learning in Down syndrome to establish whether consolidation of new vocabulary over time is impaired, in order to

reconcile findings of unimpaired immediate vocabulary learning in experimental contexts despite slow overall vocabulary growth across development.

The final research question concerned the relationship between health and cognition in Down syndrome, a link that has not yet been comprehensively studied. Chapter 5 investigated this in young children with Down syndrome as part of the central longitudinal study. Parents were interviewed about their child's medical history with a focus on congenital heart defects, childhood hearing problems, perinatal factors, sleep problems and childhood hospitalisations. The thesis examined relationship between these factors and the cognitive measures administered as part of the longitudinal study. In addition, the vocabulary training study in Chapter 6 explored whether, in line with research in typically developing children, the consolidation of new words was related to sleep quality in children with Down syndrome.

7.1 Development of the Cognitive and Adaptive Phenotype in Young Children with Down Syndrome

Previous research has detailed a characteristic pattern of cognitive and adaptive strengths and weaknesses in children with Down syndrome, with relative strengths in nonverbal and social skills compared to language and motor abilities (Chapman & Hesketh, 2000). However, most studies focus on older children and adolescents, so much less is known about how this profile emerges in the early years. Fidler, Hepburn and Rogers (2006) found that in two- to three-year-old children with Down syndrome the characteristic profile was evident when domains were compared to each other in a within-subjects fashion but not when compared to appropriate control groups, suggesting that the profile was 'emerging' at this age. In other words, these toddlers with Down syndrome showed significantly weaker motor and expressive language skills in comparison to nonverbal ability in within-profile comparisons but this was not statistically distinct from the control groups. A similar pattern emerged for adaptive skills where communication and motor skills were significantly weaker than socialisation skills, but only in within-profile comparisons.

Chapters 3 and 4 addressed the same question in a slightly older sample of four- to five-year-old children with Down syndrome. Chapter 3 showed that the expected cognitive profile had fully emerged at the group level by this age, as reflected by statistically significant differences on the expected variables in comparison to the typically developing controls. The children with Down syndrome performed significantly worse on tests of language and motor skills than a nonverbal-age matched control group, which is suggestive

of language and motor weaknesses relative to nonverbal ability. This finding indicates that the group-level cognitive phenotype associated with Down syndrome emerges early in development, before formal schooling and formal intervention programs have typically begun.

Chapter 4 partially replicated the typical adaptive profile associated with Down syndrome in four- to five-year-olds. As expected, children with Down syndrome did not differ from typically developing controls in the socialisation domain but showed significant weaknesses in the communication and daily living skills domains. However, the difference on the motor domain was only marginally significant, contrary to expectations. On the whole, though, similarly to the findings from Chapter 3, this suggests that the profile of adaptive strengths and weaknesses has also mostly emerged by the age of four in children with Down syndrome.

Previous research has largely focussed on group-level findings to establish the general profile of cognitive strengths and weaknesses. Highlighting these consistencies provides useful information for researchers and practitioners. However, there is some evidence to suggest that the nature of the profile may not be consistent across individuals with Down syndrome (Tsao & Kindelberger, 2009) and that there is a greater degree of general cognitive variability amongst those with Down syndrome compared to the typical population (Patterson et al., 2013). Chapter 3, however, did not find evidence of greater cognitive variability in the current sample of children with Down syndrome. The standard deviations of all of the cognitive test scores were similar across both groups. This may reflect the fact that most previous studies have used samples that vary widely in age, whereas the current sample did not. Thus, it is possible that previous estimates of increased variability have been inflated by sample selection, or that increased variability is a feature of the later stages of development in Down syndrome when differences in individual developmental trajectories may become more apparent. In terms of variability in the expression of the cognitive profile between individuals with Down syndrome, Chapter 3 found that only around half of the children with Down syndrome showed the characteristic profile across all of the tests administered. This level of individual variability has typically been neglected in previous research but is potentially important when considering appropriate educational intervention strategies for children with Down syndrome and when developing theoretical models of strengths and deficits in the disorder.

Understanding how different cognitive domains relate to each other over time in Down syndrome, and how this compares to typical relationships, can speak to questions about whether development in Down syndrome is qualitatively different to typical development or merely delayed. Chapter 3 found that, broadly speaking, the patterns of the relationships between language, nonverbal and motor skills were very similar in Down syndrome and typical development. There were bidirectional relationships between nonverbal and language ability, and motor ability was correlated with later language ability, in both groups. There was some evidence that motor skill may have more of an influence on language development than the reverse relationship in the children with Down syndrome, which was atypical compared to the control group. However, conclusions are tempered by the skewed distributions of scores on the motor measures in the group with Down syndrome. Overall, there was little evidence to suggest that different cognitive skills relate to each other in a qualitatively different way across this period of development in Down syndrome compared to typical development, suggesting that at this point in time cognitive development follows a delayed rather than a disordered pattern.

Objective cognitive testing with young children with disabilities can be challenging and this is reflected by significant problems with the score distributions on some of the standardised tests presented in Chapter 3. Therefore, Chapter 4 examined how effectively parent-report measures could be used to predict objectively measured cognitive skills at a later point in time, when the objective tests seem to be more reliable. The Vineland-II parent-report interview has a Communication and a Motor scale and, thus, these could potentially be used to predict language and motor skills respectively. The simple correlations suggested that the Motor scale on the Vineland was not related to later performance on objective motor tasks and thus could probably not be used as a reliable substitute for objective testing. The Communication scale of the Vineland-II, however, was equivalent to objective testing in its prediction of later language ability and it was a better predictor of grammar skills than earlier objective tests. It was also a good predictor of vocabulary, as was the parent-report CDI questionnaire, but neither was a better predictor than earlier scores on the same objective vocabulary test. This suggests that, for language ability at least, the parent-report Vineland-II and CDI measures can be acceptable substitutes for objective cognitive testing in young children with Down syndrome, particularly where there are concerns about the reliability of the objective tests. This has important implications for practitioners working with young children with Down syndrome

and their families, who need an accurate, reliable assessment of a child's abilities with confidence that their assessment tools are predictive of future ability.

In sum, the findings of this thesis suggest that the group-level cognitive phenotype associated with Down syndrome has fully emerged by the age of four and the adaptive profile of strengths and weaknesses has also largely emerged by this age. However, only half of the children showed the cognitive phenotype at the individual level, in line with previous findings about variability in the cognitive profile. There was no evidence of increased variability in cognitive performance in children of this age with Down syndrome compared to typical development. Furthermore, the relationships between the different cognitive domains over time were similar across those with Down syndrome and typical development, suggesting a delayed rather than disordered course of development. Lastly, it was established that the Vineland-II and CDI parent-report measures could be acceptable substitutes of objective language tests for practitioners and researchers interested in predicting the language abilities of young children with Down syndrome.

7.2 The Nature of the Language Impairment in Down Syndrome

The language skills of children with Down syndrome have attracted considerable research interest due to an uneven linguistic profile, which closely resembles that of children with specific language impairment. However, the precise nature of the language impairment in Down syndrome is still debated. This current study is one of the first to focus on language skills from preschool to the start of formal schooling.

Chapter 3 replicated the characteristic language profile in four- to five-year-old children with Down syndrome. Namely, receptive vocabulary was a strength compared to expressive language and grammatical skills, in line with the majority of the previous research (Abbeduto et al., 2007). Chapter 3 also found some evidence of the characteristic discrepancy between vocabulary and grammar skills, with vocabulary being the stronger of the two.

The study in Chapter 3 was also the first to look at the relationships between grammar and vocabulary across a relatively early stage of language development in Down syndrome. The results suggested that this relationship was somewhat atypical. In the typically developing group, grammar and vocabulary were related concurrently at both time points in the longitudinal study and they were related to each other over time. In the group with Down syndrome, however, there were no concurrent relationships between

grammar and vocabulary at the first time point and no relationship between them over time. However, at the second time point there were significant concurrent correlations between grammar and vocabulary. This pattern of results is similar to that seen in late talking typically developing children (Moyle et al., 2007). Without a further time point in the longitudinal study it is not possible to determine whether the pattern of results in Chapter 3 reflects a disordered trajectory of vocabulary and grammar development, where the two skills are dissociated to a greater extent than in typical development across childhood, or delayed development that is more similar to late talking typically developing children. However, these findings suggest that further examination of how vocabulary and grammar relate to each other over time is warranted in order to gain a greater understanding of the nature of the language impairment in Down syndrome.

Expressive vocabulary in Down syndrome was of particular interest to this thesis. Chapter 3 replicated findings of an expressive vocabulary impairment according to objective testing. Chapter 4 investigated whether children with Down syndrome still had expressive vocabulary impairments when signed vocabulary was taken into account using the parent-report CDI questionnaire. The results suggested that, even when signing was taken into account, expressive vocabulary was still a weakness. One interesting observation from the results of Chapters 3 and 4, however, was the noticeable improvement in expressive vocabulary over the course of the longitudinal study. According to effect sizes, the group with Down syndrome improved more on the objective expressive vocabulary measure, the expressive subdomain of the Vineland-II and the expressive sub-domain of the CDI questionnaire than on any other measure in these assessments. Although caution must be employed in interpreting effect sizes across disparate tests, this finding was remarkably consistent across all different measures of expressive language. This suggests that the period of development between the ages of four- and six-years-old may be a key time for expressive language growth in Down syndrome.

The nature of vocabulary learning in Down syndrome was also explored in an experimental vocabulary training study in Chapter 6. This study investigated the consolidation of new vocabulary over time in an attempt to reconcile findings that children with Down syndrome are relatively unimpaired in the immediate acquisition of new words in experimental contexts, even when tested expressively (Mengoni et al., 2013; Mosse & Jarrold, 2011), with findings from observational studies of slow expressive vocabulary growth in Down syndrome. Thus, it was hypothesised that impairments in the

consolidation of vocabulary in Down syndrome would bridge these disparate findings. However, contrary to expectations, the children with Down syndrome showed identical patterns of consolidation over time to language-matched typically developing children. This was true across all of the learning outcomes. This is an intriguing finding in the context of a vast literature on the memory impairments associated with Down syndrome (Jarrold, Nadel, & Vicari, 2009) and would benefit from further investigation. It is possible that the explicit nature of the training benefitted the children with Down syndrome, who were significantly older than the control group and had had several years of formal education. Future research could investigate whether a more implicit word learning task, such as story book reading, yields a similar pattern of results. However, the current results suggest that long-term consolidation of new language items is not a key underpinning of the language impairment seen in Down syndrome.

In sum, the findings from this thesis suggest that even by the age of four-years-old children with Down syndrome show an uneven language profile, with strengths in receptive vocabulary and weaknesses in expressive language and grammar. The relationships between vocabulary and grammar are atypical at this age in Down syndrome although it is not clear whether they remain atypical across development or follow a pattern more similar to typically developing late talking toddlers. The expressive vocabulary deficit in Down syndrome was replicated across all measures employed in this thesis although there was evidence of a noticeable expressive vocabulary spurt across the study period. Finally, contrary to expectations, there was no evidence that children with Down syndrome have a specific difficulty with consolidating new vocabulary that they have learned across time, suggesting that this does not account for the characteristic language impairment in Down syndrome.

7.3 Relationship Between Health and Cognition in Down Syndrome

A central concern of this thesis was the role that health might play in explaining some of the individual variability in cognitive and adaptive skills found in Chapters 3 and 4. To this end, Chapter 5 looked at the impact of a range of health factors on cognitive and adaptive outcome measures. There was evidence that children with Down syndrome who also had a congenital heart defect had poorer language and overall adaptive behaviour at four-years-old. This is in line with Visootsak, Hess, Bakeman and Adamson (2013) who found that three-year-old children with Down syndrome who also had a congenital heart defect had weaker language skills. However, the study in Chapter 5 found that these

language weaknesses had decreased in size by the age of six years and were no longer significant. There was still a moderate impact on overall adaptive behaviour. Further research would be needed to ascertain why the relationship with language changes over this developmental period. Children who are otherwise developing typically but have a congenital heart defect still show some subtle language and motor impairments compared to peers at eight-years-old (Bellinger et al., 2003). Thus, it is possible that in children with Down syndrome, impairments are still evident later in development but become less pronounced and arguably, larger samples would be required to detect an effect. However, the results from Chapter 5 build on an existing body of research to suggest that having a congenital heart defect puts young pre-school children with Down syndrome at risk of greater language difficulties. As well as raising interesting questions about the interactions between biology and cognition in Down syndrome, this finding is also of interest to practitioners as it highlights a potential risk factor for poor language development.

Chapter 5 also found that childhood hearing difficulties were related to poorer language outcomes in children with Down syndrome. These relationships increased in strength across the course of the longitudinal study. This is in line with Laws and Hall (2014) who found that children with Down syndrome who had a history of early childhood hearing problems also had significantly poorer expressive and receptive language skills in middle childhood. However, this appears to be inconsistent with several previous studies, which have found that concurrent hearing level is unrelated to performance on language tests (e.g. Jarrold & Baddeley, 1997). The hearing difficulties typical of children with Down syndrome are intermittent conductive losses, frequently caused by middle ear infections (Shott et al., 2001). It is possible that hearing level on the day of assessment might not have a strong relationship with performance on language tests but, rather, intermittent hearing losses over time, during childhood, might have an effect. Thus, studies of the language skills of children with Down syndrome should ideally take hearing history into account. Furthermore, it illustrates yet another example of the way that biology and cognition interact in the development of children with Down syndrome.

Sleep problems and measures of hospitalisation frequency were also investigated as possible correlates of cognitive ability. However, there was no strong evidence that either variable was related to performance on cognitive tests. Chapter 5 showed that at T1 of the longitudinal study there were no significant relationships between the length or frequency of hospitalisation and any of the cognitive or adaptive outcomes. It should be

noted that significant relationships with nonverbal ability and parent-reported motor ability at T2 likely reflected the abilities of one child who had spent an unusually long period of time in hospital; it is not possible to have confidence in these findings without a larger-scale replication.

Chapter 5 also failed to find a relationship between parentally reported sleep quality and cognitive and adaptive outcomes. This is, in some ways, inconsistent with previous research that has found a relationship between sleep difficulties in Down syndrome and performance on executive functioning and visuoperceptual tasks (Andreou et al., 2002; Chen et al., 2013). However, the current study did not use specific tasks to tap executive functioning and visuoperceptual skill and also involved a much younger sample. It is possible that these relationships don't emerge until later in development or are very specific to certain cognitive skills. Chapter 6 attempted to address one of these issues by looking at how parentally reported sleep quality related to the consolidation of new vocabulary, a cognitive skill known to depend on sleep. However, there were no consistent relationships between the different sleep domains assessed by the CSHQ questionnaire and performance on the word learning task. Although the failure to find the expected relationships in both studies was plausibly linked to the use of parent-report measures of sleep quality, the study by Chen et al. (2013) also used parent-report measures and yet found a relationship with cognition. However, if the reliability of parent-report were different between children, who may be less able to communicate sleep problems to their parents, and adults with Down syndrome, then this could contribute to the different pattern of results. Further research using polysomnographic measures is needed to determine whether there is a relationship between sleep and cognition in young children with Down syndrome or whether using more objective measures of sleep quality might prove more reliable and informative.

In sum, the findings of this thesis suggest that having a heart defect and a childhood history of hearing difficulties may have a negative impact on language abilities between the ages of four- and six-years-old. However, the impact of heart defects appeared to lessen somewhat over the course of the longitudinal study and there was no strong evidence of a relationship between frequency or length of hospitalisations and cognitive outcomes. Similarly, there was no evidence of a relationship between parentally-reported sleep quality and either broad cognitive abilities in the early years or performance on an experimental vocabulary consolidation task in later childhood and adolescence. Thus,

it seems that some, but not all, aspects of health may show important links with specific cognitive and adaptive outcomes demonstrating that the relationship between health and cognition in Down syndrome is complex and multifaceted.

7.4 Implications for Theory and Practice

Research into cognitive development in Down syndrome has mainly involved observational studies describing the cognitive phenotype. Discussions historically focussed on whether the development at the behavioural level provides evidence for a delayed version of typical development, with delays of different rates in different cognitive domains, or evidence of a disordered pattern of development (e.g. Cleland, Wood, Hardcastle, Wishart, & Timmins, 2010; Fowler, 1990). However, frameworks of atypical development, such as Developmental Causal Modelling (Morton, 2004), are needed to guide developmental theories about disorders. The importance of change over time has also been emphasised (Moore & George, 2011) and neuroconstructivist approaches advocate looking at developmental trajectories of cognitive skills (Thomas et al., 2009) which requires data from longitudinal studies of children within narrow age bands.

The data from this thesis can be viewed from the perspective of each of these frameworks. In relation to questions of delayed versus disordered development, the findings from Chapters 3 and 4 are compatible with the view that while there are largely patterns of delayed typical development, there may be specific skills that show a disordered trajectory (e.g. Cleland et al., 2010). The relationships between language, motor and nonverbal abilities, as broad domains, were similar to those seen in developmentally matched typical controls but there was some tentative evidence of a qualitatively different relationship between the specific areas of grammar and vocabulary.

The results of Chapter 5 can be interpreted within the Developmental Causal Modelling approach to conceptualising cognitive development in Down syndrome. This approach tends to focus on genetic and brain abnormalities at the biological level of explanation but the data from this thesis suggest that health may also be an important consideration. While the relationships between health and cognition appear to be complex, and much more research is needed to clarify these interactions, there was evidence that some health factors may have an impact on cognitive skills and therefore may warrant inclusion in future causal models.

This thesis describes, in detail, the cognitive and adaptive skills of children with Down syndrome at a very specific point in development, which is in line with neuroconstructivist approaches. The results suggest that the cognitive and adaptive profile of skills associated with Down syndrome has already largely emerged by the age of four-years-old. However, there was variability in how consistently this profile was expressed at the individual level. In line with this, questions have been raised by proponents of neuroconstructivism about the validity of conceptualising disorders as a static and fixed profile of cognitive strengths and weaknesses. There was also evidence that the period of development investigated in the longitudinal study was a particularly important time for expressive vocabulary growth. Such a finding can inform developmental trajectory approaches to modelling cognition in Down syndrome, which are a key part of the neuroconstructivist approach to disorders.

There were also several implications for education and health practitioners working with children with Down syndrome. First, understanding how early the cognitive phenotype emerges but yet simultaneously recognising that this profile will not characterise all children could inform approaches to educational assessment. Second, the evidence supporting the predictive validity of some parent-report measures of language in young children with Down syndrome could guide the selection of assessment tools, particularly in situations where the reliability of objective language tests may be questionable. Third, the impact of heart defects and childhood hearing difficulties on language outcomes highlights factors that could put children at high risk of language difficulties and thus could help target early interventions for children who can benefit the most from them. Furthermore, the links between health and cognition suggest that there could be benefit to service users if practitioners in the health and education sectors communicate and work closely with each other. Finally, Chapter 6 outlines a methodology through which children with Down syndrome can learn new vocabulary items and remember them over time, which could be of potential use to those designing effective language interventions for children with Down syndrome.

7.5 Limitations and Future Directions

The primary limitation of the central longitudinal study is its relatively small sample size, a common concern in much of the literature on developmental disorders. While the size of the sample is consistent with previous similar studies (e.g. Fidler et al., 2006), it constrains statistical analyses and places caveats on the conclusions drawn from the study.

The research field would benefit from future large-scale longitudinal studies where the data can be subjected to growth curve modelling and trajectory analyses. However, there are challenges inherent with recruiting clinical samples and this approach is likely to require collaboration across researchers and institutions. As the size of the sample precluded more sophisticated statistical analyses, the cognitive phenotype had to be determined through comparisons with a nonverbal-age-matched control group. The concerns with this approach have been well documented (see section 1.4.1) and, although measures were taken to ensure that the typically developing group were typical in their cognitive performance, their educational backgrounds were not representative of the general population of the same age and could have affected the group comparisons. However, much of the data in this thesis were derived from the group with Down syndrome alone and comparisons with the typically developing group were primarily relevant for determining the cognitive and adaptive profile, which was in line with all previous research, supporting the validity of the profile findings.

Another possible limitation of the research presented in this thesis is the selection of assessment measures. As the specific nature of the cognitive phenotype was of particular interest, cognitive tests from different assessment batteries were included to ensure that all of the cognitive skills of interest were represented in the assessment (e.g. receptive vocabulary, expressive vocabulary, grammatical skill etc.). However, there were challenges inherent in comparing the scores on these different tests to make within-profile contrasts. If the specific research aims allow, future research would benefit from using sub-tests that belong to the same assessment tool so that within-profile comparisons can be made more readily and confidently. Furthermore, while health information is often collected through parental-report in research studies (e.g. Schieve, Boulet, Kogan, Van Naarden-Braun, & Boyle, 2011), information from medical records could provide complementary information and help validate parental interviews. Although it was not possible to access such information for the current study, future research using both methods to gain a detailed health history for participating children would strengthen findings. Finally, given that this thesis failed to find a relationship between cognition and parentally reported sleep quality, future research using objective polysomnographic measures could address whether these findings were a result of the limitations of parent-report or reflect the true absence of a relationship.

The results of this thesis raise many interesting questions for future research. The nature of the relationship between grammar and vocabulary across development was particularly intriguing. Research tracing these interactions in the next stage of development would help answer questions about whether they develop in a delayed or disordered fashion. Expressive vocabulary development in Down syndrome also warrants further study. Although the current findings suggest that expressive language undergoes a noticeable improvement between the ages of four- and six-years-old in Down syndrome, it is not possible to determine whether this is due to intrinsic developmental factors or extrinsic factors such as the start of formal schooling. This would be an interesting question for future research. This thesis provides some indication that health and cognition may interact in some way during development in Down syndrome. This paves the way for a larger epidemiological study to confirm and extend such findings, which would inform both practitioners and theoretical models of Down syndrome.

7.6 Conclusion

This thesis explored the development of cognition, language and adaptive behaviour in four- to six-year-old children with Down syndrome and investigated the role of health in determining outcomes. The findings of a fifteen-month longitudinal study suggested that the cognitive, language and adaptive phenotype had largely emerged in children with Down syndrome as young as four-years-old, although there was a large degree of individual variability in the expression of this profile. In most areas, development between the ages of four- and six-years-old largely followed a delayed typical course rather than a disordered pattern. The only exception was the development of vocabulary and grammar skills, which did show some evidence of atypicality. In the prediction of later language ability, there was evidence that objective tests and parent-report measures of language can be used relatively interchangeably. In terms of the language profile in Down syndrome, there was evidence of an expressive vocabulary spurt over the course of the longitudinal study. An experimental training study investigating vocabulary consolidation failed to find evidence of a consolidation impairment, suggesting that this is not a critical underpinning of the language difficulties in Down syndrome. Finally, there was evidence that congenital heart defects and childhood hearing difficulties were related to poorer language outcomes but no relationships were found between sleep problems and cognition, either in terms of broad cognitive outcomes or performance on a vocabulary consolidation task. However, these findings still suggest that the interactions between

health and cognition may be important considerations in developmental models of Down syndrome and future research delineating the relationship would be of interest.

Appendix 1.

Intercorrelations between the Vineland-II subscales and the adapted OCDI

Correlations between the parent-report measures at T1. Correlations for the group with Down syndrome are above the diagonal and for the typically developing children are below the diagonal.

	V-II Communication	V-II Receptive	V-II Expressive	**V-II Daily Living**	**V-II Social**	**V-II Motor**	V-II Gross	V-II Fine	OCDI: words + signs	OCDI: words	OCDI: receptive
Communication	1	.583**	.955**	.384	.577**	.364	.121	.551**	.493*	.562*	.568*
Receptive	.874**	1	.345	.389	.573**	.391	.067	.673**	.326	.158	.598**
Expressive	.990**	.821**	1	.309	.471*	.274	.115	.385	.442	.625**	.447
Daily Living	.679**	.521*	.650**	1	.653**	.785**	.610**	.739**	.368	.270	.501*
Social	.470*	.505*	.490*	.135	1	.669**	.407	.775**	.251	.129	.550*
Motor	.654**	.631**	.633**	.522*	.522*	1	.886**	.802**	.446	.385	.540*
Gross	.599**	.532*	.605**	.573**	.573**	.882**	1	.433*	.330	.344	.371
Fine	.491*	.533*	.443*	.270	.270	.795**	.415	1	.454	.317	.587*
OCDI: w + s	.703**	.669**	.698**	.538**	.197	.318	.242	.302	1	.829**	.828**
OCDI: words	.703**	.669**	.698**	.538**	.197	.318	.242	.302	1	1	.528*
OCDI: receptive	.684**	.610**	.685**	.485*	.154	.338	.212	.379	.860**	.860**	1

Correlations between the parent-report measures at T2. Correlations for the group with Down syndrome are above the diagonal and for the typically developing children are below the diagonal.

	V-II Communication	V-II Receptive	V-II Expressive	**V-II Daily Living**	**V-II Social**	**V-II Motor**	V-II Gross	V-II Fine	OCDI: words + signs	OCDI: words	OCDI: receptive
Communication	1	.731**	.966**	.430	.533*	.634**	.311	.765**	.841**	.814**	.682**
Receptive	.872**	1	.626**	.380	.519*	.516*	.178	.679**	.538*	.367	.589*
Expressive	.881**	.742**	1	.370	.450*	.538*	.245	.664**	.849**	.850**	.672**
Daily Living	.722**	.646**	.549**	1	.620**	.826**	.725**	.755**	.357	.435	.193
Social	.531*	.599**	.526*	.524*	1	.674**	.571**	.633**	.139	.052	.209
Motor	.603**	.541**	.356	.690**	.308	1	.864**	.925**	.506	.590*	.290
Gross	.428*	.407	.189	.518*	.228	.770**	1	.608**	.128	.300	-.134
Fine	.553**	.479*	.376	.611**	.276	.871**	.358	1	.690**	.688**	.557*
OCDI: w+s	-.288	-.290	-.315	-.030	-.155	-.071	-.151	.001	1	.920**	.875**
OCDI: words	-.288	-.290	-.315	-.030	-.155	-.071	-.151	.001	1	1	.646**
OCDI: receptive	-.329	-.294	-.354	-.039	-.121	-.147	-.191	-.081	.981**	.981**	1

Appendix 2

Correlations between the parent-report measures from Chapter 4 and objective measures from Chapter 3 in the typically developing group

Concurrent correlations at T1:

	V-II Communication	V-II Receptive	V-II Expressive	**V-II Daily Living**	**V-II Social**	**V-II Motor**	V-II Gross	V-II Fine	OCDI words + signs	OCDI words	OCDI receptive
Mental age	.226	.249	.231	-.097	.107	.099	.072	.098	.348	.348	.439*
Object Assembly	.038	.226	.003	-.022	.240	.388	.207	.482*	.103	.103	.134
Receptive Vocabulary	.715**	.627**	.723**	.292	.469*	.544**	.401	.533*	.474*	.474*	.475*
Basic Concepts	.826**	.737**	.795**	.454*	.504*	.618**	.560**	.472*	.484*	.484*	.548**
Expressive Vocabulary	.816**	.773**	.799**	.431*	.490*	.688**	.619**	.532*	.424*	.424*	.459*
Nonword Repetition	.759**	.662**	.760**	.409	.522*	.522*	.579*	.282	.503*	.503*	.589*
Coin Posting	-.245	-.064	-.274	-.014	-.059	-.243	-.344	-.027	.051	.051	-.162
Bike Trails	-.179	-.163	-.162	-.373	-.034	-.503*	-.380	-.496*	-.221	-.221	-.185
Nonverbal composite	.172	.310	.152	-.077	.226	.317	.182	.378	.294	.294	.374
Language composite	.886**	.789**	.874**	.461*	.536*	.674**	.608**	.519*	.533*	.533*	.583**
Vocabulary composite	.828**	.757**	.824**	.391	.519*	.667**	.552**	.576**	.486*	.486*	.506*
Grammar composite	.826**	.737**	.795**	.454*	.504*	.618**	.560**	.472*	.484*	.484*	.548**
Motor composite	-.245	-.064	-.274	-.014	-.059	-.243	-.344	-.027	.051	.051	-.162

Concurrent correlations at T2:

	V-II Communication	V-II Receptive	V-II Expressive	**V-II Daily Living**	**V-II Social**	**V-II Motor**	V-II Gross	V-II Fine	OCDI: words + signs	OCDI: words	OCDI: receptive
Mental Age	.320	.301	.225	.553**	.071	.519*	.202	.604**	-.156	-.156	-.216
Object Assembly	.505*	.394	.440*	.402	.280	.320	.138	.363	.091	.091	.134
Block Design	.350	.196	.280	.314	-.053	.510*	.156	.626**	-.049	-.049	-.134
Receptive Vocab	.171	.106	-.014	.216	.154	.099	.274	-.067	-.230	-.230	-.230
Basic Concepts	.364	.211	.151	.290	-.036	.382	.417	.238	-.348	-.348	-.337
Sentence Structure	.050	.020	-.101	.361	.021	.346	.535*	.094	-.033	-.033	.023
Expressive Vocab	.487*	.419	.370	.575**	.166	.422	.322	.370	-.241	-.241	-.247
Nonword repetition	.566**	.662**	.508*	.342	.285	.323	.291	.243	-.320	-.320	-.359
Posting Coins	-.378	-.245	-.275	-.619**	-.470*	-.451*	-.379	-.369	.212	.212	.241
Bike Trails	-.536*	-.482*	-.465*	-.652**	-.216	-.455*	-.276	-.453*	.143	.143	.176
Nonverbal composite	.500*	.379	.403	.541**	.127	.574**	.211	.678**	-.052	-.052	-.100
Language composite	.457*	.389	.247	.515*	.140	.430*	.515*	.233	-.378	-.378	-.368
Vocabulary composite	.392	.313	.212	.471*	.190	.310	.355	.181	-.311	-.311	-.315
Grammar composite	.244	.136	.030	.385	-.009	.430*	.562**	.196	-.257	-.257	-.220
Motor composite	-.554**	-.441*	-.449*	-.771**	-.416	-.549**	-.397	-.499*	.215	.215	.253

Correlations between parent-report measures at T1 and objective measures at T2:

	V-II Communication	V-II Receptive	V-II Expressive	**V-II Daily Living**	**V-II Social**	**V-II Motor**	V-II Gross	V-II Fine	OCDI: words + signs	OCDI: words	OCDI: receptive
Mental Age	.173	.330	.142	-.074	.307	.233	.045	.391	.318	.318	.367
Object Assembly	.060	.220	.072	-.095	.339	.318	.328	.192	-.075	-.075	-.073
Block Design	-.002	.217	-.037	-.107	.172	.178	.040	.292	.236	.236	.233
Receptive Vocabulary	.259	.188	.276	-.235	.026	.060	.069	.026	.108	.108	.180
Basic Concepts	.260	.226	.247	-.135	.127	.168	.185	.087	.103	.103	.132
Sentence Structure	.023	-.013	.008	-.076	.046	.144	.075	.182	-.005	-.005	.112
Expressive Vocabulary	.541**	.470*	.530*	.280	.151	.477*	.387	.422	.302	.302	.378
Nonword Repetition	.786**	.752**	.761**	.517*	.255	.543*	.506*	.369	.467*	.467*	.397
Coin Posting	-.149	-.093	-.170	-.156	-.514*	-.373	-.426*	-.171	-.154	-.154	-.284
Bike Trails	-.349	-.343	-.340	-.285	-.402	-.243	-.172	-.248	-.381	-.381	-.308
Nonverbal Composite	.099	.327	.076	-.118	.348	.310	.176	.373	.204	.204	.224
Language Composite	.534*	.452*	.521*	.095	.156	.376	.329	.303	.272	.272	.342
Vocabulary Composite	.476*	.392	.480*	.027	.105	.320	.272	.267	.244	.244	.333
Grammar Composite	.167	.126	.151	-.125	.102	.185	.153	.159	.057	.057	.144
Motor Composite	-.302	-.265	-.310	-.267	-.556**	-.374	-.363	-.254	-.325	-.325	-.359

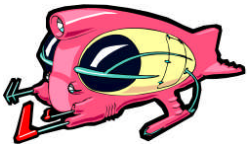
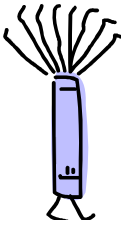
Appendix 3

Linear regression analyses showing the prediction of T2 objective outcomes from the T1 objective and parent-report measures in the typically developing group

Outcome	Predictor	R^2	F	β	*p*
T2 language composite	T1 language composite	.54	23.48	.74	<.001
	T1 Vineland Communication	.29	7.98	.53	.010
T2 vocabulary composite	T1 vocabulary composite	.55	24.85	.74	<.001
	T1 Vineland Communication	.23	5.86	.48	.025
	T1 OCDI composite	.08	1.73	.28	.203
T2 grammar composite	T1 grammar composite	.20	5.04	.45	.036
	T1 Vineland Communication	.03	.58	.17	.457

Appendix 4

The novel words and associated pictures used in Chapter 6

Novel word target	Pictures and descriptions paired with novel words	Distracter in the receptive phonology task (initial phoneme changed)	Distracter in the receptive phonology task (final phoneme changed)
Mav	 A mav lives in the alien jungle	Nav	Maf
Zem	 A zem goes under the water	Vem	Zen
Vot	 A vot stores the alien cars	Thot	Vod
Nep	 A nep is used for grinding moondust	Mep	Neb
Tus	 A tus is used for cooking alien food	Dus	Tuth
Pid	 A pid likes to tickle other aliens	Tid	Pib

Appendix 5

Planetary context used throughout the familiarisation phase in the novel word training procedure in Chapter 6

References

Abbeduto, L., Murphy, M. M., Cawthon, S. W., Richmond, E. K., Weissman, M. D., Karadottir, S., & O'Brien, A. (2003). Receptive language skills of adolescents and young adults with Down or Fragile X syndrome. *American Journal of Mental Retardation*, *108*(3), 149–60. doi:10.1352/0895-8017(2003)108<0149:RLSOAA>2.0.CO;2

Abbeduto, L., Warren, S. F., & Conners, F. A. (2007). Language development in Down syndrome: from the prelinguistic period to the acquisition of literacy. *Mental Retardation and Developmental Disabilities Research Reviews*, *261*, 247–261. doi:10.1002/mrdd

Anders, Y., Sammons, P., Taggart, B., Sylva, K., Melhuish, E., & Siraj-Blatchford, I. (2011). The influence of child, family, home factors and pre-school education on the identification of special educational needs at age 10. *British Educational Research Journal*, *37*(3), 421–441. doi:10.1080/01411921003725338

Andreou, G., Galanopoulou, C., Gourgoulianis, K., Karapetsas, A., & Molyvdas, P. (2002). Cognitive status in Down syndrome individuals with sleep disordered breathing deficits (SDB). *Brain and Cognition*, *50*(1), 145–9. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12372360

Ashworth, A., Hill, C. M., Karmiloff-Smith, A., & Dimitriou, D. (2013). Cross syndrome comparison of sleep problems in children with Down syndrome and Williams syndrome. *Research in Developmental Disabilities*, *34*(5), 1572–1580. doi:10.1016/j.ridd.2013.01.031

Aylward, E. H., Li, Q., Honeycutt, N. A., Warren, A. C., Pulsifer, M. B., Barta, P. E., … Pearlson, G. D. (1999). MRI Volumes of the hippocampus and amygdala in adults with Down's syndrome with and without dementia. *American Journal of Psychiatry*, *156*(4), 564–568.

Backhaus, J., Hoeckesfeld, R., Born, J., Hohagen, F., & Junghanns, K. (2008). Immediate as well as delayed post learning sleep but not wakefulness enhances declarative memory consolidation in children. *Neurobiology of Learning and Memory*, *89*(1), 76–80. doi:10.1016/j.nlm.2007.08.010

Backhaus, J., Junghanns, K., Born, J., Hohaus, K., Faasch, F., & Hohagen, F. (2006). Impaired declarative memory consolidation during sleep in patients with primary insomnia: Influence of sleep architecture and nocturnal cortisol release. *Biological Psychiatry*, *60*(12), 1324–30. doi:10.1016/j.biopsych.2006.03.051

Balboni, G., Pedrabissi, L., Molteni, M., & Villa, S. (2001). Discriminant validity of the Vineland scales: Score profiles of individuals with mental retardation and a specific disorder. *American Journal of Mental Retardation*, *106*(2), 162–172.

Barnes, E. F., Roberts, J., Mirrett, P., Sideris, J., & Misenheimer, J. (2006). A comparison of oral structure and oral-motor function in young males with fragile X syndrome and Down syndrome. *Journal of Speech, Language, and Hearing Research*, *49*(4), 903–17. doi:10.1044/1092-4388(2006/065)

Bates, E., & Goodman, J. C. (1997). On the inseparability of grammar and the lexicon: Evidence from acquisition, aphasia and real-time processing. *Language and Cognitive Processes*, *12*(5-6), 507–584. doi:10.1080/016909697386628

Bates, E., & Goodman, J. C. (2001). On the inseparability of grammar and the lexicon: Evidence from acquisition. In M. Tomasello & E. Bates (Eds.), *Language Development: The Essential Readings* (pp. 134–162). Oxford: Blackwell Publishers Ltd.

Beebe, D. W., Groesz, L., Wells, C., Nichols, A., & Mcgee, K. (2003). The neuropsychological effects of obstructive sleep apnea: a meta-analysis of norm-referenced and case-controlled data. *Sleep*, *26*(3), 298–307.

Bellinger, D. C., Wypij, D., duPlessis, A. J., Rappaport, L. a, Jonas, R. a, Wernovsky, G., & Newburger, J. W. (2003). Neurodevelopmental status at eight years in children with dextro-transposition of the great arteries: The Boston Circulatory Arrest Trial. *The Journal of Thoracic and Cardiovascular Surgery*, *126*(5), 1385–1396. doi:10.1016/S0022-5223(03)00711-6

Berglund, E., Eriksson, M., & Johansson, I. (2001). Parental reports of spoken language skills in children with Down syndrome. *Journal of Speech, Language and Hearing Research*, *44*, 179–192. doi:1092-4388/ 01/ 4401-0179

Bishop, D. V. M. (2006). What causes specific language impairment in children? *Current Directions in Psychological Science*, *15*(5), 217–221. doi:10.1111/j.1467-8721.2006.00439.x

Bishop, D. V. (1997). Cognitive neuropsychology and developmental disorders: uncomfortable bedfellows. *Quarterly Journal of Experimental Psychology.*, *50*(4), 899–923. doi:10.1080/713755740

Blunden, S., & Beebe, D. W. (2006). The contribution of intermittent hypoxia, sleep debt and sleep disruption to daytime performance deficits in children: consideration of respiratory and non-respiratory sleep disorders. *Sleep Medicine Reviews*, *10*(2), 109–18. doi:10.1016/j.smrv.2005.11.003

Blunden, S., Lushington, K., Kennedy, D., Martin, J., & Dawson, D. (2000). Behavior and neurocognitive performance in children aged 5-10 years who snore compared to controls. *Journal of Clinical and Experimental Neuropsychology*, *22*(5), 554–568. doi:1380-3395/00/2205-554

Boudreau, D. (2002). Literacy skills in children and adolescents with Down syndrome. *Reading and Writing*, *15*, 497–525.

Boulet, S. L., Schieve, L. A., & Boyle, C. A. (2011). Birth weight and health and developmental outcomes in US children, 1997-2005. *Maternal and Child Health Journal*, *15*(7), 836–44. doi:10.1007/s10995-009-0538-2

Breslin, J. H., Edgin, J. O., Bootzin, R. R., Goodwin, J. L., & Nadel, L. (2011). Parental report of sleep problems in Down syndrome. *Journal of Intellectual Disability Research*, *55*(11), 1086–91. doi:10.1111/j.1365-2788.2011.01435.x

Breslin, J., Spanò, G., Bootzin, R., Anand, P., Nadel, L., & Edgin, J. (2014). Obstructive sleep apnea syndrome and cognition in Down syndrome. *Developmental Medicine and Child Neurology*, *56*, 657–664. doi:10.1111/dmcn.12376

Brock, J., & Jarrold, C. (2005). Serial order reconstruction in Down syndrome: evidence for a selective deficit in verbal short-term memory. *Journal of Child Psychology and Psychiatry*, *46*(3), 304–16. doi:10.1111/j.1469-7610.2004.00352.x

Brooks, L. J., Olsen, M. N., Bacevice, A. M., Beebe, A., Konstantinopoulou, S., & Taylor, H. G. (2014). Relationship between sleep, sleep apnea, and neuropsychological function in children with Down syndrome. *Sleep and Breathing*, 1–8. doi:10.1007/s11325-014-0992-y

Brown, H., Weighall, A., Henderson, L. M., & Gaskell, G. M. (2012). Enhanced recognition and recall of new words in 7- and 12-year-olds following a period of offline consolidation. *Journal of Experimental Child Psychology*, *112*(1), 56–72. doi:10.1016/j.jecp.2011.11.010

Brownell, R. (2000a). *Expressive One-Word Picture Vocabulary Test*. Novato, CA: Academic Therapy Publications.

Brownell, R. (2000b). *Receptive One-Word Picture Vocabulary Test - Second Edition*. Novato, CA: Academic Therapy Publications.

Byrne, A., MacDonald, J., & Buckley, S. (2002). Reading, language and memory skills: a comparative longitudinal study of children with Down syndrome and their mainstream peers. *The British Journal of Educational Psychology*, *72*, 513–29. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12495564

Cairns, P., & Jarrold, C. (2005). Exploring the correlates of impaired non-word repetition in Down syndrome. *British Journal of Developmental Psychology*, *23*(3), 401–416. doi:10.1348/026151005X26813

Can, D. D., Ginsburg-Block, M., Golinkoff, R. M., & Hirsh-Pasek, K. (2013). A long-term predictive validity study: can the CDI Short Form be used to predict language and early literacy skills four years later? *Journal of Child Language*, *40*(4), 821–35. doi:10.1017/S030500091200030X

Carducci, F., Onorati, P., Condoluci, C., Di Gennaro, G., Quarato, P. P., Pierallini, A., … Albertini, G. (2013). Whole-brain voxel-based morphometry study of children and adolescents with Down syndrome. *Functional Neurology*, *28*(1), 19–28.

Carey, S., & Bartlett, E. (1978). Acquiring a single new word. *Papers and Reports on Child Language Development*, *15*, 17–29.

Carlesimo, G. A., Marotta, L., & Vicari, S. (1997). Long-term memory in mental retardation: Evidence for a specific impairment in subjects with Down's syndrome. *Neuropsychologia*, *35*(1), 60–68. doi:S0028-3932(96)00055-3

Carr, J. (1992). Longitudinal research in Down syndrome. *International Review of Research in Mental Retardation*, *18*, 197–223.

Carter, M., McCaughey, E., Annaz, D., & Hill, C. M. (2009). Sleep problems in a Down syndrome population. *Archives of Disease in Childhood*, *94*(4), 308–10. doi:10.1136/adc.2008.146845

Caselli, M. C., Monaco, L., Trasciani, M., & Vicari, S. (2008). Language in Italian children with Down syndrome and with specific language impairment. *Neuropsychology*, *22*(1), 27–35. doi:10.1037/0894-4105.22.1.27

Caselli, M. C., Vicari, S., Longobardi, E., Lami, L., Pizzoli, C., & Stella, G. (1998). Gestures and words in early development of children with Down syndrome. *Journal of Speech, Language and Hearing Research*, *41*, 1125–1135. doi:1092-4388/98/4105-1125

Cebula, K. R., Moore, D. G., & Wishart, J. G. (2010). Social cognition in children with Down's syndrome: challenges to research and theory building. *Journal of Intellectual Disability Research*, *54*(2), 113–34. doi:10.1111/j.1365-2788.2009.01215.x

Chapman, R. S. (1995). Language development in children and adolescents with Down syndrome. In P. Fletcher & B. MacWhinney (Eds.), *Handbook of Child Language* (pp. 641–663). Oxford: Blackwell Publishing.

Chapman, R. S. (2006). Language learning in Down syndrome: the speech and language profile compared to adolescents with cognitive impairment of unknown origin. *Down's Syndrome, Research and Practice*, *10*, 61–6. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16869363

Chapman, R. S., & Hesketh, L. J. (2000). Behavioural phenotype of individuals with Down syndrome. *Mental Retardation and Developmental Disabilities Research Reviews*, *6*, 84–95.

Chapman, R. S., Hesketh, L. J., & Kistler, D. J. (2002). Predicting longitudinal change in language production and comprehension in individuals with Down syndrome: hierarchical linear modeling. *Journal of Speech, Language and Hearing Research*, *45*, 902–915. doi:1092-4388/02/4505-0902

Chapman, R. S., Kay-Raining Bird, E., & Schwartz, S. E. (1990). Fast mapping of words in event contexts by children with Down syndrome. *Journal of Speech and Hearing Disorders*, *55*(4), 761–70. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/2146444

Chapman, R. S., Schwartz, S. E., & Bird, E. K. (1991). Language skills of children and adolescents with Down syndrome: I. Comprehension. *Journal of Speech, Language and Hearing Research*, *34*(5), 1106–20. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1836243

Chapman, R. S., Seung, H., Schwartz, S. E., & Bird, E. K. (1998). Language skills of children and adolescents with Down syndrome: II. Production deficits. *Journal of Speech, Language and Hearing Research*, *41*, 861–873. doi:1092-4388/98/4104-0861

Chapman, R. S., Seung, H., Schwartz, S. E., & Kay-Raining Bird, E. (2000). Predicting language production in children and adolescents with Down syndrome: the role of comprehension. *Journal of Speech, Language and Hearing Research*, *43*, 340–350. doi:1092-4388/00/4302-0340

Chapman, R. S., Sindberg, H., Bridge, C., Gigstead, K., & Hesketh, L. (2006). Effect of memory support and elicited production on fast mapping of new words by adolescents with Down Syndrome. *Journal of Speech, Language and Hearing Research*, *49*, 3–16. doi:1092-4388/06/4901-0003

Chen, C.-C. J., Spanò, G., & Edgin, J. O. (2013). The impact of sleep disruption on executive function in Down syndrome. *Research in Developmental Disabilities*, *34*(6), 2033–2039. doi:10.1016/j.ridd.2013.03.009

Childers, J. B., & Tomasello, M. (2002). Two-year-olds learn novel nouns, verbs, and conventional actions from massed or distributed exposures. *Developmental Psychology*, *38*(6), 967–978. doi:10.1037//0012-1649.38.6.967

Cleland, J., Wood, S., Hardcastle, W., Wishart, J., & Timmins, C. (2010). Relationship between speech, oromotor, language and cognitive abilities in children with Down's syndrome. *International Journal of Language & Communication Disorders*, *45*(1), 83–95. doi:10.3109/13682820902745453

Clibbens, J. (2001). Signing and lexical development in children with Down syndrome. *Down Syndrome Research and Practice*, *7*(3), 101–5. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11721535

Connolly, B. H., & Michael, B. T. (1986). Performance of retarded children, with and without Down syndrome, on the Bruininks Oseretsky Test of Motor Proficiency. *Physical Therapy*, *66*(3), 344–8. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/2937069

Contestabile, A., Benfenati, F., & Gasparini, L. (2010). Communication breaks-Down: from neurodevelopment defects to cognitive disabilities in Down syndrome. *Progress in Neurobiology*, *91*(1), 1–22. doi:10.1016/j.pneurobio.2010.01.003

Couzens, D., Haynes, M., & Cuskelly, M. (2012). Individual and environmental characteristics associated with cognitive development in Down syndrome: a longitudinal study. *Journal of Applied Research in Intellectual Disabilities*, *25*(5), 396–413. doi:10.1111/j.1468-3148.2011.00673.x

Cupples, L., & Iacono, T. (2000). Phonological awareness and oral reading skill in children with Down syndrome. *Journal of Speech, Language, and Hearing Research*, *43*(3), 595–608. doi:10.1044/jslhr.4303.595

Dale, P. S., Dionne, G., Eley, T. C., & Plomin, R. (2000). Lexical and grammatical development : a behavioural genetic perspective. *Journal of Child Language*, *27*, 619–642.

Davis, M. H., Di Betta, A. M., Macdonald, M. J. E., & Gaskell, M. G. (2009). Learning and consolidation of novel spoken words. *Journal of Cognitive Neuroscience*, *21*(4), 803–20. doi:10.1162/jocn.2009.21059

De Bildt, A., Kraijer, D., Sytema, S., & Minderaa, R. (2005). The psychometric properties of the Vineland Adaptive Behavior Scales in children and adolescents with mental

retardation. *Journal of Autism and Developmental Disorders*, *35*(1), 53–62. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15796122

Deb, S., Hare, M., & Prior, L. (2007). Symptoms of dementia among adults with Down's syndrome: a qualitative study. *Journal of Intellectual Disability Research*, *51*, 726–39. doi:10.1111/j.1365-2788.2007.00956.x

Di Nuovo, S., & Buono, S. (2011). Behavioral phenotypes of genetic syndromes with intellectual disability: comparison of adaptive profiles. *Psychiatry Research*, *189*(3), 440–5. doi:10.1016/j.psychres.2011.03.015

Diamond, A. (2000). Close interrelation of motor development and cognitive development and of the cerebellum and prefrontal cortex. *Child Development*, *71*(1), 44–56. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10836557

Diekelmann, S., Wilhelm, I., & Born, J. (2009). The whats and whens of sleep-dependent memory consolidation. *Sleep Medicine Reviews*, *13*(5), 309–21. doi:10.1016/j.smrv.2008.08.002

Dionne, G., Dale, P. S., Boivin, M., & Plomin, R. (2003). Genetic evidence for bidirectional effects of early lexical and grammatical development. *Child Development*, *74*(2), 394–412. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12705562

Dockrell, J. E., Braisby, N., & Best, R. M. (2007). Children's acquisition of science terms: Simple exposure is insufficient. *Learning and Instruction*, *17*(6), 577–594. doi:10.1016/j.learninstruc.2007.09.005

Dodd, B., Holm, A., Hua, Z., & Crosbie, S. (2003). Phonological development: a normative study of British English-speaking children. *Clinical Linguistics & Phonetics*, *17*(8), 617–643. doi:10.1080/0269920031000111348

Dolva, A.-S., Coster, W., & Lilja, M. (2004). Functional performance in children with Down syndrome. *The American Journal of Occupational Therapy*, *58*(6), 621–9. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15568546

Down Syndrome Medical Interest Group. (2011). *Schedule of health checks*. Retrieved from http://www.dsmig.org.uk/publications/pchrhealthchk.html

Dressler, A., Perelli, V., Feucht, M., & Bargagna, S. (2010). Adaptive behaviour in Down syndrome: a cross-sectional study from childhood to adulthood. *Wiener Klinische Wochenschrift*, *122*(23-24), 673–80. doi:10.1007/s00508-010-1504-0

Dumay, N., & Gaskell, M. G. (2007). Sleep-associated changes in the mental representation of spoken words. *Psychological Science*, *18*(1), 35–9. doi:10.1111/j.1467-9280.2007.01845.x

Dykens, E., Hodapp, R., & Evans, D. (2006). Profiles and development of adaptive behavior in children with Down syndrome. *Down Syndrome Research and Practice*, *9*(3), 45–50. doi:10.3104/reprints.293

Eadie, P. A., Fey, M. E., Douglas, J. M., & Parsons, C. L. (2002). Profiles of grammatical morphology and sentence imitation in children with specific language impairment and Down syndrome. *Journal of Speech, Language and Hearing Research*, *45*, 720–732. doi:1092-4388/02/4504-0720

Ellenbogen, J. M., Payne, J. D., & Stickgold, R. (2006). The role of sleep in declarative memory consolidation: passive, permissive, active or none? *Current Opinion in Neurobiology*, *16*(6), 716–22. doi:10.1016/j.conb.2006.10.006

Estigarribia, B., Martin, G. E., & Roberts, J. E. (2012). Cognitive, environmental, and linguistic predictors of syntax in fragile X syndrome and Down syndrome. *Journal of Speech, Language, and Hearing Research*, *55*(6), 1600–12. doi:10.1044/1092-4388(2012/10-0153)

Facon, B., Magis, D., & Belmont, J. M. (2011). Beyond matching on the mean in developmental disabilities research. *Research in Developmental Disabilities*, *32*(6), 2134–47. doi:10.1016/j.ridd.2011.07.029

Farrell, A. D. (1994). Structural equation modeling with longitudinal data: Strategies for examining group differences and reciprocal relationships. *Journal of Consulting & Clinical Psychology*, *62*(3), 477–487. doi:0022-006X/94

Feldman, H. M., Dale, P. S., Campbell, T. F., Colborn, D. K., Kurs-Lasky, M., Rockette, H. E., & Paradise, J. L. (2005). Concurrent and predictive validity of parent reports of child

language at ages 2 and 3 years. *Child Development*, *76*(4), 856–68. doi:10.1111/j.1467-8624.2005.00882.x

Fenn, K. M., Nusbaum, H. C., & Margoliash, D. (2003). Consolidation during sleep of perceptual learning of spoken language. *Nature*, *425*, 614–616. doi:10.1038/nature01971.1.

Fenson, L., Dale, P., Reznick, S., Thal, D., Bates, E., Hartung, J., … Reilly, J. (1993). *MacArthur Communicative Development Inventories*. San Diego, CA: Singular.

Fidler, D. J., Hepburn, S., & Rogers, S. (2006). Early learning and adaptive behaviour in toddlers with Down syndrome: evidence for an emerging behavioural phenotype? *Down's Syndrome Research and Practice*, *9*(3), 37–44. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16869373

Fidler, D. J., Most, D. E., & Guiberson, M. M. (2005). Neuropsychological correlates of word identification in Down syndrome. *Research in Developmental Disabilities*, *26*(5), 487–501. doi:10.1016/j.ridd.2004.11.007

Fidler, D. J., & Nadel, L. (2007). Education and children with Down syndrome: Neuroscience, development and intervention. *Human Development*, *271*, 262–271. doi:10.1002/mrdd

Fisher, S. E. (2006). Tangled webs: tracing the connections between genes and cognition. *Cognition*, *101*(2), 270–97. doi:10.1016/j.cognition.2006.04.004

Fitzgerald, D. a, Paul, A., & Richmond, C. (2007). Severity of obstructive apnoea in children with Down syndrome who snore. *Archives of Disease in Childhood*, *92*(5), 423–5. doi:10.1136/adc.2006.111591

Fowler, A. E. (1988). Determinants of rate of language growth in children with Down syndrome. In L. Nadel (Ed.), *The Psychobiology of Down Syndrome* (pp. 217–245). Cambridge, MA: MIT Press.

Fowler, A. E. (1990). Language abilities in children with Down syndrome: Evidence for a specific syntactic delay. In D. Cicchetti & M. Beeghly (Eds.), *Children with Down syndrome: A developmental perspective* (pp. 302–328). Cambridge University Press.

Fowler, A. E. (1998). The challenge of linguistic mastery in Down syndrome. In T. J. Hassold & D. Patterson (Eds.), *Down Syndrome: A Promising Future, Together* (pp. 165–182). Wiley-Liss.

Freeman, S. B., Taft, L. F., Dooley, K. J., Allran, K., Sherman, S. L., Hassold, T. J., … Saker, D. M. (1998). Population-based study of congenital heart defects in Down syndrome. *American Journal of Medical Genetics*, *80*(3), 213–7. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9843040

Gäddlin, P.-O., Finnström, O., Hellgren, K., & Leijon, I. (2007). Hospital readmissions and morbidity in a fifteen-year follow-up of very low birthweight children in Southeast Sweden. *Acta Paediatrica*, *96*(4), 499–505. doi:10.1111/j.1651-2227.2007.00183.x

Gais, S., & Born, J. (2004). Declarative memory consolidation: mechanisms acting during human sleep. *Learning & Memory*, *11*(6), 679–85. doi:10.1101/lm.80504

Galeote, M., Sebastián, E., Checa, E., Rey, R., & Soto, P. (2011). The development of vocabulary in Spanish children with Down syndrome: comprehension, production, and gestures. *Journal of Intellectual & Developmental Disability*, *36*(3), 184–96. doi:10.3109/13668250.2011.599317

Gathercole, S. E., & Baddeley, A. D. (1990). The role of phonological memory in vocabulary acquisition: A study of young children learning new names. *British Journal of Psychology*, *81*(4), 439–454.

Glenn, S., & Cunningham, C. (2005). Performance of young people with Down syndrome on the Leiter-R and British picture vocabulary scales. *Journal of Intellectual Disability Research*, *49*(4), 239–44. doi:10.1111/j.1365-2788.2005.00643.x

Glenner, G. G., & Wong, C. W. (1984). Alzheimer's disease: initial report of the purification and characterization of a novel cerebrovascular amyloid protein. *Biochemical and Biophysical Research Communications*, *120*(3), 885–890.

Goate, A., Chartier-Harlin, M.-C., Mullan, M., Brown, J., Crawford, F., Fidani, L., … Hardy, J. (1991). Segregation of a missense mutation in the amyloid precursor protein gene with familial Alzheimer's disease. *Nature*, *349*, 704–706.

Gottlieb, D. J., Chase, C., Vezina, R. M., Heeren, T. C., Corwin, M. J., Auerbach, S. H., … Lesko, S. M. (2004). Sleep-disordered breathing symptoms are associated wtih poorer cognitive function in 5-year-old children. *The Journal of Pediatrics*, *145*(4), 458–64. doi:10.1016/j.jpeds.2004.05.039

Guidi, S., Bonasoni, P., Ceccarelli, C., Santini, D., Gualtieri, F., Ciani, E., & Bartesaghi, R. (2008). Neurogenesis impairment and increased cell death reduce total neuron number in the hippocampal region of fetuses with Down syndrome. *Brain Pathology*, *18*(2), 180–97. doi:10.1111/j.1750-3639.2007.00113.x

Gunn, D. M., & Jarrold, C. (2004). Raven's matrices performance in Down syndrome: evidence of unusual errors. *Research in Developmental Disabilities*, *25*(5), 443–57. doi:10.1016/j.ridd.2003.07.004

Guralnick, M. J., Connor, R. T., & Johnson, L. C. (2011). The peer-related social competence of young children with Down syndrome. *American Journal on Intellectual and Developmental Disabilities*, *116*(1), 48–64. doi:10.1352/1944-7558-116.1.48.The

Hamilton, A., Plunkett, K., & Schafer, G. (2000). Infant vocabulary development assessed with a British communicative development inventory. *Journal of Child Language*, *27*(3), 689–705. Retrieved from http://europepmc.org/abstract/MED/11089344

Henderson, L. M., Weighall, A. R., Brown, H., & Gaskell, M. G. (2012). Consolidation of vocabulary is associated with sleep in children. *Developmental Science*, *15*(5), 674–87. doi:10.1111/j.1467-7687.2012.01172.x

Henderson, S. E., Sugden, D. A., & Barnett, A. L. (2007). *Movement Assessment Battery for Children - 2*. London: Pearson Assessment.

Hick, R. F., Botting, N., & Conti-Ramsden, G. (2005). Short-term memory and vocabulary development in children with Down syndrome and children with specific language impairment. *Developmental Medicine and Child Neurology*, *47*(8), 532–8. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16108453

Hill, E. L. (2001). Non-specific nature of specific language impairment: a review of the literature with regard to concomitant motor impairments. *Journal of Language and*

Communication Disorders, *36*(2), 149–171. Retrieved from http://informahealthcare.com/doi/abs/10.1080/13682820010019874

Horst, J. S., & Samuelson, L. K. (2008). Fast mapping but poor retention by 24-month-old infants. *Infancy*, *13*(2), 128–157. doi:10.1080/15250000701795598

Hulme, C., Goetz, K., Brigstocke, S., Nash, H. M., Lervåg, A., & Snowling, M. J. (2012). The growth of reading skills in children with Down Syndrome. *Developmental Science*, *15*(3), 320–9. doi:10.1111/j.1467-7687.2011.01129.x

Hulme, C., & Snowling, M. J. (2009). *Developmental Disorders of Language Learning and Cognition*. Chichester: Wiley-Blackwell.

Hung, W.-J., Lin, L.-P., Wu, C.-L., & Lin, J.-D. (2011). Cost of hospitalization and length of stay in people with Down syndrome: evidence from a national hospital discharge claims database. *Research in Developmental Disabilities*, *32*(5), 1709–13. doi:10.1016/j.ridd.2011.02.024

Irving, C., Basu, A., Richmond, S., Burn, J., & Wren, C. (2008). Twenty-year trends in prevalence and survival of Down syndrome. *European Journal of Human Genetics*, *16*(11), 1336–40. doi:10.1038/ejhg.2008.122

Jarrold, C., & Baddeley, A. D. (1997). Short-term memory for verbal and visuospatial information in Down's syndrome. *Cognitive Neuropsychiatry*, *2*(2), 101–122. doi:10.1080/135468097396351

Jarrold, C., Baddeley, A. D., & Phillips, C. (1999). Down syndrome and the phonological loop: the evidence for, and importance of, a specific verbal short-term memory deficit. *Down Syndrome Research and Practice*, *6*(2), 61–75. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11276981

Jarrold, C., Baddeley, A. D., & Phillips, C. (2007). Long-term memory for verbal and visual information in Down syndrome and Williams syndrome: performance on the Doors and People test. *Cortex*, *43*(2), 233–47. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/17405669

Jarrold, C., & Brock, J. (2004). To match or not to match? Methodological issues in autism-related research. *Journal of Autism and Developmental Disorders*, *34*(1), 81–6. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15098961

Jarrold, C., Nadel, L., & Vicari, S. (2009). Memory and neuropsychology in Down syndrome. *Down Syndrome Research and Practice*, *12*(3), 68–73. doi:10.3104/reviews/2068

Jarrold, C., Thorn, A. S. C., & Stephens, E. (2009). The relationships among verbal short-term memory, phonological awareness, and new word learning: evidence from typical development and Down syndrome. *Journal of Experimental Child Psychology*, *102*(2), 196–218. doi:10.1016/j.jecp.2008.07.001

Jenkins, J. G., & Dallenbach, K. M. (1924). Obliviscence during sleep and waking. *The American Journal of Psychology*, *35*(4), 605–612. Retrieved from http://www.jstor.org/stable/1414040

Karmiloff-Smith, A. (1998). Development itself is the key to understanding developmental disorders. *Trends in Cognitive Sciences*, *2*(10), 389–98. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21227254

Karmiloff-Smith, A. (2007). Atypical epigenesis. *Developmental Science*, *10*(1), 84–8. doi:10.1111/j.1467-7687.2007.00568.x

Kay-Raining Bird, E., Chapman, R. S., & Schwartz, S. E. (2004). Fast mapping of words and story recall by individuals with Down syndrome. *Journal of Speech, Language, and Hearing Research*, *47*(6), 1286–300. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15842011

Kenny, D. A. (1975). Cross-lagged panel correlation: A test for spuriousness. *Psychological Bulletin*, *82*(6), 887–903. doi:10.1037//0033-2909.82.6.887

Kheirandish-Gozal, L., de Jong, M. R., Spruyt, K., Chamuleau, S. A. J., & Gozal, D. (2010). Obstructive sleep apnoea is associated with impaired pictorial memory task acquisition and retention in children. *European Respiratory Journal*, *36*(1), 164–169. doi:10.1183/09031936.00114209

Klein, B. P., & Mervis, C. B. (1999). Contrasting patterns of cognitive abilities of 9- and 10-year-olds with Williams syndrome or Down syndrome. *Developmental Neuropsychology*, *16*(2), 177–196.

Kloepfer, C., Riemann, D., Nofzinger, E. A., Feige, B., Unterrainer, J., O'Hara, R., … Nissen, C. (2009). Memory before and after sleep in patients with moderate obstructive sleep apnea. *Journal of Clinical Sleep Medicine*, *5*(6), 540–8. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2792970&tool=pmcentrez&rendertype=abstract

Korenberg, J. R., Kawashima, H., Pulst, S. M., Ikeuchi, T., Ogasawara, N., Yamamoto, K., … Magenis, E. (1990). Molecular definition of a region of chromosome 21 that causes features of the Down syndrome phenotype. *American Journal of Human Genetics*, *47*(2), 236–46. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1683719&tool=pmcentrez&rendertype=abstract

Krakowiak, P., Goodlin-Jones, B., Hertz-Picciotto, I., Croen, L. a, & Hansen, R. L. (2008). Sleep problems in children with autism spectrum disorders, developmental delays, and typical development: a population-based study. *Journal of Sleep Research*, *17*(2), 197–206. doi:10.1111/j.1365-2869.2008.00650.x

Kumin, L. (1994). Intelligibility of speech in children with Down syndrome in natural settings: parents' perspective. *Perceptual and Motor Skills*. Retrieved from http://europepmc.org/abstract/MED/8177677/reload=0

Lahl, O., Wispel, C., Willigens, B., & Pietrowsky, R. (2008). An ultra short episode of sleep is sufficient to promote declarative memory performance. *Journal of Sleep Research*, *17*(1), 3–10. doi:10.1111/j.1365-2869.2008.00622.x

Lana-Elola, E., Watson-Scales, S. D., Fisher, E. M. C., & Tybulewicz, V. L. J. (2011). Down syndrome: searching for the genetic culprits. *Disease Models & Mechanisms*, *4*(5), 586–95. doi:10.1242/dmm.008078

Lanfranchi, S., Jerman, O., Dal Pont, E., Alberti, A., & Vianello, R. (2010). Executive function in adolescents with Down Syndrome. *Journal of Intellectual Disability Research*, *54*(4), 308–19. doi:10.1111/j.1365-2788.2010.01262.x

Laws, G. (2004). Contributions of phonological memory, language comprehension and hearing to the expressive language of adolescents and young adults with Down syndrome. *Journal of Child Psychology and Psychiatry*, *45*(6), 1085–95. doi:10.1111/j.1469-7610.2004.t01-1-00301.x

Laws, G., & Bishop, D. V. M. (2003). A comparison of language abilities in adolescents with Down syndrome and children with specific language impairment. *Journal of Speech, Language and Hearing Research*, *46*, 1324–1339. doi:1092-4388/03/4606-1324

Laws, G., & Bishop, D. V. M. (2004). Verbal deficits in Down's syndrome and specific language impairment: a comparison. *International Journal of Language & Communication Disorders*, *39*(4), 423–451. doi:10.1080/13682820410001681207

Laws, G., & Gunn, D. (2004). Phonological memory as a predictor of language comprehension in Down syndrome: a five-year follow-up study. *Journal of Child Psychology and Psychiatry*, *45*(2), 326–37. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/14982246

Laws, G., & Hall, A. (2014). Early hearing loss and language abilities in children with Down syndrome. *International Journal of Language & Communication Disorders*, *49*(3), 333–42. doi:10.1111/1460-6984.12077

Leddy, M. (1999). The biological bases of speech in people with Down syndrome. In J. F. Miller, M. Leddy, & L. A. Leavitt (Eds.), *Improving the Communication of People with Down Syndrome* (pp. 61 – 80). Baltimore, Maryland: Paul H Brookes.

Lee, V. M.-Y., & Trojanowski, J. Q. (1992). The disordered neuronal cytoskeleton in Alzheimer's disease. *Current Opinion in Neurobiology*, *2*(5), 653–656. doi:10.1016/0959-4388(92)90034-I

Levanon, A., Tarasiuk, A., & Tal, A. (1999). Sleep characteristics in children with Down syndrome. *Journal of Pediatrics*, *134*(6), 755–760. doi:9/21/98572

Määttä, T., Kaski, M., Taanila, A., Keinänen-Kiukaanniemi, S., & Iivanainen, M. (2006). Sensory impairments and health concerns related to the degree of intellectual disability in people with Down syndrome. *Down's Syndrome, Research and Practice*, *11*(2), 78–83. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/17048801

MacKay, D. F., Smith, G. C. S., Dobbie, R., & Pell, J. P. (2010). Gestational age at delivery and special educational need: retrospective cohort study of 407,503 schoolchildren. *PLoS Medicine*, *7*(6), e1000289. doi:10.1371/journal.pmed.1000289

Majnemer, A., Limperopoulos, C., Shevell, M. I., Rohlicek, C., Rosenblatt, B., & Tchervenkov, C. (2009). A new look at outcomes of infants with congenital heart disease. *Pediatric Neurology*, *40*(3), 197–204. doi:10.1016/j.pediatrneurol.2008.09.014

Marcell, M. M., & Cohen, S. (1992). Hearing abilities of Down syndrome and other mentally handicapped adolescents. *Research in Developmental Disabilities*, *13*(6), 533–551. doi:10.1016/0891-4222(92)90048-B

McClelland, J. L., McNaughton, B. L., & O'Reilly, R. (1995). Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. *Psychological Review*, *102*(3), 419–457. doi:0033-295X/95

McDuffie, A. S., Sindberg, H. a, Hesketh, L. J., & Chapman, R. S. (2007). Use of speaker intent and grammatical cues in fast-mapping by adolescents with Down syndrome. *Journal of Speech, Language, and Hearing Research*, *50*(6), 1546–61. doi:10.1044/1092-4388(2007/105)

McGaugh, J. L. (1966). Time-dependent processes in memory storage. *Science*, *153*, 1351–8. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/172964

McGrath, R. J., Stransky, M. L., Cooley, W. C., & Moeschler, J. B. (2011). National profile of children with Down syndrome: disease burden, access to care, and family impact. *The Journal of Pediatrics*, *159*(4), 535–40. doi:10.1016/j.jpeds.2011.04.019

Menghini, D., Costanzo, F., & Vicari, S. (2011). Relationship between brain and cognitive processes in Down syndrome. *Behavior Genetics*, *41*(3), 381–93. doi:10.1007/s10519-011-9448-3

Mengoni, S. E., Nash, H., & Hulme, C. (2013). The benefit of orthographic support for oral vocabulary learning in children with Down syndrome. *Journal of Child Language*, *40*(1), 221–43. doi:10.1017/S0305000912000396

Miano, S., Bruni, O., Elia, M., Scifo, L., Smerieri, A., Trovato, A., … Ferri, R. (2008). Sleep phenotypes of intellectual disability: a polysomnographic evaluation in subjects with Down syndrome and Fragile-X syndrome. *Clinical Neurophysiology*, *119*(6), 1242–7. doi:10.1016/j.clinph.2008.03.004

Miatton, M., De Wolf, D., François, K., Thiery, E., & Vingerhoets, G. (2006). Neurocognitive consequences of surgically corrected congenital heart defects: A review. *Neuropsychology Review*, *16*(2), 65–85. doi:10.1007/s11065-006-9005-7

Miatton, M., De Wolf, D., François, K., Thiery, E., & Vingerhoets, G. (2007). Neuropsychological performance in school-aged children with surgically corrected congenital heart disease. *The Journal of Pediatrics*, *151*(1), 73–8, 78.e1. doi:10.1016/j.jpeds.2007.02.020

Miller, J. F. (1988). The developmental asynchrony of language development in children with Down syndrome. In L. Nadel (Ed.), *The Psychobiology of Down syndrome* (pp. 167–198). Boston, MA: MIT Press.

Miller, J. F. (1999). Profiles of language development in children with Down syndrome. In J. F. Miller, M. Leddy, & L. A. Leavitt (Eds.), *Improving the Communication of People with Down Syndrome* (pp. 11–39). Baltimore, Maryland: Paul H Brookes.

Miller, J. F., & Leddy, M. (1999). Verbal fluency, speech intelligibility, and communicative effectiveness. In J. F. Miller, M. Leddy, & L. A. Leavitt (Eds.), *Improving the Communication of People with Down Syndrome* (pp. 81 – 92). Baltimore, Maryland: Paul H Brookes.

Miller, J. F., Sedey, A. L., & Miolo, G. (1995). Validity of parent report measures of vocabulary development for children with Down syndrome. *Journal of Speech and Hearing Research*, *38*(5), 1037–44. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8558873

Miolo, G., Chapman, R. S., & Sindberg, H. A. (2005). Sentence comprehension in adolescents with Down syndrome and typically developing children: Role of sentence voice, visual context, and auditory-verbal short-term memory. *Journal of Speech, Language and Hearing Research*, *48*, 172–188. doi:1092-4388/05/4801-0172

Moore, D. G., & George, R. (2011). ACORNS: a tool for the visualisation and modelling of atypical development. *Journal of Intellectual Disability Research*, *55*(10), 956–72. doi:10.1111/j.1365-2788.2011.01471.x

Morton, J. (2004). *Understanding Developmental Disorders: A Causal Modelling Approach*. Malden, MA: Blackwell Publishing.

Mosse, E. K., & Jarrold, C. (2008). Hebb learning, verbal short-term memory, and the acquisition of phonological forms in children. *Quarterly Journal of Experimental Psychology*, *61*(4), 505–14. doi:10.1080/17470210701680779

Mosse, E. K., & Jarrold, C. (2010). Searching for the Hebb effect in Down syndrome: evidence for a dissociation between verbal short-term memory and domain-general learning of serial order. *Journal of Intellectual Disability Research*, *54*(4), 295–307. doi:10.1111/j.1365-2788.2010.01257.x

Mosse, E. K., & Jarrold, C. (2011). Evidence for preserved novel word learning in Down syndrome suggests multiple routes to vocabulary acquisition. *Journal of Speech, Language and Hearing Research*, *54*, 1137–1153. doi:10.1044/1092-4388(2010/09-0244)a

Moyle, M. J., Ellis Weismer, S., Evans, J. L., & Lindstrom, M. J. (2007). Longitudinal relationships between lexical and grammatical development in typical and late-talking children. *Journal of Speech, Language, and Hearing Research*, *50*(2), 508–28. doi:10.1044/1092-4388(2007/035)

Msall, M. E., & Tremont, M. R. (1999). Measuring functional status in children with genetic impairments. *American Journal of Medical Genetics*, *89*(2), 62–74. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10559760

Neale, B. M., Medland, S. E., Ripke, S., Asherson, P., Franke, B., Lesch, K., … Elia, J. (2010). Meta-analysis of genome-wide association studies of attention- deficit/hyperactivity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *49*(9), 884–897.

Nieuwenhuis-Mark, R. E. (2009). Diagnosing Alzheimer's dementia in Down syndrome: problems and possible solutions. *Research in Developmental Disabilities*, *30*(5), 827–38. doi:10.1016/j.ridd.2009.01.010

Norbury, C. F., Griffiths, H., & Nation, K. (2010). Sound before meaning: word learning in autistic disorders. *Neuropsychologia*, *48*(14), 4012–9. doi:10.1016/j.neuropsychologia.2010.10.015

Ohayon, M. M., Carskadon, M. A., Guilleminault, C., & Vitiello, M. V. (2004). Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. *Sleep*, *27*(7), 1255–73. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15586779

Oliver, A., Johnson, M. H., Karmiloff-Smith, A., & Pennington, B. (2000). Deviations in the emergence of representations : a neuroconstructivist framework for analysing developmental disorders. *Developmental Science*, *1*, 1–23.

Oliver, C., Crayton, L., Holland, A., Hall, S., & Bradbury, J. (1998). A four year prospective study of age-related cognitive change in adults with Down's syndrome. *Psychological Medicine*, *28*(6), 1365–1377. doi:10.1017/S0033291798007417

Organisation for Economic Co-operation and Development (OECD). (2010). *PF3.2: Enrolment in childcare and pre-schools*. Retrieved from http://www.oecd.org/els/family/PF3.2 Enrolment in childcare and preschools - 290713.pdf

Owens, J. A., Spirito, A., & McGuinn, M. (2000). The Children's Sleep Habits Questionnaire (CSHQ): psychometric properties of a survey instrument for school-aged children. *Sleep*, *23*(8), 1043–51. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11145319

Palisano, R. J., Walter, S. D., Russell, D. J., Rosenbaum, P. L., Gémus, M., Galuppi, B. E., & Cunningham, L. (2001). Gross motor function of children with Down syndrome: creation of motor growth curves. *Archives of Physical Medicine and Rehabilitation*, *82*(4), 494–500. doi:10.1053/apmr.2001.21956

Patterson, D. (2007). Genetic mechanisms involved in the phenotype of Down syndrome. *Mental Retardation and Developmental Disabilities Research Reviews*, *13*, 199–206. doi:10.1002/mrdd

Patterson, T., Rapsey, C. M., & Glue, P. (2013). Systematic review of cognitive development across childhood in Down syndrome: implications for treatment interventions. *Journal of Intellectual Disability Research*, *57*(4), 306–318. doi:10.1111/j.1365-2788.2012.01536.x

Pennington, B. F., Moon, J., Edgin, J., Stedron, J., & Nadel, L. (2003). The neuropsychology of Down syndrome: evidence for hippocampal dysfunction. *Child Development*, *74*(1), 75–93. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12625437

Pereira, K., Basso, R. P., Lindquist, A. R. R., Silva, L. G. P. Da, & Tudella, E. (2013). Infants with Down syndrome: Percentage and age for acquisition of gross motor skills. *Research in Developmental Disabilities*, *34*(3), 894–901. doi:10.1016/j.ridd.2012.11.021

Pickering, S., & Gathercole, S. (2001). *Working Memory Test Battery for Children*. London: The Psychological Corporation.

Pinter, J. D., Brown, W. E., Eliez, S., Schmitt, J. E., Capone, G. T., & Reiss, A. L. (2001). Amygdala and hippocampal volumes in children with Down syndrome: a high-resolution MRI study. *Neurology*, *56*(7), 972–4. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11294940

Pinter, J. D., Eliez, S., Schmitt, J. E., Capone, G. T., & Reiss, A. L. (2001). Neuroanatomy of Down's syndrome: A high-resolution MRI study. *American Journal of Psychiatry*, *158*(10), 1659–1665.

Plihal, W., & Born, J. (1997). Effects of early and late nocturnal sleep on declarative and procedural memory. *Journal of Cognitive Neuroscience*, *9*(4), 534–547.

Prehn-Kristensen, A., Göder, R., Fischer, J., Wilhelm, I., Seeck-Hirschner, M., Aldenhoff, J., & Baving, L. (2011). Reduced sleep-associated consolidation of declarative memory in attention-deficit/hyperactivity disorder. *Sleep Medicine*, *12*(7), 672–9. doi:10.1016/j.sleep.2010.10.010

Price, J., Roberts, J., Vandergrift, N., & Martin, G. (2007). Language comprehension in boys with fragile X syndrome and boys with Down syndrome. *Journal of Intellectual Disability Research*, *51*, 318–26. doi:10.1111/j.1365-2788.2006.00881.x

Price, T. S., Dale, P. S., & Plomin, R. (2004). A longitudinal genetic analysis of low verbal and nonverbal cognitive abilities in early childhood. *Twin Research*, *7*(2), 139–48. doi:10.1375/136905204323016122

Pueschel, S., & Gieswein, S. (1993). Ocular disorders in children with Down syndrome. *Down Syndrome Research and Practice*, *1*(3), 129–132. doi:10.3104/reports.23

Pueschel, S. M., Gallagher, P. L., Zartler, A. S., & Pezzullo, J. C. (1987). Cognitive and learning processes in children with Down syndrome. *Research in Developmental Disabilities*, *8*(1), 21–37. doi:10.1016/0891-4222(87)90038-2

Raghunathan, T. E., Rosenthal, R., & Rubin, D. B. (1996). Comparing correlated but nonoverlapping correlations. *Psychological Methods*, *1*(2), 178–183. doi:10.1037/1082-989X.1.2.178

Rechetnikov, R. P., & Maitra, K. (2009). Motor impairments in children associated with impairments of speech or language: a meta-analytic review of research literature. *American Journal of Occupational Therapy*, *63*, 255–263.

Rice, M. L., Smolik, F., Perpich, D., Thompson, T., Rytting, N., & Blossom, M. (2010). Mean length of utterance levels in 6-month intervals for children 3 to 9 years with and without language impairments. *Journal of Speech, Language and Hearing Research*, *53*(April), 333–350. doi:10.1044/1092-4388(2009/08-0183)

Rihtman, T., Tekuzener, E., Parush, S., Tenenbaum, A., Bachrach, S. J., & Ornoy, A. (2010). Are the cognitive functions of children with Down syndrome related to their participation? *Developmental Medicine and Child Neurology*, *52*(1), 72–8. doi:10.1111/j.1469-8749.2009.03356.x

Roberts, J. E., Rosenfeld, R. M., & Zeisel, S. A. (2004). Otitis media and speech and language: a meta-analysis of prospective studies. *Pediatrics*, *113*, e238–e248.

Roberts, J., Long, S. H., Malkin, C., Barnes, E., Skinner, M., Hennon, E. A., & Anderson, K. (2005). A comparison of phonological skills of boys with Fragile X syndrome and Down syndrome. *Journal of Speech, Language and Hearing Research*, *48*(5), 980–95. doi:10.1044/1092-4388(2005/067)

Robertson, E. M., & Cohen, D. A. (2006). Understanding consolidation through the architecture of memories. *The Neuroscientist*, *12*(3), 261–71. doi:10.1177/1073858406287935

Rodrigue, J. R., Morgan, S. B., & Geffken, G. R. (1991). A comparative evaluation of adaptive behavior in children and adolescents with autism, Down syndrome, and normal development. *Journal of Autism and Developmental Disorders*, *21*(2), 187–96. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1830878

Roid, G. H., & Miller, L. J. (1997). *Leiter International Performance Scale - Revised*. Wood Dale, IL: Stoelting Co.

Roizen, N. J., Magyar, C. I., Kuschner, E. S., Sulkes, S. B., Druschel, C., van Wijngaarden, E., … Hyman, S. L. (2014). A community cross-sectional survey of medical problems in 440 children with Down syndrome in New York State. *The Journal of Pediatrics*, *164*(4), 871–5. doi:10.1016/j.jpeds.2013.11.032

Roizen, N. J., & Patterson, D. (2003). Down ’s syndrome. *The Lancet*, *361*, 1281–1289.

Roper, R. J., & Reeves, R. H. (2006). Understanding the basis for Down syndrome phenotypes. *PLoS Genetics*, *2*(3), e50. doi:10.1371/journal.pgen.0020050

Rowe, J., Lavender, A., & Turk, V. (2006). Cognitive executive function in Down’s syndrome. *The British Journal of Clinical Psychology*, *45*, 5–17. doi:10.1348/014466505X29594

Schieve, L. A., Boulet, S. L., Boyle, C., Rasmussen, S. A., & Schendel, D. (2009). Health of children 3 to 17 years of age with Down syndrome in the 1997-2005 national health interview survey. *Pediatrics*, *123*(2), e253–60. doi:10.1542/peds.2008-1440

Schieve, L. A., Boulet, S. L., Kogan, M. D., Van Naarden-Braun, K., & Boyle, C. A. (2011). A population-based assessment of the health, functional status, and consequent family

impact among children with Down syndrome. *Disability and Health Journal*, *4*(2), 68–77. doi:10.1016/j.dhjo.2010.06.001

Schneider, W., Eschman, A., & Zuccolotto, A. (2002). *E-Prime User's Guide*. Pittsburgh: Psychology Software Tools Inc.

Seef-Gabriel, B., Chiat, S., & Roy, P. (2008). *Early Repetition Battery*. London: Pearson Assessment.

Shapiro, B. L. (1983). Down syndrome-a disruption of homeostasis. *American Journal of Medical Genetics*, *14*, 241–269.

Shott, S. R., Amin, R., Chini, B., Heubi, C., Hotze, S., & Akers, R. (2006). Obstructive sleep apnea: should all children with Down syndrome be tested? *Archives of Otolaryngology: Head and Neck Surgery*, *132*, 432–436.

Shott, S. R., Joseph, A., & Heithaus, D. (2001). Hearing loss in children with Down syndrome. *International Journal of Pediatric Otorhinolaryngology*, *61*(3), 199–205. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11700189

Sigman, M., & Ruskin, E. (1999). Continuity and change in the social competence of children with autism, Down syndrome and developmental delays. *Monographs of the Society for Research in Child Development*, *64*, 1–139. Retrieved from http://www.jstor.org/stable/3181510

Silveri, M. C., Leggio, M. G., & Molinari, M. (1994). The cerebellum contributes to linguistic production: A case of agrammatic speech following a right cerebellar lesion. *Neurology*, *44*(11), 2047–2050. doi:10.1212/WNL.44.11.2047

Silverman, W. (2007). Down syndrome: cognitive phenotype. *Mental Retardation and Developmental Disabilities Research Reviews*, *13*, 228–236. doi:10.1002/mrdd

Singer Harris, N. G., Bellugi, U., Bates, E., Jones, W., & Rossen, M. (1997). Contrasting profiles of language development in children with Williams and Down syndromes. *Developmental Neuropsychology*, *13*(3), 345–370. doi:10.1080/87565649709540683

Snookes, S. H., Gunn, J. K., Eldridge, B. J., Donath, S. M., Hunt, R. W., Galea, M. P., & Shekerdemian, L. (2010). A systematic review of motor and cognitive outcomes after

early surgery for congenital heart disease. *Pediatrics*, *125*(4), e818–27. doi:10.1542/peds.2009-1959

So, S. A., Urbano, R. C., & Hodapp, R. M. (2007). Hospitalizations of infants and young children with Down syndrome: evidence from inpatient person-records from a statewide administrative database. *Journal of Intellectual Disability Research*, *51*(Pt 12), 1030–8. doi:10.1111/j.1365-2788.2007.01013.x

Sparrow, S. S., Cicchetti, D. V, & Balla, D. A. (2005). *Vineland Adaptive Behaviour Scales: Second Edition*. Bloomington: Pearson.

Squire, L. R. (1992a). Declarative and nondeclarative memory: Multiple brain systems supporting learning and memory. *Journal of Cognitive Neuroscience*, *4*(3), 232–43.

Squire, L. R. (1992b). Memory and the hippocampus: a synthesis from findings with rats, monkeys and humans. *Psychological Review*, *99*(2), 195–231.

Stickgold, R. (2005). Sleep-dependent memory consolidation. *Nature*, *437*(7063), 1272–8. doi:10.1038/nature04286

Stoel-Gammon, C. (1997). Phonological development in Down syndrome. *Mental Retardation and Developmental Disabilities Research Reviews*, *3*, 300–306.

Storkel, H. L. (2001). Learning new words: phonotactic probability in language development. *Journal of Speech, Language, and Hearing Research*, *44*(6), 1321–37. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11776368

Takashima, A., Bakker, I., van Hell, J. G., Janzen, G., & McQueen, J. M. (2014). Richness of information about novel words influences how episodic and semantic memory networks interact during lexicalization. *NeuroImage*, *84*, 265–78. doi:10.1016/j.neuroimage.2013.08.023

Takashima, S., Iida, K., Mito, T., & Arima, M. (1994). Dendritic and histochemical development and ageing in patients with Down ’s syndrome. *Journal of Intellectual Disability Research*, *38*, 265–273.

Thomas, M. S. C., Ansari, D., Jarrold, C., & Karmiloff-Smith, A. (2009). Using developmental trajectories to understand developmental disorders. *Journal of Speech, Language and Hearing Research*, *52*, 336–358. doi:1092-4388/09/5202-0336

Tilley, A. J., & Empson, J. A. C. (1978). REM sleep and memory consolidation. *Biological Psychology*, *6*(4), 293–300. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/213132

Tsao, R., & Kindelberger, C. (2009). Variability of cognitive development in children with Down syndrome: relevance of good reasons for using the cluster procedure. *Research in Developmental Disabilities*, *30*(3), 426–32. doi:10.1016/j.ridd.2008.10.009

Tudella, E., Pereira, K., Basso, R. P., & Savelsbergh, G. J. P. (2011). Description of the motor development of 3-12 month old infants with Down syndrome: the influence of the postural body position. *Research in Developmental Disabilities*, *32*(5), 1514–20. doi:10.1016/j.ridd.2011.01.046

Turner, S., Sloper, P. C. A., & Adrian, H. (1990). Health problems in children with Down's syndrome. *Child: Care, Health and Development*, *16*, 83–97.

Vakil, E., & Lifshitz-Zehavi, H. (2012). Solving the Raven Progressive Matrices by adults with intellectual disability with/without Down syndrome: different cognitive patterns as indicated by eye-movements. *Research in Developmental Disabilities*, *33*(2), 645–54. doi:10.1016/j.ridd.2011.11.009

Van der Rijken, R., Hulstijn, W., Hulstijn-Dirkmaat, G., Daniëls, O., & Maassen, B. (2011). Psychomotor slowness in school-age children with congenital heart disease. *Developmental Neuropsychology*, *36*(3), 388–402. doi:10.1080/87565641.2011.557456

Van der Rijken, R., Hulstijn-Dirkmaat, G., Kraaimaat, F., Nabuurs-Kohrman, L., Daniëls, O., & Maassen, B. (2010). Evidence of impaired neurocognitive functioning in school-age children awaiting cardiac surgery. *Developmental Medicine and Child Neurology*, *52*(6), 552–8. doi:10.1111/j.1469-8749.2009.03547.x

Van der Schuit, M., Segers, E., van Balkom, H., & Verhoeven, L. (2011). How cognitive factors affect language development in children with intellectual disabilities. *Research in Developmental Disabilities*, *32*(5), 1884–94. doi:10.1016/j.ridd.2011.03.015

Van Duijn, G., Dijkxhoorn, Y., Scholte, E. M., & van Berckelaer-Onnes, I. A. (2010). The development of adaptive skills in young people with Down syndrome. *Journal of Intellectual Disability Research*, *54*(11), 943–54. doi:10.1111/j.1365-2788.2010.01316.x

Vandereet, J., Maes, B., Lembrechts, D., & Zink, I. (2011). Expressive vocabulary acquisition in children with intellectual disability: speech or manual signs? *Journal of Intellectual & Developmental Disability*, *36*(2), 91–104. doi:10.1080/13668250.2011.572547

Vicari, S. (2006). Motor development and neuropsychological patterns in persons with Down syndrome. *Behavior Genetics*, *36*(3), 355–64. doi:10.1007/s10519-006-9057-8

Vicari, S., Bellucci, S., & Carlesimo, G. A. (2000). Implicit and explicit memory: a functional dissociation in persons with Down syndrome. *Neuropsychologia*, *38*(3), 240–51. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10678691

Vicari, S., Caselli, M. C., Gagliardi, C., Tonucci, F., & Volterra, V. (2002). Language acquisition in special populations: a comparison between Down and Williams syndromes. *Neuropsychologia*, *40*(13), 2461–70. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12417473

Vicari, S., Caselli, M. C., & Tonucci, F. (2000). Asynchrony of lexical and morphosyntactic development in children with Down Syndrome. *Neuropsychologia*, *38*(5), 634–44. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11721535

Visootsak, J., Hess, B., Bakeman, R., & Adamson, L. B. (2013). Effect of congenital heart defects on language development in toddlers with Down syndrome. *Journal of Intellectual Disability Research*, *57*(9), 887–92. doi:10.1111/j.1365-2788.2012.01619.x

Visootsak, J., Mahle, W. T., Kirshbom, P. M., Huddleston, L., Caron-Besch, M., Ransom, A., & Sherman, S. L. (2011). Neurodevelopmental outcomes in children with Down syndrome and congenital heart defects. *American Journal of Medical Genetics. Part A*, *155A*(11), 2688–91. doi:10.1002/ajmg.a.34252

Wechsler, D. (2003). *Wechsler Preschool and Primary Scale of Intelligence - Third Edition UK*. London: Harcourt Assessment.

Westermann, G., Mareschal, D., Johnson, M. H., Sirois, S., Spratling, M. W., & Thomas, M. S. C. (2007). Neuroconstructivism. *Developmental Science*, *10*(1), 75–83. doi:10.1111/j.1467-7687.2007.00567.x

Wiig, E. H., Secord, W. A., & Semel, E. (2006). *Clinical Evaluation of Language Fundamentals Preschool - Second UK Edition*. London: Harcourt Assessment.

Wilhelm, I., Diekelmann, S., & Born, J. (2008). Sleep in children improves memory performance on declarative but not procedural tasks. *Learning & Memory*, *15*(5), 373–7. doi:10.1101/lm.803708

Wilhelm, I., Metzkow-Mészàros, M., Knapp, S., & Born, J. (2012). Sleep-dependent consolidation of procedural motor memories in children and adults: the pre-sleep level of performance matters. *Developmental Science*, no–no. doi:10.1111/j.1467-7687.2012.01146.x

Wisniewski, T., Ghiso, J., & Frangione, B. (1994). Alzheimer's disease and soluble amyloid beta. *Neurobiology of Aging*, *15*(2), 143–152. doi:10.1016/0197-4580(94)90105-8

Woodward, A. L., Markman, E. M., & Fitzsimmons, C. M. (1994). Rapid word learning in 13- and 18-month-olds. *Developmental Psychology*, *30*(4), 553–566. doi:10.1037//0012-1649.30.4.553

World Health Organisation. (1992). *The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines*. Geneva: World Health Organisation.

Yam, W. K.-L., Tse, P. W. T., Yu, C. M., Chow, C. B., But, W. M., Li, K. Y., … Lau, J. T. F. (2008). Medical issues among children and teenagers with Down syndrome in Hong Kong. *Down's Syndrome Research and Practice*, *12*(2), 138–40. doi:10.3104/reports.2005

Yang, Y., Conners, F. A., & Merrill, E. C. (2014). Visuo-spatial ability in individuals with Down syndrome: Is it really a strength? *Research in Developmental Disabilities*, *35*, 1473–1500.

Ypsilanti, A., & Grouios, G. (2008). Linguistic profile of individuals with Down syndrome: comparing the linguistic performance of three developmental disorders. *Child Neuropsychology*, *14*(2), 148–70. doi:10.1080/09297040701632209

Zampini, L., & D'Odorico, L. (2011). Lexical and syntactic development in Italian children with Down's syndrome. *International Journal of Language & Communication Disorders*, *46*(4), 386–96. doi:10.3109/13682822.2010.508764

Zampini, L., & D'Odorico, L. (2013). Vocabulary development in children with Down syndrome: longitudinal and cross-sectional data. *Journal of Intellectual & Developmental Disability*, *38*(4), 310–7. doi:10.3109/13668250.2013.828833

Zhu, J. L., Hasle, H., Correa, A., Schendel, D., Friedman, J. M., Olsen, J., & Rasmussen, S. a. (2013). Hospitalizations among people with Down syndrome: A nationwide population-based study in Denmark. *American Journal of Medical Genetics: Part A*, *161*(4), 650–7. doi:10.1002/ajmg.a.35711

Zigman, W. B., Schupf, N., Sersen, E., & Silverman, W. (1996). Prevalence of dementia in adults with and without Down syndrome. *American Journal of Mental Retardation*, *100*(4), 403–412.