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The Effects of Early Life Stress on Affective Processing: Behavioural and Neural Correlates

By:

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Thesis abstract

Previous research has consistently demonstrated a relationship between experiences of early life stress (ELS), such as abuse or neglect, and increased risk of mental illness in adulthood. However, there has been a paucity of investigation into the neurocognitive mechanisms that could mediate this relationship. Therefore, the work presented in this doctoral thesis aimed to expand current knowledge of the neurocognitive correlates of ELS in mentally healthy young adults, with a focus on the mechanisms of emotional face processing and avoidance of threat.

The first study measured young adults' (age 18 to 19; n = 147) self-reported responses to emotional facial expressions and found that higher levels of ELS were associated with reduced avoidance and increased approach of angry facial expressions, and with reduced identification of anger in female angry facial expressions. The second and third studies used EEG to examine processing at the neural level. It was found that, relative to those with low levels of ELS, young female participants (age 18 to 25; n = 58) with high levels of ELS showed blunted responses to angry, happy and neutral facial expressions as indexed by lower peak amplitudes in the N170, an event-related potential involved in visual processing. However, the high and low ELS groups did not differ in their neural or behavioural responses to stimuli which predicted an aversive outcome in a task of active and passive avoidance.

Importantly, the effects of ELS on neurocognitive processing were independent of scores on questionnaire measures of anxiety and depression, and were present in participants who had no diagnosed mental health conditions and whose experiences of ELS were not extreme. Therefore, these findings demonstrate the pervasive nature of ELS, and highlight the need for a broader societal understanding of the impact of an individual's early environment on their neural development.

Chapter 1. Literature review

Abstract

The present literature review begins by summarising previous findings regarding the personal and societal consequences of early life stress (ELS), with a focus on the impact of ELS on the mental health of those who experience it. It also introduces the role of mental illness as a critical confounding factor in previous research into the effects of ELS on neurocognitive processing. The review then addresses the neuroanatomical and functional changes which have been associated with ELS, before moving on to provide an overview of the small body of work which has used the event-related potential technique to examine the neural correlates of ELS at a high temporal resolution. The review then describes the theory of latent vulnerability (McCrory & Viding, 2015), and introduces the two neurocognitive processes which lie at the centre of the empirical work reported in this thesis: emotional face processing, and avoidance of threat. The literature review then discusses previous behavioural and neural research into the relationship between ELS and changes in emotional face processing, most of which has been carried out with child participants. Next, the review examines the second neurocognitive process of interest, avoidance of threat. Avoidance responding is examined from a theoretical and neuroanatomical perspective, and the impact of ELS on avoidance behaviour is discussed. The literature review ends with a summary of the aforementioned research and an overview of the work that will be presented in this doctoral thesis.

1.1. Introduction

Experiences of early life stress (ELS) such as abuse or neglect increase an individual's risk of developing a mental health problem later in life (Heim & Nemeroff, 2001; Kessler et al., 2010). However, the neurocognitive mechanisms which mediate this risk are not well understood (McCrory, Gerin, & Viding, 2017). Research with children has found that ELS is associated with alterations in the processing of emotional facial expressions; children who have been maltreated show hyper-sensitivity to the emotion of anger (Pollak, Messner, Kistler, & Cohn, 2009; Pollak & Sinha, 2002), and altered patterns of neural activation in response to images of facial expressions (Maheu et al., 2010; McCrory et al., 2013; McCrory et al., 2011). It has been suggested that hyper-sensitivity to anger amongst children who have been maltreated is an adaptation which serves to help the child avoid danger (Pollak et al., 2009). This is supported by work with animals, which has found that rodents which experience ELS show atypical avoidance behaviour (Kosten, Kim, & Lee, 2012; Molet, Maras, Avishai-Eliner, & Baram, 2014). However, despite the importance of avoidance behaviour in the conceptualisation of ELS, there is a notable lack of investigation into avoidance behaviour in human participants who experienced ELS. In addition, despite the growing body of work addressing the psychological and neural correlates of ELS in children, few studies have examined the effects of ELS in adult samples, and many of those which have been carried out with adult samples have not accounted for the confound of mental illness.

The present doctoral research was therefore designed to examine the behavioural and neural correlates of ELS in mentally healthy adults. The first study, presented in Chapter 3, examined the effects of ELS on mentally healthy adults' perception of anger and happiness intensity in angry, happy and neutral facial expressions, as well as their self-reported tendency to approach or avoid the individuals displaying the expressions. In the second study, presented in Chapter 4, the effect of ELS on early perceptual responses to angry, happy and neutral facial expressions was examined using the event-related potential (ERP) technique. In the third study, presented in Chapter 5, the ERP technique was used to examine the effect of

ELS on participants' neural responses to signals that predict an aversive outcome during performance of an active and passive avoidance task.

The following literature review is arranged around three broad topics: ELS, the relationship between ELS and emotional face processing, and the relationship between ELS and avoidance learning. The review will begin by discussing the relationship between ELS and mental illness, before moving on to provide an overview of what is currently known about the anatomical and functional neural correlates of ELS, and introducing the theory of latent vulnerability (McCrory & Viding, 2015). The review will then address previous findings of a relationship between ELS and emotional face processing, initially at the behavioural level and then at the neural level. Next, there will be a discussion of avoidance behaviour and current work in rodents and humans which has examined the effect of ELS on avoidance behaviour, with a focus on outlining the unanswered questions which the research in this thesis endeavours to answer.

1.2. Early life stress

Early life stress (ELS) can be defined as any acute or chronic stress which occurs during childhood or adolescence and overwhelms an individual's ability to cope in a healthy manner (Goff et al., 2013). The most commonly studied forms of ELS include physical abuse (e.g. Pollak & Kistler, 2002), emotional abuse (e.g. Fonzo et al., 2016), sexual abuse (e.g. Coles, Lee, Taft, Mazza, & Loxton, 2015), and neglect (e.g. McLaughlin, Sheridan, & Nelson, 2017), including neglect which occurs as a result of institutional care (e.g. Young, Luyster, Fox, Zeanah, & Nelson, 2017).

A large scale study (n = 51 945) found that almost 40 % of individuals worldwide experience some form of early adversity (Kessler et al., 2010). This figure encompasses a wide range of harmful experiences, including child abuse, interpersonal loss and parental maladjustment. In terms of abuse and neglect specifically, it was found that 8 % of individuals experienced physical abuse, 1.6 % experienced sexual abuse and 4.4 % experienced neglect (Kessler et al., 2010). Similarly, a study carried out in the UK found that one in four young adults reported at least one incidence of abuse (physical, emotional or sexual) or neglect during childhood (Radford, Corral, Bradley, & Fisher, 2013). Whilst these prevalence estimates are high in themselves, it is likely that they do not represent the true scale of the problem, as many of those who endure such adversities are unwilling to disclose their experiences (Hardt & Rutter, 2004). Furthermore, the co-occurrence of different forms of ELS is common, for example, a child who lives with a drug user may experience both emotional and physical neglect. Work by Felitti et al. (1998) found that 80 % of individuals who had experienced one category of early adversity (such as physical abuse, sexual abuse or household criminal behaviour) had experienced at least one additional category of early adversity as well.

The lifetime consequences of early adversity are extensive for individuals and their families. ELS increases the risk of developing numerous physical health problems in adulthood, including diabetes, lung disease, liver problems, high blood pressure and cancer (Felitti et al., 1998; Widom, Czaja, Bentley, & Johnson, 2012). In addition, early adversity is associated with an increased risk of premature death, especially when more

than one form of adversity is encountered (Brown et al., 2009; Kelly-Irving et al., 2013). Kelly-Irving et al. (2013) found that exposure to early adversity (such as physical neglect or household contact with mental health services) was associated with increased risk of premature death (defined as death before the age of 50). Specifically, experience of two or more early adversities was associated with a 57 % increase in the risk of premature death amongst men, and an 80 % increase in the risk of premature death amongst women. In a different study, very high levels of ELS (quantified as six or more adverse childhood experiences) were associated with a reduction in life expectancy of almost 20 years (Brown et al., 2009).

ELS is also associated with substantial economic costs both to the individual and to society as a whole. Zielinski (2009) found that childhood maltreatment was associated with poorer socioeconomic outcomes in adulthood. After controlling for confounding variables such as age and childhood financial status, adults who experienced childhood maltreatment were twice as likely to be unemployed and more than twice as likely to live in poverty than those who did not experience maltreatment in childhood. At the societal level, ELS is associated with annual costs in the order of billions. Gelles and Perlman (2012) estimated that child abuse and neglect cost the USA $80 billion in 2012, a figure which incorporates costs to various services including health care and law enforcement. In the UK, it has been estimated that one form of ELS, child sexual abuse, incurs an annual cost of £3.2 billion (estimate based on the year 2012; Saied-Tessier, 2014). This incorporates economic losses caused by lost productivity as well as costs to children's services, the National Health Service and the criminal justice system.

1.2.1. The relationship between early life stress and mental illness

Whilst the costs of ELS to economic productivity and physical health are extensive, an additional striking and negative impact of ELS is its effect on the mental health of those who experience it. High levels of ELS have been shown to increase the risk of poor psychological outcomes (McCrory & Viding, 2015), and are estimated to account for 60 % of child-onset mood disorders and 30 % of all mental illness across the lifespan

(Kessler et al., 2010). People who experience ELS are more likely to develop a wide range of mental health conditions (Heim & Nemeroff, 2001; McCrory et al., 2017), including depression, anxiety and psychosis (Negele, Kaufhold, Kallenbach, & Leuzinger-Bohleber, 2015; Read, Fosse, Moskowitz, & Perry, 2014; Zlotnick et al., 2008). ELS also increases the risk of substance abuse problems (Dube et al., 2003) and rates of non-suicidal self-injury (Bolen, Winter, & Hodges, 2013). In addition, suicidal ideation and suicide attempts are elevated in adults who experienced ELS (Enns et al., 2006; Gunter, Chibnall, Antoniak, Philibert, & Black, 2013), even when accounting for the effects of mental illness (Enns et al., 2006). Not only is ELS related to increased occurrence of mental health problems, it is also associated with worse clinical prognoses. Amongst those who develop a mental health condition, high levels of ELS are associated with more severe symptomology (Barnhofer, Brennan, Crane, Duggan, & Williams, 2014; Russo et al., 2015; Zou et al., 2016), longer illness durations (Russo et al., 2015), and increased risk of relapse after treatment (Williams et al., 2014). People with high levels of ELS typically show clinical difficulties at a younger age than those without experience of ELS (Russo et al., 2015); drug-taking behaviour occurs earlier (Dube et al., 2003), and amongst those who attempt suicide, the first attempt occurs at a younger age in those with high levels of ELS (Roy, 2004).

1.2.1.1. Mental illness as a confound in research into early life stress

The close relationship between ELS and mental illness presents a critical confound for research which examines the impact of ELS on adult participants (Hart & Rubia, 2012). Many of the studies which have examined the effects of ELS in adult participants did not exclude people with mental health conditions from their analyses (e.g. Di Iorio et al., 2017; Anderson et al., 2002; Andersen et al., 2008; Choi et al., 2009). In fact, some studies in the field have compared a group of individuals with both high levels of ELS and diagnosed mental health conditions with a group of individuals with low levels of ELS and no diagnosed mental health conditions (e.g. Bremner et al., 2005; Carrion et al., 2001). This necessarily

limits the conclusions that can be made about the effects of ELS, especially in cases where the experimental design involves comparing a group of people with high levels of ELS with a group of people with low levels of ELS. This is because the positive association between ELS and adult mental illness means that there are likely to be more people with mental health problems in the high ELS group than in the low ELS group. As a result, it is impossible to establish whether any observed effects are attributable to ELS or to the mental health of the participants at the time of testing.

In light of this, the research presented in this thesis recruited adult participants with no current or past diagnoses of mental illness. Furthermore, questionnaire measures of depression and anxiety were taken and included in the analyses, in order to control for the effect of subclinical symptomology on the behavioural and neurological measures that were examined.

1.2.2. The neurobiology of early life stress

Whilst the relationship between ELS and increased risk of mental health problems is well established, the mechanisms which explain this increased risk, whether they be psychological, physiological, or social, have not been fully elucidated (McCrory et al., 2017). Though there is much still to uncover, research to date has investigated a number of physiological alterations in the central nervous system which are associated with ELS and which could explain some of the increased risk of mental illness amongst those who experienced high levels of ELS (Syed & Nemeroff, 2017). Physiological alterations which have been identified include dysregulation of the hypothalamic-pituitary-adrenal axis, a neuroendocrine pathway which is activated by stress (Callaghan, Sullivan, Howell, & Tottenham, 2014; Danese & Baldwin, 2017), and heightened inflammatory responses from the immune system (Danese & Baldwin, 2017). The next section of this literature review will focus specifically on reported relationships between ELS and the anatomy and function of specific regions of the brain.

1.2.2.1. Neuroanatomical changes associated with early life stress

Structural magnetic resonance imaging (sMRI) is a neuroimaging technique which can be used to create a high resolution anatomical image of the brain. This technique has been utilised by a number of research groups to investigate the relationship between ELS and structural alterations in the human brain. ELS has been associated with global and regional volumetric reductions in grey matter (Andersen et al., 2008; Hodel et al., 2015; Teicher & Samson, 2016). Though increases in volume have also been reported (Chaney et al., 2014), such effects are less common than decreases in volume. Volumetric reductions in adults who experienced ELS have been reported in the hippocampus (Chaney et al., 2014; Dannlowski et al., 2012; Teicher, Anderson, & Polcari, 2012; Vythilingam et al., 2002), anterior cingulate cortex (Baker et al., 2013; Cohen et al., 2006; Dannlowski et al., 2012; Treadway et al., 2009), orbitofrontal cortex (Chaney et al., 2014; Dannlowski et al., 2012), dorsal prefrontal cortex (Chaney et al., 2014; van Harmelen et al., 2010), insula (Cohen et al., 2006; Dannlowski et al., 2012), and caudate (Cohen et al., 2006; Dannlowski et al., 2012).

In addition to changes in grey matter volume, ELS has also been associated with global and regional reductions in white matter volumes (Choi, Jeong, Rohan, Polcari, & Teicher, 2009; Lu et al., 2013; Sheridan, Fox, Zeanah, McLaughlin, & Nelson, 2012). One of the most consistent findings regarding the impact of ELS on the brain concerns the corpus callosum, a thick band of fibres which connects the two cerebral hemispheres (Martin, 2006). In their review article, Teicher and Samson (2016) reported that 16 out of 21 studies which examined the corpus callosum in people who had experienced ELS found significant reductions in its area or integrity. In addition to findings involving the corpus callosum, an interesting and emerging body of work suggests that alterations in other white matter tracts may be specific to the type of ELS that was experienced. Specifically, experience of parental verbal abuse has been associated with reduced integrity in the left articulate fasciculus, a tract which is involved in language processing (Choi et al., 2009), whilst experience of witnessing domestic violence has been associated with reduced integrity in the left

inferior longitudinal fasciculus, a tract which is connected to the visual cortex (Choi, Jeong, Polcari, Rohan, & Teicher, 2012).

Of all the brain regions that have been linked to ELS, the hippocampus and amygdala appear to be particularly vulnerable to its effects (McCrory, De Brito, & Viding, 2010; Paquola, Bennett, & Lagopoulos, 2016; Teicher & Samson, 2016). ELS is associated with volumetric reductions in hippocampal grey matter in adults who experienced ELS (Chaney et al., 2014; Dannlowski et al., 2012; Teicher et al., 2012), with significant effects reported across 30 individual papers (Teicher & Samson, 2016). Evidence for volumetric reductions in the amygdala is less consistent, with reports of both increases and decreases in amygdala volume in adults who experienced ELS (Pechtel, Lyons-Ruth, Anderson, & Teicher, 2014; Tottenham et al., 2010). Other work has found no effect of ELS on amygdala structure (Andersen et al., 2008; Dannlowski et al., 2012). Though a consistent picture of the effects of ELS on amygdalar structure has yet to be elucidated, there is now compelling evidence for a relationship between ELS and functional alterations in the amygdala. This is discussed in more detail in § 1.2.2.2.

A thorough understanding of the specific effects of ELS on brain anatomy is elusive, due to the fact that many of the studies addressing this question have recruited participants with mental health conditions (§ 1.2.1.1). As a result, it has been difficult to distinguish between the effects of ELS and the effects of mental illness on brain structure. Significantly, however, there is some evidence for a relationship between ELS and alterations in adult brain morphology even in the absence of mental illness. Studies which have examined the effects of ELS in groups of people with and without mental illness have found alterations which are specific to ELS and not to diagnostic status (Chaney et al., 2014; van Harmelen et al., 2010). For example, Chaney et al. (2014) recruited four groups of participants; mentally healthy participants without any history of ELS, mentally healthy participants with a history of ELS, participants with depression and no history of ELS, and participants with depression and a history of ELS. They found that ELS was associated with reduced hippocampal volume in participants with and without depression, and that ELS group explained a

significant amount of the variance in hippocampal volumes even after controlling for depression status. In addition, studies which have recruited only mentally healthy adults have found significant associations between ELS and structural alterations in grey and white matter (Dannlowski et al., 2012; Lu et al., 2013).

Taken together, these findings provide initial evidence that ELS may be associated with anatomical alterations in the brain which cannot be fully explained by mental illness. This raises the possibility that adults who have not been diagnosed with a clinical condition could nevertheless encounter neurocognitive difficulties associated with their past experiences of ELS. However, examination of anatomical changes alone cannot determine the veracity of this possibility, as structural alterations do not necessarily predict functional alterations. For example, based on the evidence currently available, the hippocampus appears to be especially vulnerable to ELS at the structural level, whilst the amygdala is more vulnerable at the functional level (Teicher & Samson, 2016). In light of this, findings which have examined the functional neural correlates of ELS will be reviewed in the following section.

1.2.2.2. Functional alterations in neural activation in adults who experienced early life stress

In comparison to work on the structural neural correlates of ELS, there has been a paucity of investigation into the functional neural correlates of ELS (Hart & Rubia, 2012). Most of the studies which have taken a functional approach have used functional magnetic resonance imaging (fMRI), a technique which measures the ratio of oxygenated to deoxygenated cerebral blood (Harmon-Jones & Beer, 2009). Brain regions which use more oxygenated blood during a given task are assumed to be involved in performance of the task. Initial work with fMRI techniques has revealed evidence of ELS-related changes in striatal regions during reward anticipation (Boecker et al., 2014; Dillon et al., 2009; Teicher & Samson, 2016), and in limbic regions during the processing of threatening stimuli (Dannlowski et al., 2012; Hein & Monk, 2017).

Two fMRI studies measured reward anticipation in adults who experienced ELS by examining neural activation to a cue which represented a potential monetary reward (Boecker et al., 2014; Dillon et al., 2009). Both studies found that adults who had experienced ELS showed hypo-activation in striatal regions involved in reward anticipation. Teicher and Samson (2016) raise the interesting possibility that this hypo-activation to reward serves to shift the balance towards avoidance during approach-avoidance conflicts, which may in turn support survival in abusive situations. This hypothesis aligns with Pollak et al.'s (2009) suggestion that maltreated children's ability to identify threatening facial expressions faster than non-maltreated children serves the purpose of helping them to avoid danger. However, to the author's knowledge, the relationship between ELS and atypical avoidance behaviour has received very little empirical investigation, an issue which is discussed in detail in § 1.4. As a result, the doctoral research presented in this thesis aims to examine behavioural and neural correlates of avoidance responding in adults who experienced ELS. The results of this work are presented in Chapter 3 and Chapter 5, respectively.

In addition to its association with hypo-activation in reward regions, ELS has also been associated with greater amygdala responsivity to emotional facial expressions in adult participants (Hein & Monk, 2017). Numerous studies have reported an association between ELS and enhanced amygdala responsivity to angry and fearful facial expressions (Dannlowski et al., 2012; Di Iorio et al., 2017; Redlich et al., 2015), as well as to sad facial expressions (Dannlowski et al., 2013; Grant, Cannistraci, Hollon, Gore, & Shelton, 2011) and to emotional expressions in general (van Harmelen et al., 2013). A minority of studies have found either no effect of ELS on amygdala responsivity to facial expressions (Jedd et al., 2015), or a negative relationship between ELS and amygdala activity (Clark, Sweet, Morgello, Philip, & Cohen, 2017; Taylor, Eisenberger, Saxbe, Lehman, & Lieberman, 2006). Clark et al. (2017) note that both the studies that have found a negative relationship between ELS levels and amygdala responsivity to emotional expressions used a resting baseline, in which stimulus-related activity is compared to resting levels of activity, rather than

the more commonly used active baseline, in which the activity associated with a 'neutral' stimulus (e.g. neutral facial expressions) is used as the baseline. They posit that higher levels of ELS may be associated with higher resting baselines, and as such the increase in activity following stimulus presentation would not be as large in people with high levels of ELS as in people with lower levels of ELS (and lower resting baselines). Therefore, whilst there are some inconsistencies across studies, there is nevertheless substantial evidence to suggest that ELS is associated with atypical activity in the amygdala, a brain region which is involved in emotional processes such as encoding of emotional memories (LeDoux, 1993), fear conditioning, and detection of salient stimuli (Davis & Whalen, 2001).

As discussed above, studies using the fMRI technique have identified alterations in neural activity during the processing of rewarding and threating stimuli in mentally healthy adults who experienced high levels of ELS (Boecker et al., 2014; Dannlowski et al., 2012). This provides support for the possibility that even in mentally healthy people, high levels of ELS are associated with changes in the way that specific brain regions respond to social and non-social cues. However, whilst fMRI provides a high spatial resolution, it is somewhat limited in its temporal resolution. This means it is unable to capture ELS-related alterations in neural mechanisms which occur over a matter of milliseconds (Harmon-Jones & Beer, 2009; Shackman, Shackman, & Pollak, 2007). As a result, it is not possible to determine which specific neural mechanisms are related to ELS, nor to specify whether ELS-related changes in neural processing begin early, at the implicit 'automatic' level, or only appear later during more higher-order processing (see § 2.1.2 for a discussion of the concept of 'early' and 'late' neural processing). The ERP technique can overcome these limitations due to its high temporal resolution, which is in the order of milliseconds. The following section will provide a general overview of the ERP technique and then discuss the few studies to date which have used this technique to examine neural processing alterations in people who experienced ELS.

1.2.2.3. The event-related potential technique

Electroencephalography (EEG) is a neuroimaging technique in which electrical signals generated by populations of cortical pyramidal neurons are measured directly from the scalp (Luck, 2014). The recorded output is known as an electroencephalogram. The ERP technique extracts information from the electroencephalogram in order to isolate neural responses to specific stimuli (events). In this way, the time course of a neural response to a given stimuli can be mapped, and specific components of this response can be identified. A detailed description of the ERP technique can be found in § 2.1.1.

Despite its numerous advantages, the ERP technique has been relatively neglected in the ELS literature in favour of structural and functional MRI studies (Teicher & Samson, 2016). In addition, the vast majority of studies which have employed the ERP technique to investigate the effects of ELS have been carried out with children, with very few studies recruiting adult participants. The relative absence of ERP studies represents a critical gap in the ELS literature, as it means that information on the time course of ELS-related neural alterations is limited. Specifically, there remains a lack of clarity on the extent to which ELS affects early automatic processing as opposed to later higher-order processing. This is particularly important given that the timing of neural perturbations could have significant implications for potential interventions which seek to support those who experienced high levels of ELS. For example, in cases where automatic processing is biased towards threat, techniques which focus on attentional processes, such as cognitive bias modification (Teachman, Joormann, Steinman, & Gotlib, 2012), may be more beneficial than techniques which focus on making changes to higher-order processing, such as cognitive therapy. The present research therefore used the ERP technique to examine the effect of ELS on automatic processing of social and non-social cues in mentally healthy adults. Specifically, emotional facial expressions were used as social cues whilst stimuli associated with an aversive outcome were used as non-social threat cues. The findings of these studies are presented in chapters 4 and 5, respectively. The following

section will provide an overview of previous literature which has used the ERP technique to examine the effect of ELS on neural processes.

1.2.2.4. Use of the event-related potential technique to examine neural correlates of early life stress

A small number of studies have examined ERP components in participants who experienced ELS. To the author's knowledge, only two of these studies have focussed on adult participants (Boecker et al., 2014; Chu, Bryant, Gatt, & Harris, 2016); the vast majority have focussed on children or adolescents. It is important to note that some ERPs such as the P1, a visual perceptual component originating from the visual cortex, are present from birth or infancy onwards (Nelson & McCleery, 2008), whilst others, such as the later visual component the N170 have a much more protracted course of development lasting from the age of four until adulthood (Nelson & McCleery, 2008). This means that ERP findings in the child and adolescent literature may not relate directly to the adult brain, a problem that is discussed in more detail in § 1.3.2.2. However, given the lack of ERP evidence from adult populations, a brief overview of developmental ERP findings is warranted.

The majority of ERP studies which have looked at correlates of ELS have used emotional facial expressions as stimuli (Cicchetti & Curtis, 2005; Curtis & Cicchetti, 2011; Curtis & Cicchetti, 2013; Shackman & Pollak, 2014; Shackman et al., 2007), in light of behavioural evidence for atypical processing of emotional facial expressions following experiences of ELS (Pollak & Kistler, 2002; Pollak et al., 2009; Pollak & Sinha, 2002). Presentation of facial stimuli typically evokes two early visual ERP components, the P1 and the N170. Research has found that ELS may be associated with alterations in these components, both in response to emotional facial expressions in general (Moulson, Fox, Zeanah, & Nelson, 2009), and in relation to angry facial expressions specifically (Curtis & Cicchetti, 2011; Nelson, Westerlund, McDermott, Zeanah, & Fox, 2013). The effects of ELS on the P1 and N170 components are discussed in depth in § 1.3.2.2.

A series of studies by Pollak and colleagues took a slightly different approach to the study of ERP responses associated with ELS (Pollak, Cicchetti, Klorman, & Brumaghim, 1997; Pollak, Klorman, Thatcher, & Cicchetti, 2001; Shackman & Pollak, 2014; Shackman et al., 2007). As with previous studies, they used emotional facial expressions as stimuli, but the ERP component of interest was not an early visual component but a later central-parietal component, the P3b. The P3b appears relatively late in the waveform, typically occurring between 350 and 550 ms (Nelson & McCleery, 2008), and is thought to reflect allocation of attentional resources (Shackman et al., 2007). Pollak and colleagues asked maltreated children and non-maltreated controls (aged between 6 and 12 years, across all studies) to press a button when they saw a target stimulus, which consisted of an emotional facial expression. When the target stimulus was an angry facial expression, maltreated children consistently showed a larger P3b response than non-maltreated children (Pollak et al., 2001; Shackman & Pollak, 2014; Shackman et al., 2007). This effect was specific to angry expressions; maltreated and non-maltreated children did not differ in their P3b responses to happy or fearful facial expressions (Pollak et al., 2001; Shackman & Pollak, 2014). These findings indicated that, relative to non-maltreated children, maltreated children allocated more attentional resources to the processing of angry emotional expressions, according with behavioural findings of hyper-responsivity to anger in those who experienced ELS (Gibb, Schofield, & Coles, 2009; Pollak et al., 2009; Pollak & Sinha, 2002).

Atypical responses to angry facial expressions have been frequently interpreted in the literature as alterations in responsivity to threat (Hein & Monk, 2017). However, despite growing interest in enhanced threat responsivity as a neural correlate of ELS (McCrory et al., 2017), few studies have examined responsivity to non-facial threatening stimuli. Meyer et al. (2015) took an interesting approach to this topic by examining neural responsivity to the commission of errors in children who had experienced ELS in the form of authoritarian parenting. In the context of harsh parenting, errors can be conceptualised as a form of threat, as parents may respond to their children's mistakes with punishment (Meyer et al., 2015).

Meyer et al. (2015) measured the parenting style experienced by a group of children aged 3 years, then used EEG to measure the same children's neural responses during a Go/No-go task when they were 6 years old. The task required participants to make a response to a subset of stimuli, and withhold a response to another subset of stimuli. Mistakes in this task generate an ERP known as the error-related negativity (ERN) component, a negative deflection which occurs over frontal-central sites about 50 ms after an error has been made. Meyer et al. (2015) found that higher rates of authoritarian parenting when the children were aged 3 were associated with increased ERN responses to task errors when the children were aged 6. Interestingly, the amplitude of the ERN partially mediated the relationship between authoritarian parenting and anxiety in the children. In light of this, Meyer et al. (2015) suggest that authoritarian parenting may lead to an increased ERN which in turn leads to increased anxiety. Though speculative, this interpretation fits neatly with the theory of latent vulnerability (McCrory & Viding, 2015), which posits that ELS gives rise to neural adaptations which in turn increase an individual's risk of developing a mental health condition. The theory of latent vulnerability is described in detail in the following section.

1.2.3. The theory of latent vulnerability

An extensive body of research, discussed in § 1.2.1, has found that high levels of ELS are associated with increased risk of mental illness later in life (Kessler et al., 2010; Heim & Nermeroff, 2001). Similarly, as discussed in § 1.2.2.2, there is growing evidence for a link between ELS and changes in neurocognitive processes such as emotional face processing and responsivity to threat (Hein & Monk, 2017; McCrory et al., 2017). The theory of latent vulnerability, introduced in 2015 by Eamon McCrory and Essi Viding, draws upon these findings in an attempt to explain some of the ways in which ELS increases the risk of mental illness.

The theory of latent vulnerability (McCrory & Viding, 2015) posits that ELS leads to neurocognitive adaptations, or latent vulnerabilities, which help the individual to survive in a maltreating or neglectful environment. The theory suggests that these neurocognitive changes could in turn

predispose the individual to the development of mental illness later in life. Enhanced threat reactivity, seen behaviourally in maltreated individuals' hyper-responsivity to threatening (angry) facial expressions (Gibb et al., 2009; Pollak & Kistler, 2002; Pollak et al., 2009; Pollak & Sinha, 2002), and neurologically in their increased amygdala reactivity to these threatening facial expressions (Dannlowski et al., 2012; Redlich et al., 2015), is an example of a neurocognitive adaptation which may occur as a consequence of ELS. This adaptation could be seen as a beneficial in abusive contexts; it could help the individual to react to danger quickly and increase their chances of avoiding a harmful outcome. However, according to the theory of latent vulnerability, adaptations such as increased threat reactivity can cause problems when they are applied to positive normative contexts later in life (McCrory et al., 2017; McCrory & Viding, 2015). McCrory et al. (2017) suggest that this could happen both directly and indirectly. At the direct level, individuals who are hyper-responsive to threat may be limited in the extent to which they can devote cognitive resources to other, more positive aspects of social development. At the indirect level, a hyper-reactive approach to threat, and especially to social cues of threat such as angry facial expressions, could lead to high levels of interpersonal conflict and misunderstanding. Consequently, the individual could find themselves less well-equipped with positive cognitive and social resources which could act as a buffer against stress later in life. This in turn could increase their risk of developing a mental illness. Importantly, McCrory and Viding (2015) state that latent vulnerabilities are not in themselves symptoms of mental illness; rather they are adaptations which could increase the risk of a mental illness occurring in response to stressors later in life. This conceptualisation of risk can account for the fact that, in some cases, people who experience ELS do not develop mental health problems until years after the abuse itself has ended (Teicher, Samson, Polcari, & Andersen, 2009). This is illustrated by a study which examined the number of years between offset of abuse and onset of depression (Teicher et al., 2009). The researchers recruited women who had been sexually abused as children and found that, amongst the 62 % of women who met criteria for

depression, the mean number of years between the offset of the sexual abuse and the onset of depression was 9.6 years.

The theory of latent vulnerability is still in its relative infancy, and a full account of the neurocognitive mechanisms which may be vulnerable to ELS has yet to be elucidated. In light of this, research which investigates neurocognitive adaptations in adults who experienced ELS is particularly valuable, as identification of these mechanisms could be used to inform interventions which aim to reduce future vulnerability to mental illness. The present research therefore sought to investigate two neural mechanisms which could be disrupted following ELS: emotional face processing and avoidance of threat.

The selection of these two mechanisms of interest was based on an examination of the literature to first determine which neurocognitive mechanisms have been previously identified as potentially related to ELS, and then to identify the gaps in our current knowledge about the relationship between ELS and these neurocognitive mechanisms. The first neurocognitive mechanism, emotional face processing, was considered in light of behavioural evidence for altered emotional face processing in children who experienced maltreatment (discussed in detail in Section 1.3.1; da Silva Ferreira, Crippa, & Osorio, 2014; Pollak et al., 2009; Pollak & Sinha, 2002), and evidence from functional neuroimaging which has found amygdala hyper-responsivity to emotional facial expressions in adults who have experienced ELS (Dannlowski et al., 2012; Redlich et al., 2015). Despite growing interest in emotional face processing as a potential neurocognitive adaptation to ELS, the majority of behavioural and ERP studies have been carried out with either children (e.g. Cicchetti & Curtis, 2005; Pollak et al., 2009; Shackman et al., 2007) or adults with mental health problems (e.g. Nicol, Pope, & Hall, 2014; Russo et al., 2015), whilst the remainder of the neuroimaging work has largely utilised the fMRI technique (e.g. Dannlowski et al., 2012; Redlich et al., 2015). As a result, there is a dearth of research examining the potential relationship between ELS and alterations in emotional face processing in mentally healthy adults, especially at the behavioural level and in ERP paradigms. The present research therefore sought to examine the relationship between ELS and face

processing in mentally healthy adults. This was examined at the behavioural level (Chapter 3) and at the neural level (Chapter 4). A detailed review of previous work on this topic is presented in § 1.3.

The second neurocognitive mechanism examined by this research is avoidance of threat. There is now relatively substantial evidence for enhanced processing of threat in people who have experienced early maltreatment (McCrory et al., 2017). However, it is unclear whether people who experienced ELS also show altered avoidance of threat. The lack of research on this topic is surprising given the extensive evidence from animal work which suggests that avoidance behaviour is altered following ELS. In light of this, the present research examined the relationship between ELS and mentally healthy young adults' self-reported avoidance of social threat (angry facial expressions; Chapter 3), and the relationship between ELS and neural indices of avoidance of non-social threat in a group of mentally healthy young adults (Chapter 5). A detailed review of previous work on the relationship between ELS and avoidance of threat is presented in § 1.4.

1.3. Emotional face processing and early life stress

A growing body of research suggests that ELS is associated with changes in the processing of emotional facial expressions, both at the behavioural and neural levels. For the purposes of this thesis, the term 'emotional facial expression' is used to describe face stimuli displaying neutral expressions as well as those displaying specific emotions. This is because neutral facial expressions are not always perceived as neutral (Suess, Rabovsky, & Abdel Rahman, 2015), and evidence suggests that ELS may be associated with perception of negative emotions in facial expressions that have been classified as neutral (Pollak & Kistler, 2002). The following section of this review will provide an overview of the behavioural and neural evidence for alterations in emotional face processing following ELS. As discussed previously, the majority of studies, especially in the behavioural literature, have focussed on children. As a result, it remains unclear whether the alterations in emotional face processing seen in children who have experienced ELS can also be observed in adults who experienced ELS. This represents a critical gap in the literature, as it remains unclear whether the association between ELS and altered emotional face processing persists over time into adulthood. In light of this, the present research focussed on adults who had experienced ELS, in order to examine whether the effects reported previously in children are also present in adults.

1.3.1. Altered responding to angry facial expressions following early life stress

There is a lack of consistency in the behavioural paradigms used to assess the relationship between ELS and processing of emotional facial expressions, with cross-experimental differences in the stimuli used and the outcome measures recorded (Ferreira, Crippa, & Osorio, 2014). However, most of the studies in this field fall into one of two categories: identification paradigms (Gibb et al., 2009; Pollak & Kistler, 2002; Pollak et al., 2009; Pollak & Sinha, 2002), and attentional bias paradigms (McCrory et al., 2013; McCrory et al., 2011; Pollak et al., 1997; Pollak et al., 2001; Pollak & Tolley-Schell, 2003). Most identification paradigms involve the use of a continuum of face stimuli. At one end of this continuum is a prototypical

emotional expression, e.g. an angry facial expression. At the other end of the continuum is a different stimulus, most commonly a neutral facial expression. The intensity of the emotional expression is gradually increased across the continuum. For example, in an angry trial, the stimulus will begin as a neutral face which gradually displays more and more anger until it reaches a prototypical angry facial expression. Studies which have used this paradigm to examine the effect of ELS on children's emotional face processing have found that, compared to non-maltreated children, children who have been abused identify the expression of anger earlier in the continuum (Pollak & Kistler, 2002; Pollak et al., 2009; Pollak & Sinha, 2002). To the author's knowledge, only one study has used an identification paradigm to investigate the effect of ELS on emotional face processing in adult participants (Gibb et al., 2009). This study found similar effects to the studies carried out with child participants, such that higher levels of ELS were associated with earlier identification of anger (Gibb et al., 2009).

In contrast to its relationship with enhanced identification of anger; ELS does not appear to be related to changes in the identification of happiness in facial expressions, in either children or adults (Gibb et al., 2009; Pollak & Kistler, 2002; Pollak et al., 2009; Pollak & Sinha, 2002). However, studies which have examined the effect of ELS on identification of negative emotions other than anger have found mixed results. A study by Masten et al. (2008) reported that maltreated children were faster to identify the emotion of fear than non-maltreated children, though other work has found no effect of ELS on identification of fear (Pollak & Kistler, 2002; Pollak et al., 2009; Pollak & Sinha, 2002). The discrepancy in findings across studies may be explained by methodological differences; the study which found an effect of ELS on processing of fearful facial expressions used an older sample of children (mean age 11 years for the maltreated group and 12 years for the control group; Masten et al., 2008), whereas the studies which did not find this effect typically examined participants whose mean age was around 9 years old (Pollak & Kistler, 2002; Pollak et al., 2001; Pollak et al., 2009; Pollak & Sinha, 2002). This explanation is supported by research showing that recognition of fear in emotional expressions improves across childhood and adolescence, whereas

recognition of happiness and anger is well established by the age of 6 (Lawrence, Campbell, & Skuse, 2015). Alterations in the processing of another negative emotion, sadness, have been associated with ELS, though in this case in the opposite direction, such that ELS is associated with impaired identification of sadness (Pollak & Sinha, 2002). However, other studies have found no relationship between ELS and identification of sadness (Pollak & Kistler, 2002; Pollak et al., 2009). The discrepancy in findings could again be explained by methodological differences between studies; the study which found impaired identification of sadness amongst maltreated children used an atypical paradigm in which a scrambled image was morphed gradually into the emotional expression of interest (Pollak & Sinha, 2002). This differs from the other studies, in which a different expression (neutral or emotional) was gradually morphed into the emotional expression of interest. Despite some inconsistencies between findings, the studies which have used identification paradigms to examine the effect of ELS on emotional face processing are consistent in their finding that maltreated children and adults show enhanced identification of anger in facial expressions.

Whilst evidence from identification paradigms is relatively consistent, the relationship between ELS and responding in attentional bias paradigms is less clear. In attentional bias paradigms, participants are required to make a response as quickly as possible to a target. In some paradigms, the target is an emotional facial stimulus (e.g. McCrory et al., 2011; Pollak et al., 1997; Pollak et al., 2001), whilst in other paradigms, the emotional facial stimulus is presented prior to the target as a cue, and the target itself is a dot or asterisk (e.g. Gibb et al., 2009; McCrory et al., 2013; Pollak & Tolley-Schell, 2003). Studies which use attentional bias paradigms typically measure reaction time as a dependent variable, with faster reaction times towards a specific stimulus interpreted as an attentional bias towards that stimulus. Three studies with maltreated children found no effect of ELS on reaction times to emotional facial expressions presented as targets (McCrory et al., 2011; Pollak et al., 1997; Pollak et al., 2001), though one of these studies found that maltreated children were more accurate than non-

maltreated children when responding to angry targets, as measured by fewer false alarms and premature responses (Pollak et al., 2001).

In four other studies with maltreated children, the emotional expression was presented as a cue that occurred prior to the target, which was a dot or asterisk (Kelly et al., 2015; McCrory et al., 2013; Pine et al., 2005; Pollak & Tolley-Schell, 2003). Pollak and Tolley-Schell (2003) found that maltreated children showed faster reaction times to targets which followed angry expressions than targets which followed happy expressions, an effect that was not present in the non-maltreated children. This was interpreted as an attentional bias towards angry facial expressions in children who had been maltreated. On the other hand, two additional studies with maltreated children found the opposite effect, such that maltreated children showed an attentional bias away from angry facial expressions (Kelly et al., 2015; Pine et al., 2005). This was interpreted by the authors as attentional avoidance of angry facial expressions. The discrepancy between these findings could be explained by the paradigm that was used; Pollak and Tolley-Schell (2003) used a paradigm in which children were presented with a single facial expression stimulus on either the left or the right of the screen, followed by a target on either the left or the right of the screen. In contrast, both Kelly et al. (2015) and Pine et al. (2005) used a paradigm in which a pair of facial expressions were presented on either side of the screen, followed by a target which was presented on one side of the screen. Therefore, when the angry facial expression was the only cue present, maltreated children showed a bias towards it, but when the angry facial expression was presented alongside a neutral facial expression, the maltreated children showed a bias away from the angry facial expression. A different study by McCrory et al. (2013) presented facial stimuli pre-consciously for 17 ms, and found no evidence for an attentional bias towards or away from angry facial expressions. This suggests that, at least at the behavioural level, attentional biases towards or away from angry facial expressions may only emerge when the stimuli are presented for long enough to reach the level of conscious processing.

The effect of ELS on adults' attentional biases towards emotional facial expressions was investigated by Gibb et al. (2009) using a paradigm

similar to that employed by Pine et al. (2005) and Kelly et al. (2015). Gibb et al. (2009) found that high levels of ELS were associated with a significant attentional bias towards angry facial expressions but not towards happy or sad facial expressions. This finding is at odds with the findings of Pine et al. (2005) and Kelly et al. (2015), who found an attentional bias away from angry facial expressions. The difference in findings may be explained by differences in stimulus presentation time, which was 1000 ms in Gibb et al.'s (2009) study and 500 ms in the other two studies. Alternatively, differences in the age of the participants may explain the effects; the participants in the studies by Pine et al. (2005) and Kelly et al. (2015) were children (mean age 10.3 years and 12.7 years in the maltreated groups respectively), whilst the participants in Gibb et al.'s (2009) study were young adults (mean age 19.2 years). This highlights the need for more studies which address the effects of ELS in adult participants, as it cannot be assumed that the effects of ELS will present in the same way in adults as they do in children. In light of this, the research presented in this thesis focussed on adult participants.

Taken together, evidence from behavioural measures of emotional face processing provides support for enhanced identification of anger in emotional facial expressions in children and adults who experienced ELS, as well as alterations in attentional biases which are specific to angry facial expressions. These findings can be interpreted in the context of latent vulnerability; earlier identification of anger is likely to be highly adaptive in an abusive environment, as it provides the individual with more time to avoid or prepare for the abuse (McCrory & Viding, 2015; Pollak et al., 2009). However, given the importance of emotional face processing for successful social interactions, approaching healthy relationships with an adaptation suited to unhealthy relationships could lead to social difficulties, which could in turn increase the risk of developing a mental illness (McCrory et al., 2013).

1.3.2. Neural alterations in emotional face processing following early life stress

Behavioural studies have highlighted the relationship between ELS and alterations in emotional face processing (§ 1.3.1). However, these studies are limited in their ability to examine the mechanisms which underlie this relationship. An approach that has been used to investigate these mechanisms in more depth is functional neuroimaging. The following section will provide an overview of the findings of neuroimaging studies which have examined the relationship between ELS and alterations in emotional face processing, beginning with findings from fMRI work and moving on to address findings from the small number of ERP studies which have been conducted in this field.

1.3.2.1. Amygdala hyperactivity to emotional facial expressions following early life stress

Functional magnetic resonance imaging (fMRI) studies with children and adolescents (mean age between 12 and 14 years) have found enhanced amygdala activation to angry facial expressions in those exposed to violence, physical abuse, caregiver deprivation and emotional neglect (Maheu et al., 2010; McCrory et al., 2013; McCrory et al., 2011). As discussed in § 1.3.2.1, higher levels of ELS are also associated with greater amygdala activation to angry facial expressions in adult participants (Dannlowski et al., 2012; Di Iorio et al., 2017; Redlich et al., 2015). These findings are consistent with behavioural evidence for enhanced identification anger in facial expressions amongst people who have experienced ELS (§ 1.3.1). However, there have also been reports of ELS-related enhancements in children and adults' amygdala activity to other facial expressions, including happy expressions (McCrory et al., 2013; van Harmelen et al., 2013), fearful expressions (Clark et al., 2017; Dannlowski et al., 2012; Maheu et al., 2010; Tottenham et al., 2011) and sad expressions (Dannlowski et al., 2013; Grant et al., 2011). The fact that ELS is associated with amygdala hyperactivity to a range of facial expressions, and not just to angry expressions, raises the possibility that individuals with ELS show abnormal hyper-arousal to all facial stimuli (van Harmelen et al., 2013).

This introduces a paradox into the literature on ELS and emotional face processing, such that the behavioural and neuroimaging evidence are not in alignment with one another. Specifically, the behavioural evidence mostly converges on a conclusion of hyper-sensitivity to anger, with limited evidence for hyper-sensitivity to other emotional expressions (§ 1.3.1). In contrast, a number of neuroimaging studies have found a non-specific hyperactivity to emotional facial expressions in general (van Harmelen et al., 2013; Di Iorio et al., 2017; McCrory et al., 2013). This paradox could reflect a lack of sensitivity in the behavioural paradigms, such that they are unable to detect some of the functional changes observed at the neural level. Indeed, reports of group-specific alterations in neural activity in the absence of behavioural differences are common in the wider neuroscientific literature. For example, research has found that adolescents and adults show similar behavioural performance across a number of cognitive tasks, yet at the neural level these same tasks engage different brain regions in adolescents and adults (Luna, Padmanabhan, & O'Hearn, 2010). Often these neural differences are reflected in more widespread activation in adolescents with more focal activation in adults (Durston et al., 2006).

Another potential explanation for the differential effect of ELS on behavioural and neural indices of emotional face processing concerns the involvement of compensatory neural processes. For example, ELS may indeed be associated with amygdala hyperactivity to all emotional facial expressions (and not just to threatening facial expressions), but this hyper-activation may not result in altered behavioural responding to non-threatening stimuli because other brain regions act in a compensatory manner to prevent inappropriate responding. McCrory et al. (2013) carried out an fMRI study in which children who had been maltreated viewed angry and happy facial expressions presented pre-consciously (i.e., implicitly) for 17 ms. In contrast to their prediction of anger-specific amygdala hyper-activation in the group of maltreated children, they found that maltreated children showed amygdala hyper-activation to both angry and happy facial expressions. Supporting the idea presented above, they interpreted this finding as an early hypervigilance for emotional valence in individuals with

high levels of ELS, and suggested that a selective response to threat may depend upon later stages of neural processing.

The idea that ELS is associated with an early hyper-activity to all emotional valance followed by later hyper-activity to threat specifically is intriguing, but neither behavioural nor fMRI methodologies are well equipped to examine this possibility. As discussed in § 2.1, the ERP technique has a high temporal resolution which allows for the examination of neural processes occurring in the first 200 ms after stimulus presentation. In light of this, the present research used the ERP technique to examine early perceptual processing of emotional facial expressions in young adults who experienced ELS (Chapter 4), with a specific focus on the N170. The N170 is an early visual component which is thought to be modulated by re-entrant connections from the amygdala (Dolan, Heinze, Hurlemann, & Hinrichs, 2006). If ELS were associated with enhanced amygdala activation to emotional valence in general, as suggested by McCrory et al. (2013), then it would be expected that the N170 would be enhanced in response to all emotional facial stimuli, irrespective of the emotion being depicted. Alternatively, if the ELS-related amygdalar hyper-activity were specific to threat rather than emotional valence in general, it would be expected that the N170 would be enhanced in response to angry facial expressions but not to happy or neutral facial expressions. The results of the present investigation into these two possibilities are presented in Chapter 4.

1.3.2.2. Alterations in early perceptual processing of emotional facial expressions following early life stress

The ERP technique used in the present research is well equipped to address the inherent limitations of fMRI and behavioural paradigms, as it allows for examination of the time course of neural responses to specific stimuli. As described in detail in § 2.1.1, the ERP technique involves the examination of ERP components, positive and negative voltage deflections which are time-locked to the onset of a sensory, motor, or cognitive event. Two ERP components, the P1 and the N170, are of particular interest in the study of emotional face processing. The N170, and to a lesser extent the P1, are considered to be ‘face-sensitive’, that is, their amplitude is

increased in response to faces in comparison to objects (Dering, Martin, Moro, Pegna, & Thierry, 2011; Eimer, 2011b). The P1 and N170 have subsequently garnered interest in ELS research, as they represent neural correlates of a mechanism (emotional face processing) that has been previously linked to ELS in behavioural and fMRI studies.

The vast majority of studies examining the electrophysiological indices of face processing following ELS have been carried out with children and infants, with only one study, to the author's knowledge, focussing on mentally healthy adults (Chu et al., 2016). In light of this, it is important to acknowledge the complicated relationship between ERPs observed in adults and ERPs observed in children. One consideration is that similar ERP components may represent different neural mechanisms in adults and children. For example, perceptual processing of facial stimuli is indexed in adult participants by the aforementioned N170, which occurs over occipital-temporal regions of the scalp. However, the N170 has a protracted course of development which does not reach maturity until at least adolescence (Nelson & McCleery, 2008). Therefore, whilst an N170 component can be seen in children as young as four, it may not necessarily reflect the same functional mechanisms as the N170 observed in adults (Nelson & McCleery, 2008). In fact, it is thought that other components, such as the P400, a positive deflection with an occipital-temporal scalp distribution, may better reflect early perceptual processing of facial expressions in infants and young children (Nelson & McCleery, 2008).

Attempts to synthesise literature on the ERP correlates of face processing across development are further complicated by the fact that terms such as 'N170' or 'N150' are occasionally used in developmental studies to label a component which does not correspond to the adult N170, due to its different topographical distribution to the adult N170 (Cicchetti & Curtis, 2005; Parker & Nelson, 2005). It is therefore important to acknowledge that ERP findings in child populations are unlikely to show a direct correspondence with ERP findings in adult populations. Nevertheless, a discussion of the developmental literature may offer insights that could inform hypotheses about the likely effect of ELS on adults' ERP responses to emotional facial expressions.

A notable portion of the work assessing ERP responses to emotional facial expressions in those who experienced ELS has come from a series of studies carried out with children participating in the Bucharest Intervention Project (BEIP). The BEIP is an ongoing randomised control trial which follows children who were recruited from Romanian institutions and a control group of children who have never experienced institutional care (Zeanah et al., 2003). The project has provided an opportunity to study the effects of ELS at different developmental stages. Research carried out during infancy found that the infants who had been raised in institutions showed reductions in the peak amplitude of the P1 and the N170 to facial emotional stimuli, irrespective of the specific emotion portrayed (Moulson et al., 2009). However, later work carried out when the children were aged 8, and aged 12, found no effect of institutional care on the peak amplitude of the P1 or N170 in response to emotional facial expressions in general (Nelson et al., 2013; Young et al., 2017). Whilst there was no effect of ELS on responses to emotional facial expressions in general, Nelson et al. (2013) did find an emotion-specific effect in the eight year old children, such that, compared to the control group, children living in institutions showed reduced P1 peak amplitudes to angry facial expressions, an effect that did not occur in response to fearful or neutral facial expressions. However, this effect was no longer apparent when the cohort was tested again at the age of 12 years (Young et al., 2017).

Whilst the BEIP focusses on individuals who experienced early institutionalisation, other work has focussed on individuals who did not live in institutions but experienced maltreatment documented by child protection services. Curtis and Cicchetti (2011) found that young children (mean age 42 months) exposed to maltreatment showed an overall reduction in N170 peak amplitudes to emotional facial expressions relative to non-maltreated children. However, within the maltreated group there was a trend towards a larger N170 response to happy facial expressions than to angry or neutral facial expressions, whilst the non-maltreated group showed no difference in N170 peak amplitude to individual emotional expressions. On the other hand, the researchers found that P1 peak amplitudes were larger in maltreated children relative to non-maltreated children, and within the

maltreated group, P1 peak amplitudes were larger to angry facial expressions than to happy or neutral facial expressions. These findings are at odds with a different study carried out by the same authors, which found that P1 peak amplitudes to angry facial expressions were reduced in a group of maltreated infants (age 15 months) relative to non-maltreated infants, and that amongst the maltreated group only, the P1 peak amplitude was larger to happy expressions than to angry expressions (Cicchetti & Curtis, 2013).

There is clearly a lot of inconsistency across studies which have examined the effect of ELS on children's early perceptual responses to emotional facial expressions. The finding of enhanced P1 peak amplitudes to angry facial expressions in children who have been maltreated (Curtis & Cicchetti, 2011) is in accordance with behavioural studies showing hyper-sensitivity to anger in children who have been maltreated. However, this interpretation is at odds with other work which has found reduced P1 peak amplitudes to angry facial expressions following institutionalisation and maltreatment (Curtis & Cichhetti, 2013; Nelson et al., 2013), and larger P1 peak amplitudes to happy facial expressions than to angry facial expressions in children who have been maltreated (Curtis & Cicchetti, 2013).

Curtis and Cicchetti (2011) suggest that heightened responding to happy expressions in early perceptual components could be explained by the relative novelty of the stimuli. Specifically, for children who experience ELS, happy facial expressions may be more novel, and consequently more salient, than angry facial expressions. This could explain the finding of increased P1 peak amplitudes to happy facial expressions in this population. However, whilst this suggestion provides an elegant explanation for the heightened responsivity to happy facial expressions in the P1 component, as the P1 is thought to index attention to salient stimuli (Luck, Heinze, Mangun, & Hillyard, 1990), it is less able to explain the heightened responsivity to happy facial expressions in the N170 component, which is thought to index face processing (Eimer, 2011b). An alternative explanation could be that heightened activity in maltreated infants' perceptual responses to happy facial expressions serves as a survival adaptation for the infant; in an abusive or neglectful environment, an ability to respond quickly to any display of affection may help the infant to attain much-needed care.

The only study (to the author's knowledge) which has looked at ERP responses to emotional facial expressions in mentally healthy adults who experienced ELS focussed specifically on the N170 component (Chu et al., 2016). It was found that higher levels of ELS were associated with less differentiation in N170 peak amplitudes to angry and happy facial expressions; specifically, whilst those with no experience of ELS showed greater N170 amplitudes to angry facial expressions than to happy facial expressions, those who experienced high levels of ELS showed similar N170 peak amplitudes to both angry and happy expressions (Chu et al., 2016).

A thorough picture of the ways in which ELS affects the neural time course of emotional face processing is absent from the current literature. This limits our ability to provide an explanation for the hyper-responsivity to anger documented at the behavioural level in children and adults who experienced high levels of ELS. In addition, the almost complete focus on children in this area of ERP research means that there is a dearth of evidence regarding the relationship between ELS and neural responses to emotional facial expressions in adult participants. Young adulthood and late adolescence are periods of time in which many individuals leave home and begin to develop their own social relationships outside of home or school environments. An ability to respond appropriately to social cues of emotion is essential to success in this transitional stage of life. In light of this, it is necessary to establish whether young adults who experienced ELS show alterations in neural responding to emotional facial expressions, as such alterations could represent a significant vulnerability in this population. The present research therefore used the ERP technique to investigate early perceptual responses to emotional facial expressions in a sample of mentally healthy young adults.

1.4. Avoidance and early life stress

As discussed in § 1.2, emotional face processing is not the only neurocognitive mechanism that may be altered following experiences of ELS. An extensive body of research in the animal literature suggests that rats which experienced ELS show changes in their avoidance of cues which represent threat. However, despite this evidence, and the fact that avoidance has played a prominent role in attempts to understand why children who have been abused show hyper-responsivity to angry facial expressions (Pollak et al., 2009), empirical assessment of avoidance as a construct has been all but absent from work with humans who experienced ELS. In light of this, the research presented in this thesis was designed to examine whether young adults who experienced ELS show atypical avoidance of social and non-social threat. This was first examined at the behavioural level by asking young adults to indicate the extent to which they would approach or avoid a series of individuals displaying angry, happy and neutral facial expressions (Chapter 3). Later, avoidance was examined at the neural level by using EEG to record ERP responses to non-social threat cues in a paradigm in which participants could learn to avoid an aversive outcome (Chapter 5).

The following section of this review will provide an overview of avoidance and its relationship with ELS. First, there will be a description of two prominent theories of avoidance, and an overview of the role of anxiety in avoidance behaviour. This will be followed by a description of the brain anatomy involved in avoidance responding. The section will then cover findings from the rat literature regarding the relationship between ELS and avoidance behaviour. Finally, there will be a brief description of two studies which provide some insight into the effect of trauma on avoidance processing in human participants.

1.4.1. Theories of avoidance learning

Successful avoidance of danger is fundamental for survival. However, avoidance can also be maladaptive, with pathological avoidance thought to play a key role in the aetiology and maintenance of various anxiety disorders (Krypotos, Effting, Kindt, & Beckers, 2015). A number of

models of avoidance learning have been described over the years, one of the most influential of which is the two-factor theory proposed by Orval Mowrer (Krypotos et al., 2015; Mowrer, 1951). Mowrer's two-factor theory combined the learning principles of classical and operant (instrumental) conditioning. It states that avoidance learning occurs in two stages. In the first stage, an initially neutral conditioned stimulus (CS) is paired with an aversive unconditioned stimulus (US), such as an electric shock or loud noise. After such pairing, the CS elicits a conditioned fear response due to its association with the aversive US. The presence of this conditioned fear response to the CS can drive an animal to learn that emitting a certain action during the presence of the CS can stop the aversive event from happening (second stage, instrumental conditioning). This leads to negative reinforcement of the action. Instrumental avoidance can be either active, in which the emission of a response allows the animal to avoid the aversive outcome, or passive, in which the omission of a response allows the animal to avoid the aversive outcome.

This can be illustrated by the following example. A rat is placed in a cage with a small barrier through the middle. A flashing warning light (CS) is presented, followed by a foot-shock (US; classical conditioning). The rat learns the association between the warning light (CS) and the shock (US) and becomes fearful of the warning light. It then learns that it can make an avoidance response by jumping over the barrier whenever the warning light (CS) is presented. The avoidance response to the CS is negatively reinforced by a reduction in the fear evoked by the CS. The two-factor theory posits that avoidance learning occurs without the need for the animal to learn a direct relationship between the avoidance response and the prevention of the US. Instead, the animal learns to avoid the fear-inducing CS (Lovibond, Saunders, Weidemann, & Mitchell, 2008).

Whilst Mower’s two-factor theory has been very influential, more recent work has shown that this theory does not fully explain avoidance behaviour (Krypotos et al., 2015). For example, the two-factor theory posits that fear in the presence of the CS acts as the motivation for the avoidance response. However, once an avoidance response to a CS has been learned, the conditioned fear to this CS reduces over time. This represents a problem

for the two-factor theory, which would predict that avoidance responding would stop if fear to the CS was reduced or absent. This is at odds with evidence showing that avoidance of a CS is maintained even when the CS itself no longer gives rise to fear (Rachman & Hodgson, 1974). In addition, the two-factor theory assumes that avoidance behaviour requires reinforcement learning. As a result, it cannot explain why animals avoid fatal sources of danger, nor why maladaptive avoidance can occur in the absence of direct experience with the feared event (Krypotos et al., 2015).

In light of these issues with the two-factor theory of avoidance learning, additional models to explain avoidance and behaviour have been proposed. These include the Species-Specific Defence Reactions (SSDR) theory, proposed by Bolles (1970) and discussed in § 1.4.6, and Seligman and Johnson's cognitive theory of avoidance learning (Seligman & Johnston, 1973), which prioritised the importance of expectancies in instrumental learning. Expectancies refer to what the organism learns to expect; they expect the US to occur if they do not perform the avoidance response, and expect the US not to occur if they perform the avoidance response. Seligman and Johnston's theory marked a deviation from previous theories of avoidance learning, as it assumed a role for explicit cognitive processing during instrumental learning (Krypotos et al., 2015). Some decades later, Lovibond (2006) took this cognitive approach further in his expectancy model of avoidance learning, which proposes that both the classical and instrumental stages of avoidance learning are driven by higher-order cognitive processes.

Specifically, the expectancy model posits that the presence of the CS will increase the individual's expectancy of the US occurring, which in turn will increase the individual's anxiety. The individual will then make or withhold an avoidance response to the CS based on their expectancy of what a (non) response would entail (Lovibond et al., 2008). If the aversive outcome is successfully avoided, anxiety will be reduced. The expectancy model is supported by the observation that when individuals are prevented from performing a learned avoidance response, their anxiety increases (Lovibond et al., 2008). This outcome would be predicted by the expectancy model, which holds that anxiety is generated by the expectation of the

aversive outcome (US), but not by the two-factor theory, which assumes that fear is generated by the presence of the CS. In addition, the expectancy model can explain some of the findings, discussed above, which cause problems for the two-factor theory. For example, it can explain why an organism continues to avoid a CS even when fear of the CS itself is diminished or virtually absent. It can also explain why individuals show maladaptive avoidance in the absence of a traumatic experience with the aversive US. For example, an individual may take extensive measures to avoid heights despite never having experienced a traumatic experience involving heights.

Whilst models of avoidance learning, including the two-factor theory and the expectancy model, disagree in various ways, they converge on the importance of anxiety as a central component of avoidance behaviour. For example, the two-factor theory assumes that fear (anxiety) of the CS motivates avoidance behaviour, whilst the expectancy model suggests that the expectation of an aversive outcome (US) elicits anxiety in the individual, and that this anxiety can be reduced by the performance of an avoidance response (Lovibond et al., 2008). Given the close relationship between avoidance behaviour and anxiety, it is perhaps unsurprising that atypical avoidance has been found to play a crucial role in the aetiology and maintenance of anxiety disorders (Beckers & Craske, 2017; Dymond & Roche, 2009). To this end, the following section focusses on the relationship between avoidance and pathological anxiety.

1.4.2. The relationship between anxiety and avoidance

As discussed in the previous section, anxiety is a central component in a number of theories of avoidance, including Lovibond's (2006) expectancy model and Mowrer's (1951) two-factor theory. Similarly, atypical patterns of avoidance behaviour feature in pathological anxiety. For example, people with pathological anxiety may show excessive avoidance of objective physical threat (e.g. excessive avoidance of heights), inappropriate avoidance of physical situations which are not objectively dangerous (e.g. avoidance of social situations), or even psychological

avoidance of internal states and thoughts (e.g. persistent worry; Arnaudova, Kindt, Fanselow, & Beckers, 2017).

Given the close relationships between avoidance and anxiety, and between ELS and anxiety, it is important that research examining the effect of ELS on avoidance behaviour controls for levels of anxiety. Therefore, in the present research, care was taken to by ensure that none of the participants had a current or past diagnosis of an anxiety disorder, and a measure of anxiety was included in all the relevant statistical analyses. This was additionally important for the investigation of the relationship between ELS and avoidance at the neural level, as evidence suggests that anxiety may be related to alterations in brain regions involved in avoidance learning such as the amygdala and striatum (White et al., 2017; Yassa, Hazlett, Stark, & Hoehn-Saric, 2012). The following section provides an overview of the brain regions involved in avoidance behaviour.

1.4.3. Brain regions involved in avoidance behaviour

At the neural level, avoidance learning recruits an extensive network of structures, including regions involved in emotional processes, such as the amygdala, and regions involved in motivational processes, such as the striatum (Ilango, Shumake, Wetzel, & Ohl, 2014). Interestingly, functional alterations in both the amygdala and the striatum have been reported in individuals who experienced ELS (§ 1.2.2.2). As discussed in § 1.4.1, prominent models of avoidance suggest that avoidance learning involves two stages; fear conditioning and instrumental avoidance. The amygdala plays a central role in the first stage of avoidance learning, classical fear conditioning (LeDoux, 1993; Maren, 2001), and also contributes to instrumental avoidance (Levita, Hoskin, & Champi, 2012).

Whilst fear conditioning is heavily dependent on the amygdala, the second stage of avoidance learning, instrumental avoidance (active or passive avoidance), relies on a network of regions which includes the anterior insula, caudate nucleus and dorsal anterior cingulate cortex (Levita et al., 2012). Two of these regions, the insula and anterior cingulate cortex, are thought to form part of a ‘salience network’ which supports the detection of important stimuli (Levita et al., 2012). The caudate nucleus is

part of the striatum, and may be involved in learning the relationships between a stimulus and the resultant response (Levita et al., 2012). Stimulus detection and knowledge of stimulus-response contingencies are both important processes in avoidance learning.

Whilst Levita et al. (2012) found extensive overlap in the brain regions involved in active and passive avoidance, there were some differences in the brain regions that were active during the two forms of instrumental avoidance. Specifically, active avoidance was associated with greater activation in the amygdala and the nucleus accumbens (NAcc), part of the ventral striatum. This accords with findings from other human neuroimaging studies which have shown that the striatum is involved in active avoidance learning, and interacts with the amygdala during the acquisition of active avoidance responses (Boeke, Moscarello, LeDoux, Phelps, & Hartley, 2017; Delgado, Jou, LeDoux, & Phelps, 2009; Levita et al., 2012). Passive avoidance, in contrast, was associated with deactivation in the NAcc, and was not associated with activation in the amygdala (Levita et al., 2012). This absence of amygdala activation during passive avoidance does not necessarily mean the amygdala had no involvement at all, as animal studies of passive avoidance have reported amygdala involvement in the acquisition of conditioned fear (Nomura, Nishiyama, Saito, & Matsuki, 1994), an important component of passive avoidance. However, unlike in active avoidance, the amygdala is not involved in the storage or retrieval of learned passive avoidance (Parent, Quirarte, Cahill, & Mcgaugh, 1995). Levita et al. (2012) used an analysis which involved taking an average of the activation across multiple passive avoidance trials. In light of this, it is possible that amygdala activity which occurred only on early trials (during acquisition of the passive avoidance response) would not have been detected.

In summary, active and passive avoidance in humans is supported by numerous neural regions, including the amygdala and striatum (Delgado et al., 2009; Levita et al., 2012). As discussed in § 1.2.2.2, functional alterations in both the amygdala and the striatum have been reported in participants who experienced ELS. Despite this, few, if any, studies have examined how ELS affects avoidance learning in the human brain. The

potential relationship between ELS and avoidance responding in human participants has also received very little attention in the behavioural literature. However, extensive evidence in support of such a relationship can be found in the animal literature. The following section will discuss this evidence in more detail.

1.4.4. The impact of early life stress on avoidance behaviour

As discussed in § 1.4.1, avoidance learning is thought to involve two stages, a fear conditioning stage and an instrumental learning stage. This latter stage can be subdivided into two distinct processes, active avoidance, in which an animal avoids an aversive outcome by making a response to a CS, and passive avoidance, in which an animal avoids an aversive outcome by withholding a response to a CS. Work with rats has found that ELS is associated with alterations in all three components of avoidance learning: fear conditioning (§ 1.4.5.2), active avoidance (§ 1.4.5.3.1) and passive avoidance (§ 1.4.5.3.2). The following section will discuss these findings in detail.

1.4.5. Early life stress and avoidance behaviour in rats

1.4.5.1. Rat models of early life stress

The vast majority of studies examining the effect of ELS on avoidance learning have used animals, usually rats, instead of human participants. This is primarily because, in contrast to studies with humans, studies with non-human animals allow for precise experimental control over the timing and type of stress that is experienced. Animal models of ELS typically involve a daily manipulation which lasts for a pre-determined length of time, often from post-natal day one (PND1) to PND21, the day on which rat pups are usually weaned (Kosten et al., 2012). Common daily manipulations include early handling, in which the pups are handled by the experimenter, maternal separation, in which the dam is removed from the litter, and early isolation, in which the pup is removed from its dam and littermates (Kosten et al., 2012). Other models of ELS involve subjecting the pups to foot shocks (e.g. Quinn, Skipper, & Claflin, 2014), and providing insufficient bedding material for the dam, resulting in rough

maternal handling and decreased nursing of the pups (Perry & Sullivan, 2014).

1.4.5.2. Early life stress and fear conditioning in rats

As discussed in § 1.4.1, fear conditioning is considered to be an important component in many models of avoidance learning. Fear conditioning in rats is typically induced by pairing a neutral conditioned stimulus (CS) with an aversive unconditioned stimulus (US). Repeated presentation of the CS with the US will result in a conditioned fear response to the CS. In rats, the US is usually a foot shock, whilst the CS is either a context (the cage in which the rat receives the US) or a cue (typically a light or a tone). Fear conditioning is usually quantified by the amount of time the rat spends freezing, or the duration of the ultrasonic vocalisations it makes when it encounters the CS (Curzon, Rustay, & Browman, 2009). More fear is indicated by more time spent freezing and longer-lasting ultrasonic vocalisations. Fear conditioning is said to be impaired in cases where the rat makes fewer fear responses to the CS.

The relationship between ELS and fear conditioning in rats is somewhat unclear. Regarding fear conditioning to a context which has been paired with a US, there are numerous reports of impaired fear conditioning following ELS. This effect has been found with early handling (Madruga, Xavier, Achaval, Sanvitto, & Lucion, 2006; Meerlo, Horvath, Nagy, Bohus, & Koolhaas, 1999), daily maternal separation (Chocyk et al., 2014) and neonatal isolation (Kosten, Lee, & Kim, 2006; Kosten, Miserendino, Bombace, Lee, & Kim, 2005). However, there are also reports of enhanced fear conditioning to a conditioned context, following ELS induced by one 24 hour period of maternal separation (Lehmann, Pryce, Bettschen, & Feldon, 1999; Oomen et al., 2010), neonatal isolation (Kosten et al., 2005), and early experience of repeated foot-shocks (Quinn et al., 2014). Other studies have found no relationship between fear conditioning to a context and ELS as induced by early handling (Stevenson, Spicer, Mason, & Marsden, 2009), daily maternal separation (Stevenson et al., 2009) or one 24-hour period of maternal separation (Lehmann et al., 1999). The relationship between ELS and fear conditioning to a cue (such as a tone)

that has been paired with a US is similarly unclear, with studies variously reporting no effects of ELS (Kosten et al., 2005; Lehmann et al., 1999), ELS-related impairments (Kosten et al., 2006), and ELS-related enhancements (Oomen et al., 2010). In their review article, Kosten et al. (2012) suggest that differences in the timing and duration of the ELS manipulations may explain some of the discrepancies across studies. However, though a clear picture of the directionality is yet to emerge, there is increasing evidence to suggest that ELS is associated with alterations in fear conditioning later in life (Callaghan & Richardson, 2013; Quinn et al., 2014).

1.4.5.3. Early life stress and instrumental avoidance responses in rats

To the author's knowledge, there have not been any studies examining the effect of ELS on instrumental avoidance behaviour, whether active or passive, in human participants. However, a number of studies have investigated the relationship between ELS and active and passive avoidance in rats.

1.4.5.3.1. Early life stress and active avoidance in rats

In a typical active avoidance paradigm, a rat is placed in a box with two compartments. It can learn to avoid a US (usually a foot-shock) by crossing a barrier to the other compartment when it is presented with the CS (usually a light and/or a tone). Numerous experiments have reported more active avoidance responses in adult animals which experienced ELS relative to adult animals which did not experience ELS (Abraham & Gruss, 2010; Catalani et al., 2002; Catalani et al., 2000; Nunez et al., 1995; Pryce, Bettschen, Nanz-Bahr, & Feldon, 2003; Rio-Alamos et al., 2015; Rio-Alamos et al., 2017; Schable, Poeggel, Braun, & Gruss, 2007). However, there have also been reports of fewer active avoidance responses in rats which experienced ELS (Toth, Avital, Leshem, Richter-Levin, & Braun, 2008; Weiss, Domeney, Moreau, Russig, & Feldon, 2001).

The contradictory findings with regards to the effect of ELS on active avoidance may be related to the timing of the stress exposure during

infancy. Lehmann et al. (1999) found that male rats which experienced maternal separation at 4 days old showed fewer active avoidance responses than rats which did not experience maternal separation. In contrast, male rats which experienced maternal separation at 9 days old showed more active avoidance responses than rats which did not experience maternal separation. This shows that the impact of ELS on active avoidance behaviour in adult rats is not uniform. Instead, the nature of the changes in active avoidance behaviour may vary according to the time at which the early stress occurred.

1.4.5.3.2. Early life stress and passive avoidance in rats

Whereas in active avoidance paradigms animals need to make a response in order to avoid an aversive outcome, in passive avoidance paradigms (also called 'inhibitory avoidance' paradigms), animals have to withhold a response in order to avoid the aversive outcome. Passive avoidance experiments typically use one of two paradigms (Ögren & Stiedl, 2010). The first, the 'step-through' paradigm, is carried out in a box with two compartments, a lit compartment and a dark compartment (Ögren & Stiedl, 2010). In the training session, the rat is placed in the lit compartment and the time it takes to enter the dark compartment (its preferred environment), is recorded. When the rat enters the dark compartment it receives a foot-shock. In the testing session, which takes place either immediately after training or a set amount of time later, the rat is once again placed in the lit compartment and the time it takes to enter the dark compartment is recorded. The difference between the two recorded times is taken as a measure of passive avoidance, with longer latencies indicating better passive avoidance performance. In the second paradigm, the 'step-down' paradigm, the rat is placed on a platform from which it can step down onto the floor (Ögren & Stiedl, 2010). When the rat steps onto the floor it receives a foot-shock. At test, the rat is again placed on the platform and the amount of time it takes to step down is recorded. As with the previous paradigm, longer latencies to step down at test indicate better passive avoidance performance.

Studies which have used these paradigms have consistently reported impaired passive avoidance, as indicated by shorter latencies, in rats which experienced ELS (Benetti, da Silveira, da Silva, Cammarota, & Izquierdo, 2012; Benetti, da Silveira, Rosa, & Izquierdo, 2015; Kosten, Karanian, et al., 2007; Kosten et al., 2012; Kosten, Lee, & Kim, 2007; Mello, Benetti, Cammarota, & Izquierdo, 2009; Neves, Menezes, Souza, & Mello-Carpes, 2015; Vivinetto, Suarez, & Rivarola, 2013; Zugno et al., 2013; though see Gschanes, Eggenreich, Windisch, & Crailsheim, 1998). Rats which experienced ELS in the form of maternal deprivation (Benetti et al., 2012; Benetti et al., 2015; Mello et al., 2009; Neves et al., 2015; Vivinetto et al., 2013; Zugno et al., 2013), neonatal isolation (Kosten, Karanian, et al., 2007) and neonatal handling (Kosten, Lee, et al., 2007) showed shorter latencies to enter a dark compartment or step down from a platform, irrespective of the time between the training and test sessions. Shorter latencies (indicating impaired passive avoidance) have been reported immediately after training (Zugno et al., 2013), one hour after training (Vivinetto et al., 2013), one and a half hours after training (Zugno et al., 2013), three hours after training (Neves et al., 2015), 24 hours after training (Benetti et al., 2012; Benetti et al., 2015; Mello et al., 2009; Neves et al., 2015; Zugno et al., 2013), 48 hours after training (Kosten, Karanian, et al., 2007; Kosten, Lee, et al., 2007) and one week after training (Kosten, Lee, et al., 2007). Therefore, work with rats suggests that ELS is associated with impaired passive avoidance in adulthood.

1.4.6. Early life stress and avoidance in human participants

Although there has been some investigation into the relationship between ELS and avoidance as an attentional process (Section 1.3.1; Kelly et al., 2015), investigation of the relationship between ELS and avoidance learning is virtually absent from the human literature. As discussed in § 1.4.1, models of avoidance learning emphasise the role of both Pavlovian (classical) and instrumental conditioning in successful avoidance responding. However, it is also important to note that under some circumstances avoidance may be purely Pavlovian (Bolles, 1970; Krypotos et al., 2015). This is the suggestion put forward by Bolles in his Species-

Specific Defence Reactions theory (SSDR theory; Bolles, 1970). The SSDR theory builds on the observation that animals possess a repertoire of species-specific responses that they make when they experience fear (Krypotos et al., 2015). For example, when a rat experiences fear it is likely to respond by fleeing, fighting or freezing. The SSDR theory posits that these species-specific defence reactions occur without the need for instrumental learning. As a result, all that is required for the emission of an avoidance response is for the animal to learn the association between the CS and the US (classical conditioning).

In light of this, it is useful to examine the effect of ELS on classical (Pavlovian) fear conditioning, as alterations in classical conditioning may contribute to the effect of ELS on avoidance learning and behaviour. To this end, Bremner et al. (2005) used two techniques to measure neural and physiological responding during fear conditioning, positron emission tomography (PET) and skin conductance responding (SCR). PET is a technique that can indirectly index neural activity by measuring blood flow, metabolism, neurotransmitters, and the position of radio-labelled drugs in the brain. This technique can be used to identify brain regions which are involved in the performance of a specific task. SCR, also known as the electro-dermal response, is a measure of variation in the electrical conductance of the skin. Skin resistance varies with the state of sweat glands in the skin. As sweating is controlled by the sympathetic nervous system, SCR can be used as measure of emotional/physiological arousal. Bremner et al. (2005) used these techniques to investigate the effect of childhood sexual abuse on fear conditioning. To do this, they recruited a group of women who had post-traumatic stress disorder (PTSD) and were sexually abused as children, and a group of women who did not have PTSD and had not experienced childhood trauma.

Each participant attended two sessions one week apart. The order of these two sessions was counterbalanced across participants. In Session A, the participants underwent paired fear conditioning, in which a CS (a blue square) was paired with a US (a shock). This procedure should result in conditioned fear responses to the CS. This was followed by an extinction procedure, which was designed to extinguish the conditioned fear response

to the CS. In Session B, the experiment was repeated, but critically in this session participants received unpaired CS and US presentations, which should lead to fear of the context rather than conditioned fear to the CS. As before, this session ended with an extinction procedure.

The authors then examined the difference in neural activation between the fear acquisition in Session A (paired, discrete fear conditioning) and the fear acquisition in Session B (unpaired, contextual fear conditioning). They did this in order to determine which brain regions were differentially active in response to the presentation of a CS that had been associated with an aversive outcome (when the CS and US were paired), relative to fear conditioning in which the US was present but was not paired with the CS. Unlike the paired condition, this unpaired condition should not result in conditioned fear to the CS. They found that the group of women with PTSD and a history of childhood sexual abuse showed greater activation than the control group in a number of brain regions during paired fear acquisition. These regions included the left amygdala, left superior temporal gyrus, right inferior frontal gyrus, cerebellum and posterior cingulate (Bremner et al., 2005). Regarding the physiological arousal as measured by SCR during the study, Bremner et al. (2005) found that the group of participants with PTSD and ELS showed greater SCR in the paired fear acquisition block compared to the unpaired fear acquisition block, a pattern that was not present in the control group.

A different study, by Cacciaglia et al. (2017), also used SCRs to examine the relationship between experience of trauma and emotional physiological arousal during fear acquisition. They recruited a group of adult participants (mean age 22.8 years) who had been exposed to trauma an average of 7.4 years before the study, and a control group of adults who had not experienced trauma (mean age 21.7 years). Experiences of trauma included a severe vehicle accident, the traumatic loss of a loved one, experience of domestic violence, and childhood abuse. The authors used a differential fear conditioning paradigm, where one stimulus (conditioned stimulus, CS+) was paired with a shock (unconditioned stimulus, US) whilst another stimulus (conditioned stimulus, CS-) was never paired with the shock. The researchers examined the difference in SCRs to the CS+ and the

CS- across two acquisition blocks. Both trauma-exposed and non-trauma-exposed groups showed greater SCRs to the CS+ (relative to the CS-) in the first block of fear acquisition (showing a conditioned fear response to the CS+). However, only the trauma-exposed group continued to show enhanced SCRs to the CS+ in the second block of fear acquisition.

Taken together, these studies suggest that Pavlovian fear conditioning differs between participants who experienced trauma and those who did not. The findings from Bremner et al (2005) and Cacciaglia et al. (2017) suggest that individuals with a history of trauma show enhanced classical fear conditioning, as demonstrated by greater fear responding to a CS after fear conditioning. Therefore it is possible that avoidance learning which does involve an instrumental component will also be affected by past trauma, as Pavlovian conditioning is thought to be an important component of avoidance learning (Krypotos et al., 2015). Put another way, if classical fear conditioning is altered, it is possible that avoidance learning will also be altered in a situation where the participant is required to make an active or passive response to a CS.

However, it is important to be aware that firm conclusions regarding the effects of ELS on avoidance learning cannot be inferred from the findings of Bremner et al. (2005) and Cacciaglia et al. (2017). This is because neither of these studies was able to fully determine whether ELS itself was associated with altered fear learning in human adults. Bremner et al. (2005) used a sample of participants with PTSD as well as ELS, and as such it is not possible to determine whether their findings were due to ELS or PTSD. Though Cacciaglia et al. (2017) used healthy participants, only a small portion of the trauma-exposed group reported childhood abuse. Whilst some of the participants' experiences of trauma undoubtedly occurred during development (given that the mean age was 22.3 years and the mean onset of trauma was 7.4 years prior to study participation), the study included participants who experienced trauma at any time, not specifically during early life. Given that the neural and behavioural effects of trauma may vary depending on the age at which the trauma occurred (Andersen et al., 2008), it is not possible to establish the extent to which Cacciaglia et al.'s (2017) findings would be repeated if the study were to be restricted to

individuals who experienced trauma in early life. Due to these limitations, and the absence of additional research with human participants, the impact of ELS on human avoidance learning remains unclear.

In order to address this, the present research took a complementary approach to investigate the effect of ELS on avoidance learning in mentally healthy adult participants. The first study (presented in Chapter 3) was designed to examine young adults' self-reported approach and avoidance of emotional facial expressions. Though ELS has previously been associated with alterations in the processing of emotional facial expressions, the question of whether these alterations extend to atypical avoidance of such expressions remains unanswered. Whilst the study presented in Chapter 3 took a behavioural approach to the investigation of avoidance learning in young adults who experienced ELS, the research presented in Chapter 5 used EEG to examine the neural correlates of avoidance learning in this population. Each of these studies therefore aims to shed light on the relationship between ELS and avoidance behaviour in human participants, a topic which, despite extensive investigation in the rat literature, has been previously neglected in the human literature.

1.5. Summary and thesis overview

The theory of latent vulnerability (McCrory & Viding, 2015) states that ELS is associated with neurocognitive adaptations which increase an individual's risk of developing a mental health problem later in life. Research to date suggests that two neurocognitive mechanisms, processing of emotional facial expressions (§ 1.3), and avoidance of threat (§ 1.4), may be particularly susceptible to the effects of ELS. However, the vast majority of studies which have examined face processing following ELS have been carried out with children (McCrory et al., 2013; Pollak & Kistler, 2002; Shackman et al., 2007), or adults with mental health problems (Grant et al., 2011; Russo et al., 2015), whilst investigation into the relationship between ELS and avoidance has been largely confined to the animal literature (Kosten et al., 2012; Lehmann et al., 1999).

The human brain undergoes extensive and prolonged maturation from childhood to adulthood (Sowell, Thompson, Holmes, Jernigan, & Toga, 1999). As a result, despite the growing body of evidence showing a relationship between ELS and neurocognitive changes in children's processing of emotional facial expressions (McCrory et al., 2017), it remains unclear whether these effects persist into adulthood in those who experienced ELS. This represents a significant gap in the literature. Though studies with adults with mental health problems can offer insight into the neurocognitive effects of ELS, they are necessarily limited in their ability to delineate the effects of ELS from the effects of the mental health condition. Finally, whilst animal work is highly beneficial for the examination of neurological changes associated with ELS, research with humans is critical if such work is to achieve its ultimate goal of informing clinical interventions.

In light of this, the research presented in this thesis sought to investigate the effect of ELS on behavioural and neural processing in young adults with no current or lifetime diagnoses of mental health problems. A series of studies were carried out, with a focus on face processing and avoidance responding. In the first study (Chapter 3), young adults were presented with images of male and female angry, happy and neutral facial expressions and asked to indicate how angry and happy they perceived the

stimuli to be, and the extent to which they would approach and avoid the stimuli. In this manner, it was possible to examine whether the enhanced perception of anger previously reported in children who experienced ELS would also be present in adults who experienced ELS. Furthermore, the study extended previous work by addressing whether ELS would also be associated with changes in the way that individuals responded to emotional facial expressions, specifically in terms of approach and avoidance.

The second study (Chapter 4) used EEG to examine the neural correlates of face processing in young adults who experienced ELS. Participants were presented with angry, happy and neutral male and female facial expressions in a passive viewing task. A focus on early visual ERPs allowed for investigation of the effects of ELS on early, automatic processing, complementing the behavioural investigation which necessitated more effortful, voluntary responding. Finally, the third study (Chapter 5) examined the neural correlates of avoidance responding to non-social threat cues in young adults who experienced ELS. EEG was recorded whilst participants either made (active avoidance) or withheld (passive avoidance) an action to conditioned stimuli (CS) in order to avoid an aversive outcome (unconditioned stimulus, US). This study allowed for the first examination of the effect of ELS on the neural correlates of avoidance in young adults, and extended previous work by investigating the effect of ELS on processing of learned threat cues that were not social in nature. Taken together, this research provides a body of work which has been designed to help elucidate neurocognitive alterations in young adults who experienced ELS, with a particular focus on changes in the affective mechanisms involved in processing social and non-social threat.

Chapter 2. Methodology

Abstract

The present chapter describes the methodology that was used to implement the studies involved in this research project. The first section of this chapter focusses on the ERP technique, providing a brief overview of the technique itself before describing the apparatus and procedure used to record the present EEG data, and the steps involved in the processing of these data. The chapter then addresses the statistical analysis of the data collected throughout the course of this research, with a focus on the use of the Benjamini-Hochberg (Benjamini & Hochberg, 1995) procedure to correct for multiple comparisons. Finally, the chapter provides details of the questionnaire measures used in the present research.

2.1. Electroencephalography

2.1.1. Overview of electroencephalography and the event-related potential technique

Neurons in the brain transmit information using chemicals known as neurotransmitters. These neurotransmitters are typically released from one neuron, the presynaptic neuron, into a synaptic cleft, the space between neurons (Purves et al., 2001). Once a neurotransmitter has crossed the synaptic cleft, it binds to a postsynaptic neuron, generating a voltage known as a post synaptic potential (PSP). When large groups of neurons (in the order of thousands or millions) are oriented in the same direction, their PSP activity summates to produce an electrical signal that can be measured at the scalp using EEG (Harmon-Jones & Beer, 2009; Luck, 2014). Activity from populations of neurons which occurs following an 'event', such as the presentation of a stimulus or the generation of a response, is known as an event-related potential (ERP). ERPs are generated by activity in cortical pyramidal cells, neurons located in the cerebral cortex which are oriented perpendicular to the cortical surface (Luck, 2014).

Studies which use the ERP technique typically present the same stimuli multiple times, then average together the electrical activity from all the stimulus presentations. This is necessary in order to isolate the neural activity associated with the event from the activity produced by other neural processes, and from electrical 'noise' produced by non-neural sources such as eye movements, muscle activity or the participant's environment. The process of averaging across trials results in an ERP waveform which contains a series of components (Luck, 2014). ERP components are positive or negative voltage deflections which occur in the order of milliseconds over certain areas of the scalp. Over the years a number of ERP components have been identified. Most ERP components are labelled with a letter denoting their direction (P for positive and N for negative), and a number. In some cases, the number represents the ordinal position of the component in the ERP waveform, as in the N1 or the P3, with the N1 being the first negative component and the P3 being the third positive component (Luck, 2014). In other cases, the number denotes the latency at which the component occurs. For example, the N170 is a negative component which

occurs about 170 ms after the presentation of a visual stimulus (Eimer, 2011a).

2.1.2. Early neural processing and its relationship with early life stress

There is a lack of clarity in the literature as to the definition of 'early' and 'late' neural processing. In this body of work, 'early processing' is used to describe neural activity which occurs within the first 200 ms after the presentation of a stimulus. The N170 component, which is the focus of the ERP analyses in this research, is a visually-evoked component which is generated in response to a visual stimulus. In light of this, it can be described as a perceptual component, though it is important to acknowledge that the N170 does not index perceptual processing exclusively, as it can be modulated by the emotional properties of the stimulus (Blau, Maurer, Tottenham, & McCandliss, 2007; Levita, Howsley, Jordan, & Johnston, 2015). The N170 occurs irrespective of whether or not the participant is consciously aware that a stimulus has been presented (Pegna, Landis, & Khateb, 2008). Therefore, within this thesis, the N170 is considered to be a component that reflects 'automatic' or implicit processing, as it occurs without the need for explicit voluntary processing.

Very few studies have examined the effect of ELS on early neural processing, and of the few studies that do exist, the majority have focussed on children and found conflicting results (see § 1.2.2.4). In light of this, examination of this stage of processing in adults is required in order to clarify whether ELS is associated with alterations in early visual processing mechanisms. It is important to establish the stage(s) of processing which is altered following ELS, as only then can therapeutic interventions be tailored to the specific changes which could be responsible for increased vulnerability to mental illness in this population (see § 1.2.2.3, for additional discussion). In addition, investigation of potential alterations in early processing is warranted, as changes in perceptual and other early processes could have knock-on effects on later higher-order processes (Portella et al., 2012). Therefore, a clear elucidation of the extent to which relatively early processes are altered or spared following experiences of ELS is necessary

for a full understanding of any ELS-related changes that may be found in higher-order processing or behavioural responding.

2.1.3. The N170 ERP component

The N170 is a face sensitive component, that is, its amplitude is larger in response to face stimuli than to other visual stimuli (Eimer, 2011a). Significantly, it is also modulated by emotion (Blau et al., 2007; Mienaltowski, Chambers, & Tiernan, 2015). The N170 typically occurs over occipital-temporal regions approximately 170 ms after stimulus onset. Given the low spatial resolution of the EEG technique, attempts to localise the source of the N170 have been inconclusive, though there is evidence for the involvement of the occipital-temporal cortex, fusiform gyrus and superior temporal sulcus (Eimer, 2011a). In addition, it is thought that the N170 response to threatening stimuli may be modulated by re-entrant projections from the amygdala (Dolan et al., 2006).

The N170 component was chosen as the focus of the present research for a number of reasons. Firstly, as an index of early neural processing, it provides an opportunity to study the effects of ELS on implicit processes (see § 2.1.2). Secondly, the face-sensitivity of the N170 makes it an ideal candidate for examination of the effects of ELS on emotional face processing. Investigation of the effects of ELS on early processing of emotional facial expressions is particularly important in light of the growing number of behavioural and fMRI studies which have found a relationship between ELS and alterations in face processing. Thirdly, recent work with a community sample of adult participants found that the N170 was sensitive to learned signals of threat in a task of instrumental avoidance learning (Levita et al., 2015). Consequently, the N170 represents a component which can be used to examine not just potential ELS-related alterations in emotional face processing but also ELS-related alterations in responsivity to cues of threat during instrumental avoidance. Therefore, the N170 is an ideal candidate for the investigation of the relationship between ELS and the two mechanisms central to the present research: emotional face processing and avoidance of threat.

2.2. The present EEG research

2.2.1. Participant recruitment

2.2.1.1. Recruitment of young adult participants

The present doctoral research was designed to examine potential neurocognitive alterations associated with ELS in young adult participants. Young adulthood is a time of extensive social change during which final brain maturational processes are still taking place (Arnett, 1994; Lebel, Walker, Leemans, Phillips, & Beaulieu, 2008). In addition, young adulthood is a period of time which is associated with increased risk for the emergence of clinically significant mental health problems (Kessler et al., 2005). This developmental stage therefore represents a period of time in which the brain may be particularly vulnerable. In spite of this, young adulthood has received relatively little attention in research examining potential neurocognitive alterations associated with ELS, with most studies focussing on childhood. Therefore, the present body of work recruited young adult participants with the aim of shedding light on the potential neurocognitive correlates of ELS in this population.

2.2.1.2. Procedure for recruitment of participants

All the research presented in this thesis received ethical approval from the Department of Psychology Ethics Committee, University of Sheffield. The research involved recruitment of two samples of participants, with one sample participating in the first study (presented in Chapter 3) and the second sample participating in the two EEG studies (presented in chapters 4 and 5). The first sample (n = 147) consisted of male and female participants aged 18 to 19 (M = 18.45). Recruitment of these participants involved a variety of methods. First year undergraduate Psychology students were invited to participate in exchange for course credits, emails were sent to staff and students at the University of Sheffield using a pre-existing volunteer list, and the study was listed on Prolific Academic, an online platform which matches interested participants with research studies (www.prolific.ac). Participants who took part via Prolific Academic received £2.10 for completing the study; the remainder were offered entry to a £20 prize draw. Participants were asked to leave their email address if they

were willing to take part in future studies. Initially, it was expected that participants for the EEG studies would be recruited from this first sample, via emails sent to interested individuals. However, of the individuals who were invited to participate in the EEG studies, only two people who fulfilled the screening criteria (described below) expressed an interest in taking part. Therefore, information about the EEG studies was sent to the University of Sheffield volunteer list and to first year undergraduate Psychology students.

2.2.1.2.1. Screening criteria for the EEG studies

Potential participants were asked to complete a screening form which determined their suitability to take part in the EEG studies. A copy of this screening form can be found in Appendix A. Young adults aged 18 to 25 were invited to participate. Individuals were only asked to take part if they stated that their country of origin was the United Kingdom, in order to minimise any confounding effects of cultural background on experiences of ELS. Evidence suggests that women are more likely than men to experience negative outcomes associated with ELS (Cooke & Weathington, 2014); in the UK, rates of depression and anxiety, both of which are associated with ELS, are higher in women than in men (McManus, Bebbington , Jenkins, & Brugha, 2016). In light of this, the present EEG research focussed on female participants. In addition, individuals were only invited to participate if they were right handed, had no history of significant loss of consciousness, were not taking any psychoactive medication, had no problems with their sight or hearing, had no present or past diagnosis of a mental health condition or developmental disorder, and were not receiving treatment for any mental health problems.

Interested participants were asked to fill in the Child Abuse and Trauma Scale (CATS; Sanders & Becker-Lausen, 1995), and were only invited to participate if they fulfilled the criteria for either ‘low’ or ‘high’ levels of ELS. The cut-off values for these groups were generated by taking the data collected during the first study (Chapter 3) and splitting it into three equal groups. This produced a range of 0 to 15 for the ‘low’ group, 16 to 24 for the ‘medium’ group and 25 and above for the ‘high’ group. Interested individuals who met the screening criteria were invited to take part if their

CATS score fell in either the ‘low’ or ‘high’ range. Individuals who scored in the ‘medium’ range were not invited to take part in the EEG studies.

Approximately 230 individuals filled in the screening form to take part in the EEG studies. The majority of people who filled in the screening form were not eligible to take part, typically because they either scored in the ‘medium’ range for ELS experience, or reported that they had been diagnosed with a mental health problem. As a result, the final sample size for the EEG studies was 62 participants, with 28 in the low ELS group and 34 in the high ELS group. In order to thank them for their participation, individuals who completed the study were given either course credits, or £5 and entry to a £50 prize draw.

2.2.2. Collection of EEG data

2.2.2.1. Apparatus

2.2.2.1.1. Electrodes

EEG signals were recorded using a Biosemi Active Two 64 channel + CMS/DRL electrode set, with 'pin-type' Ag-AgCl active electrodes designed to reduce unwanted electrical noise (www.biosemi.com). The electrodes were labelled according to the 10/20 system (Figure 2.2) and organised in two groups of 32, with each group sharing a common connector that could be plugged into the AD-box (§ 2.2.2.1.3). After each use the electrodes were washed with warm water to remove the gel. They were then dried carefully using paper towels. If electrode signals became excessively noisy, the electrodes were soaked in salt water for five to ten minutes. In addition to the pin-type electrodes, four flat-type electrodes were used to record electrooculography (EOG) data.

2.2.2.1.2. Head-caps

The electrodes were affixed to one of three 64-channel BioSemi head-caps (www.biosemi.com). The three head-caps differed only in their size and colour (Small: 50-54cm head circumference, yellow; Medium: 54-58cm head circumference, red; Large: 58-62cm head circumference, blue). Each head-cap consisted of an elastic cap with a Velcro chin strap and ear-slits on either side. The head-caps contained 66 plastic electrode holders (to hold the 64 active electrodes and the two reference electrodes), arranged according to the 10/20 system (Figure 2.2). After each use the head-cap was cleaned with warm water and left to dry on a towel. In cases where multiple participants attended on the same day, a cool fan was used to dry the cap quickly.

2.2.2.1.3. AD-Box

Electrical signals from the brain are continuous (analogue) in nature. Therefore, in order to store the data on a computer, it is necessary to convert the signal to discrete numerical representations (digital information). This process is carried out by an analogue-to-digital converter. In the present research, a BioSemi ActiveTwo AD-Box was used to amplify the signal and

convert it from analogue to digital data. The data were recorded with a sampling-rate of 2048 Hz. From the AD-Box, the data were sent to a BioSemi USB receiver via an optic fibre. The USB receiver then added the triggers to the data. Triggers, also known as event codes, are numbers which are used to indicate the time at which an event, such as the presentation of a specific stimulus, occurred. After adding the triggers, the USB receiver sent the resulting data to the computer on which the information was stored.

2.2.2.1.4. Additional apparatus

EEG recording took place in an electrically shielded room in order to limit interference from external sources of electrical activity. A Viglen LCD monitor set to a spatial resolution of 1024 by 768 pixels was used to present the stimuli. An 'EchoTubez Radition-Free Air-Tube headset' was used to deliver the aversive sound in the avoidance study (Chapter 5). This headset consisted of earbuds which were connected to 'air tubes' in place of electrical wires. The headset was used instead of a standard set of headphones in order to minimise electrical interference with the EEG signal. Signa Gel, produced by Parker Laboratories Inc. (http://www.parkerlabs.com/signagel.asp), was used to support the conduction of electrical activity from the scalp to the electrodes.

2.2.2.2. Procedure for EEG data collection

Data for both the EEG experiments (chapters 4 and 5) were collected during one recording session. Participants who had been selected to take part in the study (recruitment procedure described in § 2.2.1.2) were asked to complete a series of questionnaires in their own time before they attended the EEG recording session. These questionnaires were presented using Qualtrics (www.qualtrics.com), an online survey platform. Informed consent was obtained using a form which was presented prior to the questionnaires. The questionnaires were the Hospital Anxiety and Depression Questionnaire (HADS; Zigmond & Snaith, 1983), the State Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) the Behavioural Inhibition/Behavioural Activation Scales (BIS/BAS; Carver & White, 1994) and the Sensitivity to Punishment and Reward

Questionnaire (SPSRQ; Torrubia, Avila, Molto, & Caseras, 2001). Further details about these questionnaires can be found in § 2.4. The order in which the questionnaires were presented was counterbalanced across participants.

When participants arrived for the EEG recording session they were invited to take a seat in a room opposite the room which contained the EEG equipment, provided with a copy of the information sheet and asked if they had any questions. Once the experimenter had answered any questions the participant was asked to sign a consent form regarding their participation in the study. The participant was then taken into the EEG room and asked to take a seat on a chair which was facing the monitor. The experimenter asked the participant to position themselves so that they could easily reach the space bar on the keyboard in front of them, but not so close that the glare from the screen would be uncomfortable. The experimenter then measured the circumference of the participant's head and used this to select one of the three head-caps described in § 2.2.2.1.2. The head-cap was placed on the participant and secured by its Velcro chin strap. The participant was then asked to place the ear buds of the headphones into their ears. A tape measure was used to ensure that the cap was in the correct position, such that the plastic holder for electrode Cz lay in a central position, which was equidistant from both ears. Once the cap was in place, electrode gel was added to each of the electrode holders. The electrodes were then inserted into their respective holders. Next, the four EOG electrodes were attached to the participant's face using circular stickers. These electrodes were positioned above and below the left eye, and on the left and right temples.

Once all the electrodes were in place, their wires were plugged into the AD box, and the box was turned on. The experimenter then examined the traces produced by the electrodes using BioSemi ActiView software (www.biosemi.com/software.htm). In cases where the signal was noisy, or where the electrode offsets were larger than +/-25μV, more gel was added to the holder for the corresponding electrode. This process was repeated until a clear signal could be obtained from all the electrodes.

Once all electrodes showed a clear signal, the experiment began. Participants completed two tasks, an emotional face processing task, and an avoidance task. The order of the tasks was counterbalanced across

participants. These tasks are described in detail in § 4.2.4 and § 5.2.4. Briefly, the emotional face processing task required participants to fixate on the screen whilst images of male and female individuals displaying angry, happy and neutral facial expressions were presented. Occasionally, participants would be presented with an image of a house. They were instructed to make a response (press the space bar) when one of these images appeared. In the active and passive avoidance task, participants were presented with four unique stimuli. Two of these stimuli were warning signals that were associated with an aversive outcome (loud sound), whilst the other two were control stimuli which were never associated with the aversive outcome. Participants could avoid the aversive outcome by making the correct (non) response to the warning stimuli. One warning stimulus required the participant to make a response (press the space bar) and the other required the participant to withhold a response. In addition, one control stimulus required a response from the participant whilst the other did not. The inclusion of these control stimuli ensured that neural processing involved in active and passive avoidance of threat could be delineated from neural processing involved in making or withholding a response to a stimulus. Participants were made aware of the response contingencies for the control stimuli (i.e. they were told which stimulus required a response and which did not), but had to learn the response contingencies for the warning stimuli by trial and error. Participants completed a series of practice trials in which they learned the response contingencies. Once the participant was confident that they were aware of the contingencies, they were allowed to progress to the experimental trials.

Both the emotional face processing task and the avoidance task were divided into four blocks of equal length. There were breaks in between blocks, with the length of each break determined by the participant themselves. Altogether the emotional processing task took approximately 15 to 20 minutes, and the avoidance task took approximately 35 to 40 minutes. There was some variation between participants in the length of time taken to complete the studies, due to differences in the amount of time individuals took for their breaks, and differences in the amount of time taken to learn the response contingencies in the avoidance task.

Once the EEG recording session was finished, the experimenter removed the electrodes from the head-cap and then informed the participant that they could remove the head-cap itself. The participant was given a towel to remove some of the electrode gel from their hair, and was invited to return to the room in which they had completed the consent form when they first arrived. Once participants returned to this room they were given a laptop computer and asked to fill in an additional series of questionnaires which were presented using Qualtrics online survey software (www.qualtrics.com). These questionnaires were the Beck Depression Inventory II (BDI-II; Beck, Steer, & Brown, 1996), the Beck Anxiety Inventory (BAI; Beck, Brown, Epstein, & Steer, 1988) and the Paulhus Deception Scales (PDS; Paulhus, 1998). The order of these questionnaires was counterbalanced across participants. Once the participant had completed the questionnaires the experimenter thanked them for their attendance and gave them either £5 or course credits.

2.2.3. Pre-processing of EEG data

Pre-processing of the EEG data was carried out using MATLAB R2014b. Much of the pre-processing was carried out using in-house scripts which utilised various functions provided by EEGLAB version 13 and ERPLAB version 5.0.0.0, though some of the pre-processing was carried out manually. For example, bad channels and ICA components representing ocular artefacts were identified through manual examination of the data. Datasets from each experiment (emotional face processing and avoidance) were pre-processed separately, such that pre-processing was carried out for 122[1] individual datasets. A diagram of the pre-processing stages is presented in Figure 2.1.

[1] This figure is 122 rather than 124, as although EEG data were recorded from 62 participants, one participant's EEG data were too noisy for meaningful analysis.

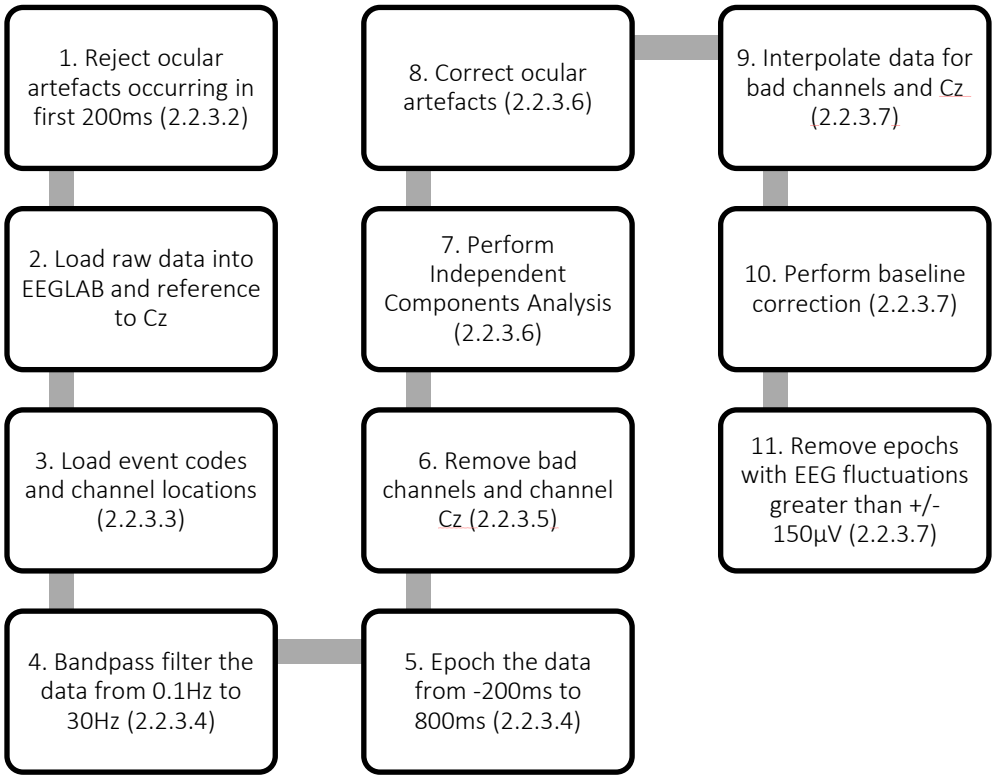

Figure 2.1. Pre-processing steps used in the analysis of the EEG data. Flow chart illustrating the order of steps for the EEG pre-processing. The numbers following each step refer to the section in which they are described in detail.

2.2.3.1. Preparation of data files

The data were recorded at a sampling rate of 2048Hz and saved in BDF files. During offline pre-processing these BDF files were downsampled to 512 Hz using the BioSemi Decimator86 (www.biosemi.com/download.htm). This reduced the files to a manageable size. The BDF files contained the data from the whole recording session. Therefore, in order to allow for the separate pre-processing of the data from the two experiments, the files were cut into two portions using the BioSemi Cropper86 tool (www.biosemi.com/download.htm). From this point onwards, datasets from the two experiments were processed separately.

BDF files contain both the EEG data and its associated event codes, also known as triggers. Due to an error in the experimental scripts, the BDF files contained numerous superfluous event codes that were not relevant to

the experiments. Therefore, instead of using the event lists stored in the BDF files, new event lists were created. This was achieved by comparing the event lists from the BDF files with separate results files created by MATLAB during the course of the experiments.

Once the accurate event lists had been prepared, event codes which were not required for analysis of the N170 response to the stimuli of interest were removed. In addition, event codes which corresponded to a trial in which a participant responded incorrectly were removed. In the emotional face processing experiment this involved the removal of trials in which a participant incorrectly responded to a face stimulus, and in the avoidance experiment this involved the removal of trials in which the participant responded to stimuli which required the omission of a response, and trials in which they did not respond to stimuli which required the emission of a response. Details of the number of incorrect (non) responses made in each task are presented in § 4.2.7 for the emotional face processing experiment and § 5.3.1.2 for the active and passive avoidance experiment. Once the event lists had been processed, they were stored as tab delimited files ready for use in the pre-processing of the EEG data.

2.2.3.2. Rejection of ocular artefacts

Once the data files with the EEG data and the correct event codes had been created, a procedure was used to reject ocular artefacts from the data. Ocular artefacts are disturbances in the EEG data which are caused by the eyes. The largest of these artefacts are blinks and lateral eye movements.

2.2.3.2.1. Rationale for the rejection of ocular artefacts

It was decided that, prior to the processing of the EEG data, trials on which an ocular artefact occurred within the first 200 ms post stimulus onset would be removed. The rationale behind this was that eye movements or blinks during this period of time could interfere with the processing of the stimulus. For example, if a participant blinked or made an eye movement when the stimulus was first presented, they would not see the stimulus until later in the time course of the trial. This would result in the ERP response to the stimulus beginning later. Furthermore, in the emotional face processing

study (Chapter 4), the facial stimuli were only presented for 200 ms. Consequently, a blink which occurred during this time period could prevent the participant from seeing the stimulus at all. Given that analysis of ERP data involves taking a mean of the ERP activity across a number of trials, inclusion of multiple trials in which the stimulus-locked activity is delayed or absent could affect the quality of the final ERP waveform. Therefore, trials in which blinks or large eye movements occurred during the first 200 ms post stimulus onset were removed from the data.

2.2.3.2.2. Procedure for the rejection of ocular artefacts

Ocular artefacts typically produce a large voltage deflection in the data which vastly exceeds the amplitude of any voltage deflections caused by neural activity. In light of this, it is possible to identify ocular artefacts by selecting an absolute voltage threshold, and removing all epochs in which the EOG signal exceeds this threshold. However, this method is a blunt tool, as drifts in the signal can lead to the erroneous removal of data containing large voltage changes that are not due to blinks (false positives), or to a failure to identify blinks which do not cross the absolute threshold (misses). To deal with this, Luck and his colleagues created a more sensitive procedure for the detection of ocular artefacts, the moving window peak-to-peak amplitude method (Luck, 2014). This method determines the voltage difference between the most positive and most negative amplitudes within a given time window. It then shifts the time window rightwards by a pre-determined step size, and repeats the process. The maximal voltage difference across all these tests is then compared to a pre-selected threshold.

The moving window peak-to-peak method was used to identify blinks and large eye movements in the present EEG data. Each set of data was split into epochs, periods of time which surround a given event code. Each epoch was 1000 ms in length and ranged from 200 ms prior to an event code (presentation of a stimulus) to 800 ms after the event code (i.e. -200 ms to 800 ms, with stimulus presentation at 0 ms). The epoched data was then processed using the moving window peak-to-peak function in ERPLAB. Given that the aim at this stage of pre-processing was to identify ocular artefacts that occurred during the first 200 ms post stimulus

presentation, the moving window peak-to-peak function was applied only to this period of time (0 ms to 200 ms), rather than applied across the whole 1000 ms epoch. For clarity, this period of time (0 ms to 200 ms) will be referred to as the 'search window'. The 'moving window' used in this stage of processing was set at 100 ms, with a step size of 20 ms. It is important to note that the search window is different to the moving window. The search window encompasses all the data that is examined for a given trial, whilst the moving window represents the amount of time that is examined at each step of the process. To illustrate, in the present analysis, the moving window was first applied over 0 ms to 100 ms, then it was moved across by 20 ms (the step size), so that the next window of time that was examined was 20 ms to 120 ms. This procedure continued until the whole of the search window (0 ms to 200 ms) had been examined.

The size of the signals generated by ocular artefacts differs across individuals. As a result, the threshold used to detect the ocular artefacts was set on a case-by-case basis, as recommended by Luck (2014). In most cases, a threshold of 75μV allowed for a high level of accuracy in detecting ocular artefacts. However, due to individual differences in the EOG signal, this threshold occasionally resulted in high numbers of misses or false positives. In these cases, the threshold was moved up or down by 25μV and the procedure was re-run. The information produced by the moving window peak-to-peak function was used to generate a new event list for each participant. These new event lists omitted any trials in which an ocular artefact occurred during the first 200 ms post stimulus onset.

2.2.3.3. Creation of EEG datasets

Once event codes followed by ocular artefacts had been removed from the event lists, new, separate datasets for the two experiments were created for each participant. These datasets were generated by loading the participant's BDF file into EEGLAB along with the corresponding event list and the channel locations. In EEG research, the term 'channel' is used somewhat interchangeably with the term 'electrode'. Typically, 'electrode' is used to refer to the physical electrodes which are placed on the scalp, whilst 'channel' is used when referring to the data recorded from a given

electrode. Channel locations provide information about the position of the electrodes on the scalp. Although BioSemi data are recorded reference-free, EEGLAB recommends allocating a reference channel when loading in the BDF files. Therefore, the BDF files were loaded into EEGLAB using Cz as the reference. Cz was selected as the reference electrode due to its equidistant position from the left and right occipital-temporal regions over which the N170 is typically recorded.

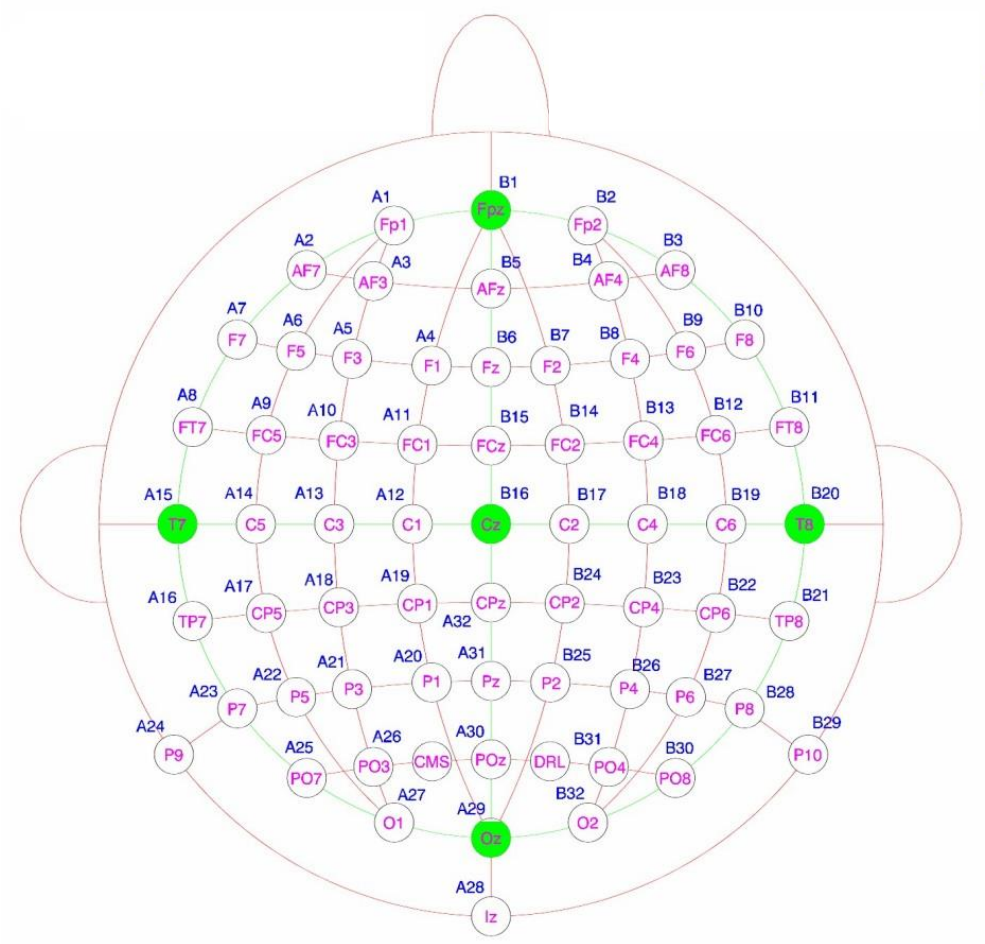

Figure 2.2. Channel locations. Illustration of the position of the electrodes (channels) in the 64 channel array used in the present research. Image taken from www.biosemi.com/headcap.htm.

2.2.3.4. Filtering and epoching the EEG data

The data were filtered using a band-pass filter with a slope of 12 dB/octave. This included a high-pass half-amplitude cut-off frequency of 0.1 Hz and a low-pass half-amplitude cut-off frequency of 30 Hz. Following this, the data were epoched into 1000 ms time periods, ranging from 200 ms

prior to stimulus presentation to 800 ms following stimulus presentation (i.e. -200 ms to 800 ms, with stimulus presentation at 0 ms). Epochs were categorised by the stimulus that was presented. In the emotional face processing study there were six categories of stimulus (event): male angry, female angry, male happy, female happy, male neutral and female neutral. In the avoidance learning study there were four stimulus categories: active avoid, passive avoid, control go and control no-go.

2.2.3.5. Removal of bad channels from the EEG data

Occasionally in EEG research, one or more EEG channels show a high level of noise throughout the EEG recording. This can affect the signal-to-noise ratio in the data, making detection of small neural fluctuations more difficult. Researchers may exclude data from bad channels altogether, or interpolate new data for the bad channels using the data recorded by their surrounding channels. There are various methods which can be used to identify whether a channel is 'bad', including visual examination of the data and the use of software which labels channels as bad if they do not meet pre-defined criteria. Manual identification of bad channels necessarily introduces a level of subjectivity into the analysis, and it can be very difficult to determine the point at which the level of noise in a given channel becomes unacceptable. This is especially difficult when working across multiple datasets that cannot be examined at the same time. On the other hand, automatic methods for the removal of bad channels can lead to spurious results, such that some bad channels are missed whilst some acceptable channels are removed. In light of this, and given Luck's (2014) recommendation that researchers should avoid removing channel data wherever possible, channels in the present research were only classified as 'bad' if they showed a uniform oscillatory pattern of noise which indicated electrode failure. This pattern of noise is illustrated in Figure 2.3. Extreme noise of this nature was rare, and only occurred in 10 % of datasets from the emotional face processing experiment and 5 % of datasets from the avoidance experiment. Once a bad channel was identified, it was removed from the data. As one channel, Cz, was used as a reference when the data

were loaded into EEGLAB, this channel did not contain any signal. Therefore, Cz was removed during the processing of each dataset.

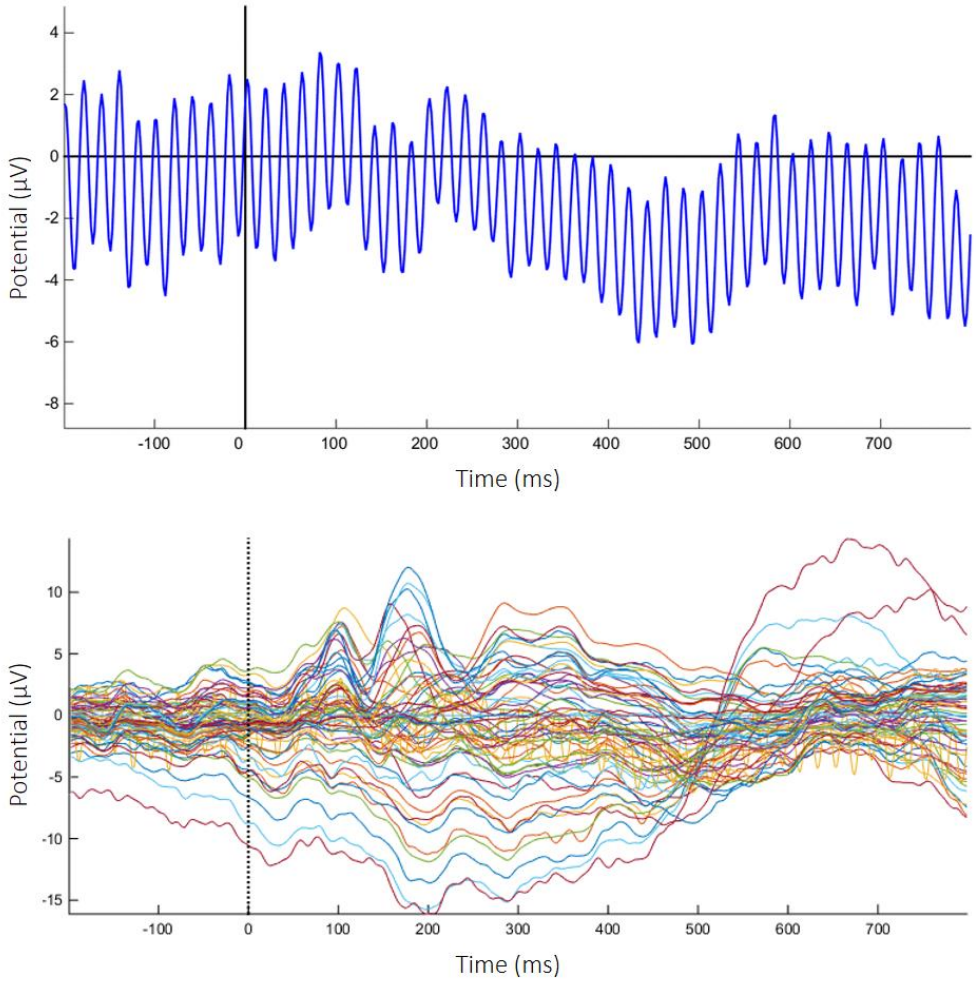

Figure 2.3. Examples of oscillatory activity in 'bad' channels. The top figure (A) depicts the oscillatory pattern which can be seen when the electrical activity from a single bad channel is averaged across all trials in a single dataset. The bottom figure (B) shows the activity averaged across all trials for each channel in a single dataset. Each channel is represented by a single coloured line. Here, the bad channel (presented in yellow) shows the oscillatory pattern which is distinct from the pattern of activity shown in the other channels.

2.2.3.6. Correction of ocular artefacts in the EEG data

As described in § 2.2.3.2, epochs in which an ocular artefact occurred within 200 ms post stimulus presentation were removed from the data. However, whilst these epochs were removed, there remained a number of cases in which ocular artefacts occurred at a different time within the epoch. For example, an epoch which contained an ocular artefact beginning at 400 ms would not be removed from the data as the artefact did not occur during the 200 ms post-stimulus onset. However, inclusion of this epoch in the averaged ERP waveform could present problems for identification of the ERP components, as voltage fluctuations which occur as a result of ocular artefacts are typically much larger than voltage fluctuations caused by neural activity (Luck, 2014).

Independent component analysis (ICA) is a statistical technique used to estimate distinct patterns of activity which together produce the recorded EEG signal. Each component represents the electrical activity associated with a specific scalp distribution (Luck, 2014). In this way, ICA can be used to identify the components which represent ocular artefacts. The activity produced by these artefacts can then be removed from the data. The present research used ICA to identify ocular artefacts and remove them from the data. Separate ICAs were run for each dataset.

Once the independent components had been extracted, the scalp topography and time course of each component was examined manually. Components denoting blinks were identified by their pattern of positive activation over frontal regions (Figure 2.4) and large voltage deflections in the waveform which typically lasted between 200 ms and 400 ms (Figure 2.5; Luck, 2014). Components denoting lateral eye movements were identified by their pattern of bilateral frontal activation (Figure 2.4) and sudden large steps from one voltage to another (Figure 2.5; Luck, 2014). In some cases, one component contained both blinks and eye movements; in other cases, blinks and eye movements were represented by separate components. Once identified, components representing ocular artefacts were removed from the data.

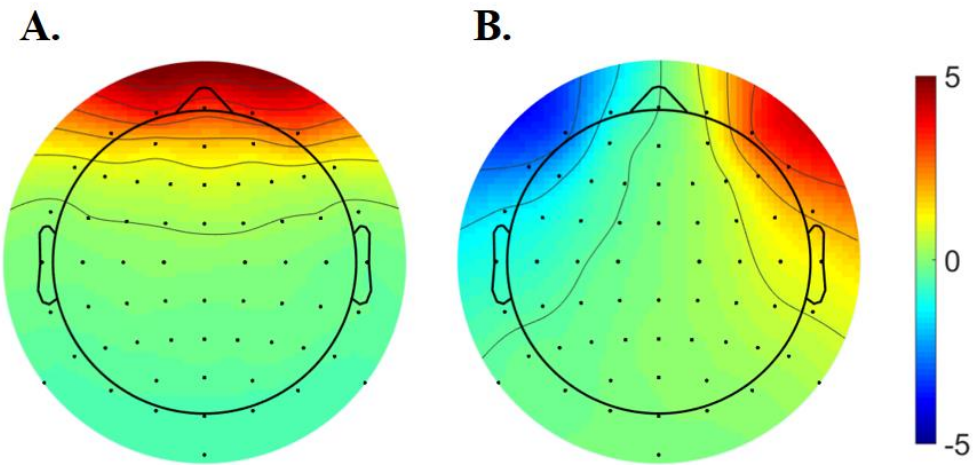

Figure 2.4. Scalp topography of ocular artefacts. Examples of the classical scalp topography of components depicting an eye blink (A) and a lateral eye movement (B). The topography of an eye blink shows high levels of positive activity in the frontal regions above the eyes, with minimal activity across other regions of the scalp. The topography of a lateral eye movement shows either left lateralised frontal negativity along with right lateralised frontal positivity, as in B, or the opposite pattern of right lateralised frontal negativity along with left lateralised frontal positivity (not shown).

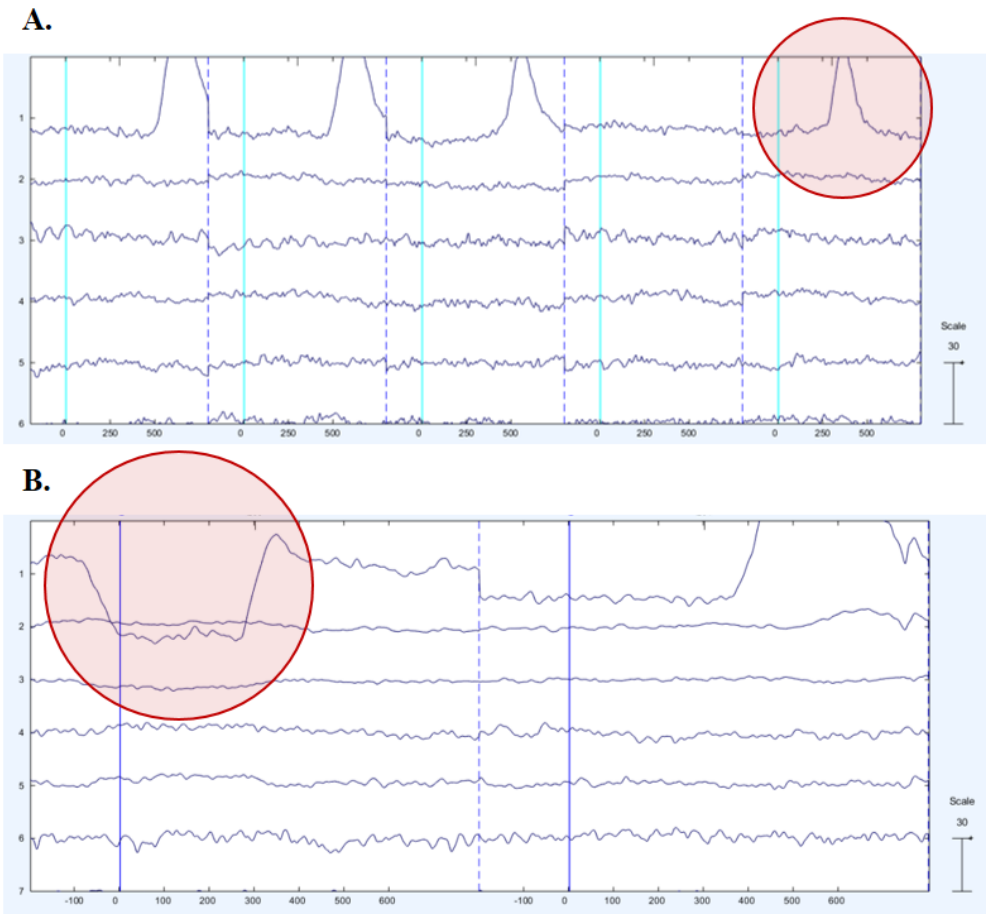

Figure 2.5. Time course of ocular artefacts. Examples of the typical time course of an eye blink (A) and a lateral eye movement (B). Eye blinks typically appear as large positive voltage deflections which last between 200 ms and 400 ms. Lateral eye movements typically appear as a 'step down' in the waveform, followed by a 'step up' when the individual shifts their gaze back in the opposite direction.

2.2.3.7. Baseline correction of EEG data and rejection of epochs containing large voltage fluctuations

Following correction of ocular artefacts, data for channels which had been removed earlier in pre-processing (Cz and any bad channels) were interpolated based on the data recorded by the surrounding channels. This procedure was carried out in order to ensure that all datasets contained the same number of channels. Baseline correction was then performed in order to reduce the effect of voltage offset on subsequent measures of ERP amplitude (Luck, 2014). Following baseline correction, epochs containing voltage fluctuations greater than +/-150μV were removed from the dataset. This process was carried out because fluctuations of this magnitude are likely to represent non-neural sources of electrical activity which could have an undue influence on the averaged ERP waveforms.

2.2.4. Measurement of ERPs

After the data had been pre-processed, measures of the N170 response were extracted for each stimulus category in each dataset. The following section will discuss the various methods which can be used to quantify ERP components, and will explain why peak amplitude was used to measure the ERP components in the present analyses. It will then provide an overview of the process that was used to select the electrodes and the time window for the present analyses. Finally, the procedure that was used to extract peak amplitude values from the present data will be described.

2.2.4.1. Methods for the quantification of ERP components

Numerous methods for the measurement of ERP components were explored over the course of this research project. Initially, a measurement of the area amplitude (also known as 'area under the curve') was used to examine the ERP components of interest. There are a number of ways to quantify area amplitude, one of which is the measurement of the signed area. This involves finding the area between the ERP waveform and the baseline. In the case of a positive-going component such as the P1, the area is defined as the region above the baseline. In the case of a negative-going component such as the N170, the area is defined as the region below the

baseline. Signed area has a number of advantages over peak amplitude and mean amplitude measures, as it is not heavily biased by the selected time window (Luck, 2014), and is relatively resilient to noise. In many experiments, measuring signed area is an effective way to quantify the size of an ERP component. However, signed area makes assumptions about the nature of the waveform which reduces its utility in certain circumstances. To use an example, signed area assumes that the N170 always crosses the baseline (which is approximately zero volts), resulting in a peak with a negative sign. However, amongst the present sample there were a large number of cases in which the N170 was clearly present but did not peak below the baseline. Therefore, signed area was not appropriate for use with the data collected in this research, as in many cases this measure would produce a value of zero, despite the clear presence of the component of interest. Consequently, another method for quantifying the area amplitude, rectified area, was examined. However, rectified area is typically used in the measurement of electromyograms (EMG; muscle activity), and is rarely used to examine ERP data (Luck, 2014). Therefore this measure was not used as it would be difficult to compare the findings with those of other EEG studies.

Given that area amplitude was not an appropriate measure for use with the present data, peak amplitude and mean amplitude were considered as potential measures. Mean amplitude has advantages over peak amplitude, such as less sensitivity to noise (Luck, 2014). However, very few previous studies have examined early visual ERP components in relation to ELS, and most of those which did measured peak amplitude (Curtis & Cicchetti, 2011; Nelson et al., 2013; Young et al., 2017). Importantly, the only one of these studies which examined the relationship between ELS and ERP responses in adult participants also examined peak amplitude (Chu et al., 2016). Therefore, in order to allow for comparisons with the small number of previous studies, the present research used peak amplitude to measure the ERP components of interest.

2.2.4.2. Selection of electrodes for ERP analysis

The N170 component is maximal over bilateral occipital-temporal regions of the scalp. In light of this, the N170 is typically measured from one or more electrodes located over the left and right occipital-temporal regions (Levita et al., 2015). Visual examination of the grand average waveforms from the first EEG study (emotional face processing; presented in Chapter 4) revealed that a large N170 component was present in electrodes P7 and P9 over the left hemisphere, and electrodes P8 and P10 over the right hemisphere. Therefore, the data were averaged across each set of two electrodes to produce a left hemisphere cluster and a right hemisphere cluster. As the component of interest (the N170) was the same across both the EEG studies (emotional face processing and avoidance), and in order to allow for comparison across studies, the same electrode clusters were used in the analysis of the data from the active and passive avoidance study (Chapter 5).

2.2.4.3. Selection of a time window for ERP analysis

Once the clusters had been created, it was necessary to identify a time window for the N170 component. To do this, the data from the emotional face processing study was used to create a grand average waveform which encompassed responding across both hemispheres, both ELS groups and all stimulus categories. This grand average included only the four occipital-temporal electrodes selected in the previous stage of analysis, as the other electrodes were not used in the measurement of the N170. The grand average waveform was then used to select a time window for the N170.

Specifically, it was decided that the time window would begin at the positive peak which preceded the N170 component and end at the positive peak which followed the N170 component. For the emotional face processing data, this resulted in a time window from 121.1 ms to 234.4 ms. The first value was rounded down to the nearest 5 ms, and the second value was rounded up to the nearest 5 ms. The values were rounded in this manner to ensure that the full time-course of the N170 waveform was included in the time window. This resulted in a time window of 120 ms to 235 ms.

However, during subsequent analysis it became apparent that, in a small number of cases, this time window was not optimal for the measurement of the N170 peak amplitude. Specifically, in these cases there were negative deflections at the very end of the time period which were identified by ERPLAB's measurement tool as the N170 peak, but which clearly did not represent the peak of the N170 when the waveform was examined by visual inspection. In light of this it was decided that the N170 time window would be shortened to allow for more accurate measurement by ERPLAB's measurement tool, and to bring it in line with the parameters used in previous research (Chu et al., 2016). In light of this, a time window of 120 ms to 220 ms was chosen. This time window was used in the measurement of the N170 in both the emotional face processing study (Chapter 4) and the active and passive avoidance study (Chapter 5).

2.2.4.4. Procedure for the measurement of the N170 peak amplitude

The measurement tool provided by ERPLAB was used to measure the peak amplitude of the N170 response to each stimulus category in both the emotional face processing experiment and the avoidance experiment. The measurement tool was used to search for a negative peak between 120 ms and 220 ms (the selection of this time window is described in § 2.2.4.3). A screen shot of the parameters entered into the measurement tool can be found in Figure 2.6, and the measurement of a peak value is illustrated in Figure 2.7. In cases where no peak could be found (Figure 2.8), ERPLAB returned a value of 'NaN' (not a number). Once all measures had been taken, cases with a value of NaN in at least one condition were removed from further analysis. In the emotional face processing study, this resulted in the removal of data from three participants. In the avoidance study, this resulted in the removal of data from eight participants. Further information about these participants can be found in § 4.2.1 and § 5.2.1, respectively. Once a value for the N170 peak amplitude in each stimulus category had been extracted, the data were transferred to SPSS for further analysis.

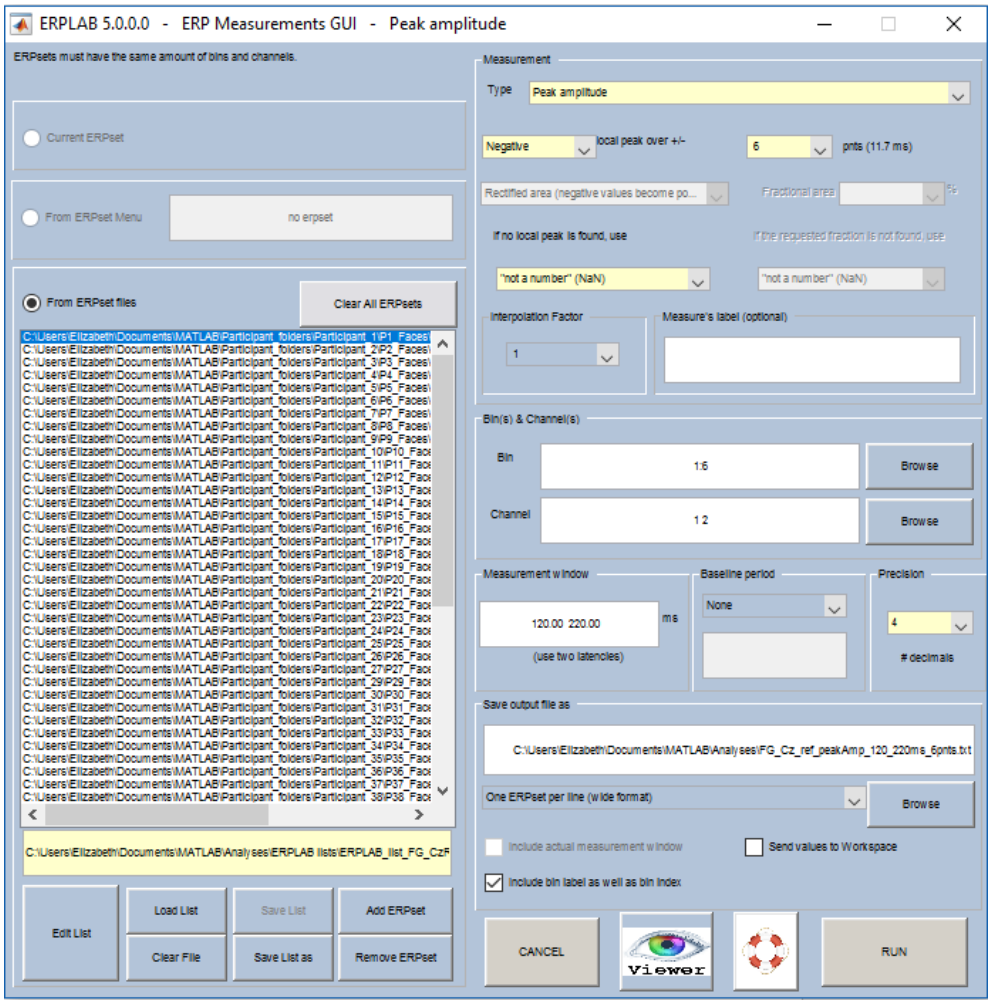

Figure 2.6. Parameters used in the measurement of the N170 peak amplitude. Screenshot of the ERPLAB Measurement Tool dialogue window. The peak amplitude was measured as a negative local peak which occurred between 120 ms and 220 ms. In cases where no local peak was found, ERPLAB returned a value of NaN (not a number). Note this image represents the parameters used in the measurement of the N170 peak amplitudes in the emotional face processing task. The parameters used in the avoidance task were the same, apart from the 'Bin' entry, which was 1:4 rather than 1:6, as this experiment contained four stimulus categories.

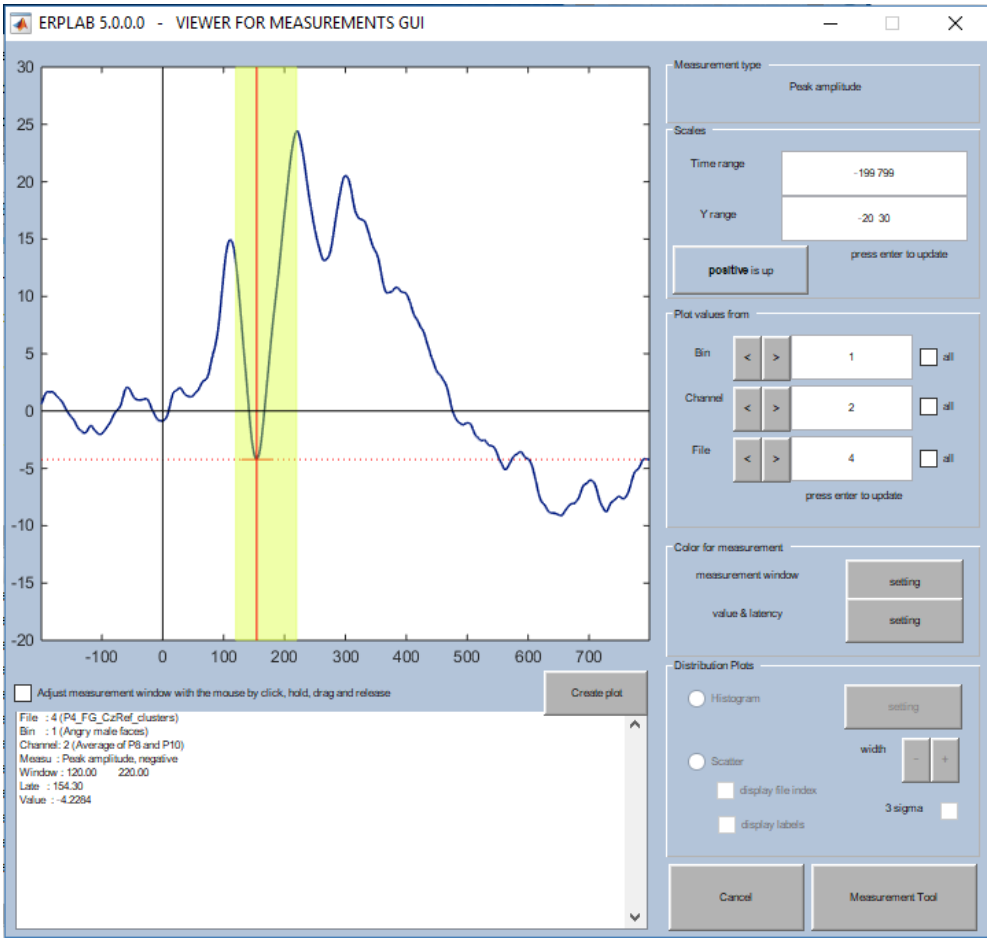

Figure 2.7. Use of the ERPLAB Measurement Tool to quantify the N170 peak amplitude for one participant in one condition. The yellow shaded area demonstrates the time window (120 ms to 220 ms). The image shows the average ERP response to angry male facial expressions (Bin 1) in the right hemisphere (Channel 2), for Participant 4. The point at which the red lines cross is used to identify the peak amplitude of the N170.

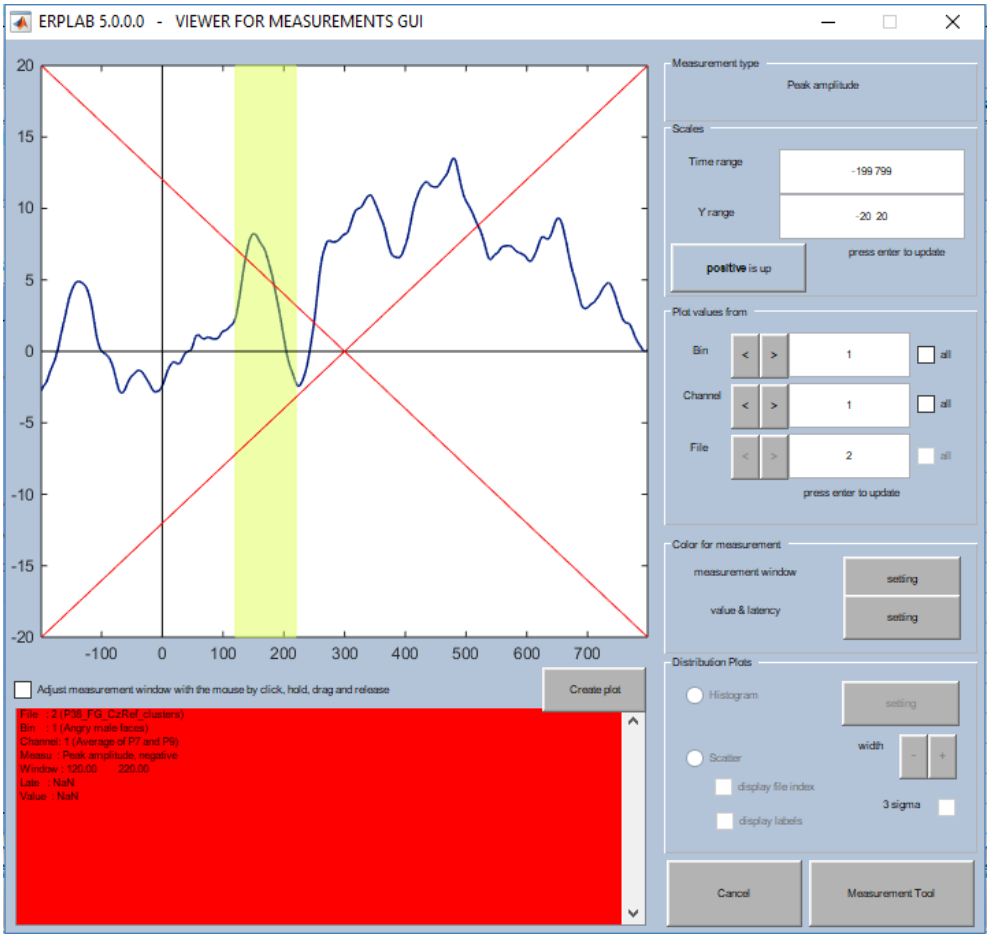

Figure 2.8. Example of a case in which the ERPLAB Measurement Tool was unable to identify a peak for the N170 response, resulting in a measurement of NaN (not a number). Due to the absence of a measurement, this participant was moved from subsequent analyses. The present figure depicts the average ERP response to angry male facial expressions (Bin 1) in the left hemisphere (Channel 1), for Participant 38.

2.3. Statistical analysis

Statistical analyses were carried out using IBM SPSS Statistics for Windows, Version 22.0. Full details of the analysis procedures used in each study can be found in the Methods sections of their corresponding chapters. As the present thesis was exploratory in nature, there were a number of cases in which multiple comparisons were carried out. The problem of multiple comparisons, and how it was dealt with in the present research, will be discussed below.

2.3.1. The problem of multiple comparisons

The problem of multiple comparisons refers to the fact that the more statistical tests are computed, the more likely it is that a 'significant' result will be discovered by chance. For example, if a single test produces a *p* value that is less than .05, this means that the chance that the experimenter incorrectly accepts their experimental hypothesis is less than 5 %. However, if 100 tests were carried out using an alpha threshold of .05, it would be expected that five of these tests would produce a *p* value that was less than .05, even if none of the tests had found a genuine effect (McDonald, 2014). This leads to an inflated family-wise error rate, which is the probability of incorrectly identifying an experimental effect in a family (group) of statistical tests when no genuine effect is actually present (known as a type I error; Field, 2005). One way to address this problem is to use the Bonferroni correction (McDonald, 2014). The Bonferroni correction involves dividing the alpha value by the number of tests that are carried out. For example, in a family of four tests, the Bonferroni corrected alpha value would be .05 divided by 4, which is .01. However, in many cases, the Bonferroni correction is too stringent, and genuine effects can be missed.

2.3.1.1. The Benjamini-Hochberg procedure

An alternative method for dealing with the problem of multiple comparisons is the Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995). This method focusses on controlling the 'false discovery rate', which is the proportion of significant findings which are actually false positives (McDonald, 2014). This procedure is especially useful for exploratory analyses, such as those used in the present research, in which the goal is to identify interesting effects which can be examined in more detail in future work. As part of the Benjamini-Hochberg procedure, a false discovery rate (FDR) is selected by the researcher. A common FDR is 10 %, which means that the researcher is willing to accept that 10 % of the significant results are actually false positives (McDonald, 2014).

The Benjamini-Hochberg procedure is illustrated in Table 2.1. This table contains the results of a hypothetical investigation in which *t*-tests were used to examine whether adults and children differed in their desire to

own various different pets. The Benjamini-Hochberg procedure is carried out as follows. First, the family of tests is performed, and the resultant *p* values are listed in order from smallest to largest (Table 2.1; Columns A and B). Next, each *p* value is given a rank according to its position in the list, with the smallest allocated a rank of one, the second smallest as two, and so on (Table 2.1; column C). The following calculation is then performed for each test: (rank/total number of tests)*FDR. This provides a list of 'critical values', with one value for each test (Table 2.1; column D). The next step in the Benjamini-Hochberg procedure is to determine the tests for which the *p* value is smaller than its corresponding critical value (Table 2.1; Column E). If a test has a *p* value which is smaller than its critical value it is classified as significant. In addition, if a test is not significant, but has a lower ranking than a test which is significant, both these tests are classified as significant (Table 2.1; Column F). For example, in Table 2.1, the variable for Dog is not significant, but as the variable for Cat, which is ranked higher, is significant, both Cat and Dog are considered to be significant.

Table 2.1

Illustration of the Benjamini-Hochberg procedure

A. Variable	B. *p* value	C. Rank	D. Critical value	E. *p* < critical value?	F. Significant?
Guinea pig	.01	1	(1/4)*0.1 = 0.03	Yes	Yes
Dog	.06	2	(2/4)*0.1 = 0.05	No	Yes
Cat	.07	3	(3/4)*0.1 = 0.08	Yes	Yes
Fish	.12	4	(4/4)*0.1 = 0.10	No	No

Note. Data from a hypothetical study examining the difference between adults' and children's desire to own each species of pet (A). The data are ranked according to their *p* value (B, C), then this *p* value is compared to a critical value calculated as (rank/number of tests)*FDR (D). The test with the highest rank for which the *p* value is less than the critical value is designated as significant (E). All tests with lower rankings than this test are also considered significant, even if their *p* values are larger than their critical values (F).

2.3.2. Assumptions of multiple linear regression analysis

Multiple linear regression analysis was used extensively throughout the work presented in this thesis. In cases where multiple regression is used, it is important to examine whether its assumptions have been met. Violation of these assumptions can result in a poorly fit model which is unable to provide reliable information about the hypotheses it is being used to test. In light of this, the following section provides a brief overview of the assumptions of multiple regression, and the ways in which each assumption can be tested.

2.3.2.1. Outliers and influential points

Outliers are cases where the value of the observed case is substantially different to the value predicted by the regression model. The difference between these values is known as the residual, or error. Outliers are typically classified as cases where the standardised residual is greater than +/- 3 *SD*s from the mean (Field, 2005). If an outlier is identified, the data should be re-examined to determine whether the data point is a true observation, as opposed to an error in data entry. If the data point is a true observation, the experimenter may choose to remove the case. When deciding whether to remove the case it is useful to examine the corresponding Cook's Distance. Cook's Distance provides a measure of the extent to which the case is influencing the regression model. A Cook's Distance greater than 1 suggests that the case may be a highly influential point which is having an undue impact on the model (Field, 2005).

2.3.2.2. Independence of residuals

An additional assumption of multiple linear regression is that there is independence of residuals, that is, the residuals do not correlate with one another. Correlation between the residuals is known as autocorrelation. This assumption can be tested using the Durbin-Watson statistic. Savin and White (1977) provide a table in which acceptable upper and lower bounds for the Durbin-Watson statistic are listed. These bounds vary according to the number of cases and the number of predictors in the analysis. In cases where the observed value is lower than the lower bound, then

autocorrelation is present in the data, and the residuals are not independent. In cases where the observed value is higher than the upper bound, then autocorrelation is not present in the data. In cases where the observed value falls between the lower and upper bounds, the test is inconclusive.

2.3.2.3. Presence of linearity

Multiple linear regression assumes a linear relationship between the dependent variable and each of the independent variables. This assumption can be investigated by visual examination of partial regression plots between the dependent variable and each independent variable. If the assumption has been met, the scatterplot will show a broadly linear relationship, with no indication of a non-linear relationship such as an exponential relationship. Multiple regression also assumes a linear relationship between the dependent variable and the independent variables collectively. This can be assessed by generating a scatterplot which plots the studentised residuals against the unstandardised predicted values. Visual examination can then be used to determine the presence or absence of linearity.

2.3.2.4. Homoscedasticity of residuals

The assumption of homoscedasticity, also known as equality of error variances, refers to the variance at each level of the predictor. Specifically, the variance should be similar at each level. This assumption can be tested by visual examination of the residual plot described in the previous section (studentised residuals plotted against unstandardised predicted values). If the assumption has been met, the data points will be approximately randomly spread, with no identifiable patterns such as a funnel with large dispersion at one end and small dispersion at the other.

2.3.2.5. Absence of multicollinearity

Multicollinearity concerns correlation between the predictors included in the model. Whilst some correlation is to be expected between psychological variables, multiple regression assumes that no two variables are highly correlated with one another. This assumption can be tested by

examination of the correlations between variables, with correlation coefficients greater than 0.8 indicating the presence of multicollinearity (Field, 2005). The assumption can be tested further by examination of the Tolerance values for each predictor. Tolerance values above 0.2 indicate that the assumption has been met, and that there is no multicollinearity in the data.

2.3.2.6. Normal distribution of residuals

Multiple regression assumes that the residuals are normally distributed. This can be examined using histograms of the standardised residuals and probability plots which plot the observed cumulative probability against the expected cumulative probability. If the assumption of normality has been met, the histogram will show a pattern which broadly follows the normal distribution, and the probability plot will show data points which follow a diagonal line across the graph.

2.4. Questionnaire measures

As discussed in Chapter 1, there is a paucity of research which examines the relationship between ELS and neurocognitive alterations in mentally healthy adults. Therefore, as part of this doctoral research, a number of questionnaire measures were used to generate a psychological profile of young adults who had experienced ELS but had not been diagnosed with any mental health conditions. The measures that were taken covered a number of categories. These were: experience of ELS; level of anxiety and depression; approach and avoidance tendencies; and (self) deception. In addition to providing an overview of the psychological profile of mentally healthy adults with differing experiences of ELS, some of the measures were used as control variables in analyses examining the effect of ELS on the measures of neurocognitive processing examined in this research (emotional face processing and avoidance of threat). Specifically, in the first study (Chapter 3), measures of anxiety and depression were included as co-variates in the regression analyses, whilst in the EEG studies (Chapters 4 and 5), scores on any questionnaire measure for which the two ELS groups differed significantly were included as co-variates in the regression analyses. This reduced the risk of incorrectly attributing between-group effects to ELS itself if this effect could have been explained by a different variable which also differed between the two ELS groups (e.g. depression scores). This was particularly important in the case of anxiety and depression, as both anxiety and depression are positively associated with ELS, and have presented a potential confound in many previous studies of ELS (§ 1.2.1.1). The following section provides information about each of the questionnaire measures used in the present doctoral research.

2.4.1. Measurement of early life stress

Many studies within the field of ELS classify participants as having experienced ELS if they have encountered extreme abuse or neglect which has been recorded by governmental authorities. For example, much of the work carried out by Pollak and his colleagues, as well as that led by McCrory and Viding, involves comparing children who have experienced documented physical abuse with children who have not experienced

documented abuse (e.g. McCrory et al., 2011; Pollak & Kistler, 2002). Other influential work, such as that carried out as part of the Bucharest Intervention Project, focusses on early institutionalisation as a form of neglect (e.g. Moulson et al., 2009). The use of objective records as a method for measuring ELS is particularly common in studies with child participants. By contrast, cross-sectional studies with adult participants typically use retrospective self-report questionnaires to measure ELS. These measures are useful in cases, such as the present research, where obtaining legally substantiated evidence of ELS is not possible.

A number of self-report questionnaires have been used to measure experiences of ELS across the literature. Commonly used measures include the Adverse Childhood Experience questionnaire (ACE; Felitti et al., 1998), the Childhood Trauma Questionnaire (CTQ; Bernstein & Fink, 1998), and the Child Abuse and Trauma Scale (CATS; Sanders & Becker-Lausen, 1995). The ACE questionnaire (Felitti et al., 1998) comprises a series of 12 questions with binary ('yes'/'no') responses. Based on these responses, participants are sorted into those who experienced a given form of ELS (e.g. physical abuse) and those who did not. In contrast, both the CTQ (Bernstein & Fink, 1998) and the CATS (Sanders & Becker-Lausen ,1995) require participants to respond to a series of questions using a five-point Likert scale. In this way, respondents can be ranked in terms of the severity of their experiences.

As discussed in Section § 1.2.1, there is a positive relationship between experiences of ELS and increased risk of negative psychosocial outcomes, such as mental illness, later in life. Given that the present research specifically recruited individuals who had reached early adulthood without being diagnosed with any mental health problems, it was anticipated that extreme experiences of ELS would be relatively scarce within the sample. Therefore it was decided that the present research would benefit from the use of a questionnaire which provides a nuanced measure of the early environment, as opposed to a questionnaire that takes a more categorical approach, such as the ACE. In light of this the CATS was chosen as the measure of ELS in the present research, as it was able to provide a good overview of the respondents' early environments.

Furthermore, at 38 items, its length was appropriate for the studies included in this project, and unlike the CTQ, it was freely accessible for use in research.

2.4.1.1. The Child Abuse and Trauma Scale

In all studies, ELS was measured using the Child Abuse and Trauma Scale (CATS; Sanders & Becker-Lausen, 1995). The CATS is a retrospective self-report measure of home environment during childhood and adolescence. It consists of 38 items covering four broad areas: negative home environment/neglect, punishment, sexual abuse and emotional abuse (Kent & Waller, 1998). Examples of items included in the scale are: 'How often were you left at home alone as a child?', 'As a child were you punished in unusual ways (e.g., being locked in a closet for a long time or being tied up)?' and 'Did your parents ever verbally abuse each other?' Participants are asked to rate each item on a scale of 0 (never) to 4 (always). This produces a total score between 0 and 152. Kent and Waller (1998) examined the reliability and validity of the CATS in a sample of mentally healthy women. They found that it showed high internal consistency as indicated by a Cronbach's alpha of 0.90 (Kent & Waller, 1998; Sanders & Becker-Lausen, 1995). Given the close relationship between high levels of ELS and increased rates of anxiety and depression in adulthood, it would be expected that scores on a measure of ELS would be correlated with scores on measures of depression and anxiety. Kent and Waller (1998) tested this and found that total CATS scores were significantly positively correlated with previously validated measures of anxiety and depression (Hospital Anxiety and Depression Scale; Zigmond & Snaith, 1983). This provides evidence for the concurrent validity of the CATS.

2.4.2. Measurement of anxiety and depression

As described above, the present research aimed to examine the effects of ELS on the psychological profile of mentally healthy young adults. In the first study (Chapter 3), anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) and the Spielberger State Trait Anxiety Inventory (STAI; Spielberger et al., 1983). The HADS was used as, at 14 items in length, it is

a quick way to collect an overview of participants' anxiety and depression symptoms. The STAI was used as, unlike the HADS, it provides separate measures of trait and state anxiety, with one subscale for each construct. The inclusion of the STAI therefore allowed for examination of whether ELS was differentially related to these two subcomponents of anxious experience. In addition, given how extensively the STAI has been utilised across the wider literature (Julian, 2011), it was decided that employing this measure would facilitate comparisons between the present sample and those recruited by a broad range of related studies.

However, whilst the STAI is widely used across the literature, there are questions as to the ability of its trait subscale to measure trait anxiety as a construct (Bados, Gomez-Benito & Balaguer, 2010). Specifically, it has been suggested that the trait subscale of the STAI represents a measure of negative affect rather than trait anxiety, in light of work which has found that this subscale correlates more closely with measures of depression than measures of anxiety (Bados et al., 2010). In light of these concerns, additional measures of anxiety and depression, the Beck Anxiety Inventory (BAI; Beck et al., 1988) and the Beck Depression Inventory II (BDI-II; Beck et al., 1996), were included in the second two studies (Chapters 4 and 5). The BAI has particular strengths in the measurement of somatic anxiety (Julian, 2011), and shows better discriminant validity than the STAI-T with respect to distinguishing between anxiety and depression (Fydrich, Dowdall, & Chambless, 1992). The BDI-II is able to detect depression even after accounting for negative affect (Hill, Musso, Jones, Pella & Gouvier, 2013), and has been described as the 'gold standard for self-rating scales [of depression]' (Cusin, Yang, Yeung & Fava, 2009, p. 10). Participants in the second two studies (Chapters 4 and 5) were also presented with the HADS and STAI to allow for comparison with the data collected in the first study. The following section describes each of the measures of mental distress in more detail.

2.4.2.1. Hospital Anxiety and Depression Scale (HADS)

The HADS (Zigmond & Snaith, 1983) is a 14-item measure of psychological distress. It is comprised of two scales, an anxiety scale and a

depression scale, each of which contains seven items. Each item takes the form of a statement, such as 'I can laugh and see the funny side of things' or 'Worrying thoughts go through my mind'. Participants indicate the extent to which they experience the symptom(s) described in the statement by selecting one of four response options. Possible scores on each of the HADS subscales range from 0 to 21. The HADS has good internal consistency and shows relatively good concurrent validity, as evidenced by its medium to strong correlations with other measures of anxiety and depression, such as the STAI (Spielberger et al., 1983) and the Beck Depression Inventory (BDI; Beck, Erbaugh, Ward, Mock, & Mendelsohn, 1961; Bjelland, Dahl, Haug, & Neckelmann, 2002; Lisspers, Nygren, & Soderman, 1997).

2.4.2.2. Beck Depression Inventory II (BDI-II)

The BDI-II (Beck et al., 1996) is a 21-item self-report measure which assesses symptoms of depression. For each item, participants are presented with a number of statements and asked to select the statement that best describes the way they have been feeling during the previous two weeks. For example, item 1, which concerns sadness, includes the statements 'I do not feel sad', 'I feel sad much of the time', 'I feel sad all the time' or 'I am so sad or unhappy that I can't stand it'. The measure has a minimum possible score of 0 and a maximum possible score of 63. A review of the psychometric properties of the BDI-II found high internal consistency, with an average Cronbach's alpha of around 0.9 across studies (Wang & Gorenstein, 2013). Similarly, correlations between scores on the BDI-II and other measures of depression were relatively high, indicating good concurrent validity (Wang & Gorenstein, 2013).

2.4.2.3. Beck Anxiety Inventory (BAI)

The BAI is a 21-item self-report measure which assesses symptoms of anxiety (Beck et al., 1988). Participants are asked to indicate the extent to which they experienced each symptom of anxiety over the previous month. Examples of anxiety symptoms assessed are: 'feeling hot', 'unable to relax', and 'fear of dying'. Possible scores on the BAI range from 0 to 63. The BAI has high levels of internal consistency (Contreras, Fernandez, Malcarne,

Ingram, & Vaccarino, 2004) and good discriminant validity, such that it can reliably discriminate anxiety from depression (Creamer, Foran, & Bell, 1995; Fydrich et al., 1992).

2.4.2.4. State-Trait Anxiety Inventory (STAI)

The STAI (Spielberger et al., 1983) is a 40-item measure of anxiety. It is divided into two 20-item subscales which measure the participant's current level of anxiety (state anxiety, STAI-S), and the participant's general disposition towards anxiety (trait anxiety, STAI-T). On the state anxiety scale participants are asked to read a series of statements and respond on a four point scale ranging from 'not at all' to 'very much so'. Examples of statements used in the state anxiety scale are 'I am tense' and 'I feel frightened'. On the trait anxiety scale participants respond on a four point scale ranging from 'almost never' to 'almost always'. Examples of statements used in the trait anxiety scale are 'I worry too much over something that really doesn't matter' and 'I feel inadequate'. The minimum possible score for each of the two subscales is 20, and the maximum possible score is 80. Both the STAI-T and STAI-S show good internal consistency (Barnes, Harp, & Jung, 2002), and test-retest scores are more highly correlated for the STAI-T than for the STAI-S, as would be expected if the two subscales were providing reliable measures of trait and state anxiety, respectively (Barnes et al., 2002).

2.4.3. Measurement of approach and avoidance tendencies

Gray (1981, 1982) suggests that approach and avoidance behaviour are supported by two distinct motivational systems, the behavioural inhibition system (BIS) and the behavioural activation system (BAS). The BIS, which is associated with anxiety and negative affect, is sensitive to signals of punishment, whilst the BAS, which is associated with impulsivity and positive affect, is sensitive to signals of reward (Carver & White, 1994). It is thought that the relative sensitivity of the BIS and BAS will mediate an individual's approach and avoidance responding to cues of punishment and reward. Despite evidence for alterations in avoidance behaviour following ELS (§ 1.4.5), very few studies have examined whether experiences of ELS

are associated with changes in the BIS and BAS. Therefore, as an exploratory measure, participants in the EEG studies (Chapters 4 and 5) were asked to complete two questionnaires, each of which measure constructs derived from Gray's model of personality. These questionnaires, the Behavioral Inhibition System/Behavioral Activation System Scales (BIS/BAS Scales; Carver & White, 1994) and the Sensitivity to Punishment/Sensitivity to Reward Questionnaire (SPSRQ; Torrubia et al., 2001), are described below.

2.4.3.1. Sensitivity to Punishment/Sensitivity to Reward Questionnaire (SPSRQ)

The SPSRQ (Torrubia et al., 2001) is designed to measure individual differences in anxiety or sensitivity to punishment (BIS) and in impulsivity or sensitivity to reward (BAS). The questionnaire contains 48 items, each of which requires a 'Yes' or 'No' response from the participant. Half of the items concern sensitivity to punishment, whilst the other half assesses sensitivity to reward. Examples of questions examining sensitivity to punishment are, 'Do you often refrain from doing something because you are afraid of it being illegal?' and 'Would it be difficult for you to ask your boss for a raise (salary increase)?'. Examples of items assessing sensitivity to reward are, 'Do you often do things to be praised?' and 'Are you interested in money to the point of being able to do risky jobs?'. Responses receive a score between 0 and 24 for each subscale (punishment and reward). In a sample of university students (n = 538), both the Sensitivity to Punishment (SP) and Sensitivity to Reward (SR) scales showed acceptable internal consistency, with Cronbach's alpha values of 0.83 and 0.76, respectively (Caseras, Avila, & Torrubia, 2003). In terms of concurrent validity, Caseras et al. (2003) found that the SP was negatively associated with extraversion and positively associated with neuroticism as measured by the Eysenck Personality Questionnaire (EPQ; Eysenck & Eysenck, 1975). Similarly, the SR was positively associated with extraversion and neuroticism. These associations are in the directions that would be expected if the scales were indeed measuring sensitivity to punishment and sensitivity to reward.

2.4.3.2. Behavioural Inhibition System/Behavioural Activation System (BIS/BAS) Scales

Like the SPSRQ, the BIS/BAS scales (Carver & White, 1994) are based upon Gray's model of personality, and are designed to measure the sensitivity of a respondent's BIS and BAS. Unlike the SPSRQ, which provides one score for each scale (punishment/BIS and reward/BAS), the BIS/BAS Scales provide one measure of BIS functioning and three sub-scales measuring different dimensions of BAS functioning. These subscales are labelled Drive, Fun-seeking and Reward Responsiveness. The scales contain 24 items, four of which are fillers. The BIS scale contains seven items (minimum score: 7, maximum score: 28), the BAS: Drive and BAS: Fun-seeking scales each contain four items (minimum score: 4, maximum score: 16), and the BAS: Reward Responsiveness scale contains five items (minimum score: 5, maximum score: 20). Examples of items are: 'Even if something bad is about to happen to me, I rarely experience fear or nervousness' (BIS), 'I go out of my way to get things I want' (BAS: Drive), 'I'm always willing to try something new if I think it will be fun' (BAS: Fun-seeking), and 'It would excite me to win a contest' (BAS: Reward Responsiveness).

Sava and Sperneac (2006) examined the relationship between the BIS/BAS scales and the anxiety and impulsivity dimensions derived from a measure of personality, the EPQ (Eysenck & Eysenck, 1975). As would be expected if the scales were indeed measuring behavioural inhibition and activation, the BIS scale was positively correlated with anxiety, whilst each of the BAS scales was positively correlated with impulsivity. This provides evidence for the validity of the scales. In terms of reliability, Ross, Millis, Bonebright, and Bailley (2002) found that the BIS/BAS Scales showed an acceptable level of internal consistency when tested with a sample of undergraduate participants, such that all scales had a Cronbach's alpha greater than 0.70.

2.4.4. Measurement of (self) deception

The final measures included in the present research were the Paulhus Deception Scales (PDS; Paulhus, 1998), which are designed to assess a respondent's tendency to give socially desirable responses on self-report measures. The PDS is a 40-item measure which is comprised of two 20-item subscales measuring different aspects of deception: deception of others (Impression Management) and deception of the self (Self-deceptive Enhancement). Both subscales have a minimum potential score of 0 and a maximum potential score of 20. The Impression Management subscale assesses social desirability and contains items such as 'I never swear' and 'I have taken sick-leave from work or school even though I wasn't really sick'. The rationale behind this measure is based on an assumption that the majority of people occasionally do undesirable things, and that those who report that they do not do these things (and hence score highly on the Impression Management subscale) are being either wilfully or unintentionally untruthful due to high social desirability bias. The Self-deceptive Enhancement subscale assesses respondents' insight into their own psychological and behavioural abilities. Examples of items on the Self-deceptive Enhancement scale are 'I always know why I like things' and 'I am not a safe driver when I exceed the speed limit'. High scores on this subscale represent overconfidence in one's abilities accompanied by positive self-esteem and potentially poor interpersonal judgement (Paulhus, 1998).

When the EEG studies (Chapters 4 and 5) were first designed, it was anticipated that the Impression Management subscale of the PDS would be used as a 'validity check' to exclude participants who were not responding truthfully. However, contrary to expectations, the high and low ELS groups differed significantly on the measure of impression management, and exclusion of participants who scored above the cut-off value for 'lying' proposed by Paulhus (1998) would have resulted in the exclusion of more than twice as many participants from the low ELS group (n = 5) than from the high ELS group (n = 2). In addition, a high score on the Impression Management subscale could indicate that an individual is very virtuous, rather than 'lying'. Therefore, it was decided that participants would not be

excluded from subsequent analyses on the basis of their impression management scores. Instead, the PDS Impression Management scores were used in the same way as the other questionnaire measures; to provide an overview of the effect of ELS on measures of psychological functioning in mentally healthy young adults, and to act as a control variable in subsequent analyses.

The PDS subscales show good convergent validity and internal reliability (Paulhus, 1998). When tested with both a college (university) student sample and a sample from the general population, Cronbach's alpha values for the two subscales were greater than 0.7 for the Self-deceptive Enhancement subscale and greater than 0.8 for the Impression Management subscale (Paulhus, 1998), indicating acceptable to good internal consistency. In addition, the PDS Impression Management subscale showed good concurrent validity with measures of exaggerated virtue in an undergraduate sample of participants (Lanyon & Carle, 2007).

Chapter 3. The relationship between early life stress and young adults' self-reported responses to emotional facial expressions: atypical identification of anger and reduced avoidance of threat

Abstract

Early neglect or maltreatment often results in maladaptive changes to neurocognitive processes which subsequently increase vulnerability to mental illness in adulthood (McCrory & Viding, 2015). One such change is altered processing of emotional facial expressions. However, despite compelling evidence for atypical identification of emotional expressions in children who experience ELS, few studies have investigated whether these effects persist into adulthood, nor whether experiences of ELS affect individuals' approach and avoidance of these threat and safety signals. Therefore, the present study aimed to examine the impact of ELS on 18-19 year olds' (n =147) ratings of angry, happy and neutral facial expressions, and their behavioural tendencies to approach or avoid these cues. Significantly, higher levels of ELS were associated with greater approach and reduced avoidance of angry facial expressions. ELS was also associated with reduced identification of anger in female, but not male, angry facial expressions. ELS-related approach behaviour towards threatening facial expressions could reflect an adaptation to an early abusive environment. This adaptation could have a negative impact on social interactions later in life, acting as a latent vulnerability which increases the risk of the development of mental illness. The presence of this adaptation in a sample of young adults is particularly salient given that young adulthood is a sensitive period of neurodevelopment when the risk of mental illness is high and final brain maturation processes are still taking place.

3.1. Introduction

As discussed in Chapter 1, the research presented in this thesis focusses on two neurocognitive mechanisms which may be altered following ELS: emotional face processing, and avoidance of threat. The present study examines both of these constructs at the behavioural level, by addressing the relationship between ELS and self-reported identification of emotion in emotional facial expressions (emotional face processing), and the relationship between ELS and self-reported avoidance of angry facial expressions (avoidance of threat). The present study had two specific aims, the first of which was to examine the relationship between ELS and young adults' self-reported identification of anger and happiness in angry, happy and neutral facial expressions displayed by male and female individuals. The second aim was to examine the relationship between ELS and young adults' self-reported tendencies to approach or avoid individuals displaying angry, happy and neutral facial expressions.

As detailed in § 1.3.1, work with children has shown that individuals who experienced high levels of ELS require less information to identify anger (Pollak et al., 2009), and misattribute the emotion of anger to neutral facial expressions (Pollak & Kistler, 2002). According to the theory of latent vulnerability (McCrory & Viding, 2015), this hyper-sensitivity to anger could represent a neurocognitive adaptation to a maltreating environment. Though initially adaptive, this neurocognitive alteration (latent vulnerability) becomes maladaptive when applied to non-maltreating environments later in life, potentially leading to social difficulties and increasing the risk of mental illness (§ 1.2.3). In line with this theory, it has been suggested that hyper-sensitivity to anger may represent an environmental adaptation which develops in order to help an individual avoid harm in a maltreating context (Pollak et al., 2009). However, despite the intuitive value of this explanation, very little research has examined whether ELS is associated with changes in individuals' explicit behavioural tendencies to avoid angry facial expressions.

Furthermore, the vast majority of behavioural research into the relationship between ELS and emotional face processing has been carried out with children, and the relationship between ELS and emotional face

processing in adults remains unclear. Initial evidence suggests that the association between high levels of ELS and hyper-sensitivity to anger found in children may also be present in adults. Gibb et al. (2009) gave young adults a task in which images of facial expressions were 'morphed' from a neutral expression to an emotional expression in 10 % increments (i.e. 90 % neutral, 10 % angry; 80 % neutral, 20 % angry and so on). As such, the intensity of each emotion (e.g. anger) could be said to increase as the facial expression moved from a neutral expression to a display of a prototypical emotion (e.g. an angry facial expression). Participants were asked to identify the emotion that was being displayed in each image as it morphed from a neutral expression to a specific emotional expression. Gibb et al. (2009) found that young adults with high levels of ELS showed enhanced sensitivity to the emotion of anger, as evidenced by their ability to detect anger at lower levels of emotional intensity. However, high levels of ELS were not associated with changes in the identification of happiness or sadness.

Whilst Gibb et al.'s (2009) findings offer promising insight into a possible relationship between ELS and adults' emotional face processing, the authors of the study did not exclude people with diagnosed mental health conditions from their analyses. This represents a potential confound, as the close relationship between ELS and mental illness makes it difficult to determine whether the findings can be reliably attributed to differences in ELS itself, rather than to differences in mental health status. This represents a particular concern for studies of emotional face processing, as there is evidence to suggest that mental illness is itself associated with changes in emotional face processing. Studies have shown that depression in particular is related to reduced identification of happiness in emotional facial expressions (Gur et al., 1992; Joormann & Gotlib, 2006; Munkler, Rothkirch, Dalati, Schmack, & Sterzer, 2015), and increased self-reported avoidance of images depicting emotional facial expressions in general (Derntl et al., 2011; Seidel et al., 2010).

Due to the dearth of previous research, it remains unclear whether experiences of ELS are associated with alterations in emotional face processing or avoidance of threat (angry facial expressions) in mentally

healthy young adults. In light of this, the present study examined the effect of ELS on self-reported responses to emotional facial expressions in a sample of young adults with no past or present diagnoses of mental illness. The present study focussed on young adulthood (age 18 to 19) because it represents a time of substantial social and neurodevelopmental change (Sowell et al., 1999) during which an ability to respond accurately to social cues of emotion becomes particularly important for the creation and maintenance of interpersonal relationships.

The present study used a similar approach to Seidel et al. (2010). Specifically, participants were presented with images of male and female individuals displaying angry, happy and neutral facial expressions. For each image, participants indicated how happy and angry they perceived the individual to be, as well as how likely they would be to approach and to avoid the individual displaying the facial expression. In light of previous work showing gender effects in participants' responses to male and female individuals (Miller, Chabriac, & Molet, 2013; Seidel et al., 2010), responses to male and female faces were analysed separately, and the effect of participant gender on responses was examined.

It was hypothesised that higher levels of ELS would be associated with increased avoidance of angry facial expressions, and that female participants would show greater avoidance of angry facial expressions than male participants. It was also predicted that higher scores on a measure of depression would be associated with reduced identification of happiness in happy facial expressions, and that higher levels of ELS would be associated with increased perception of anger in neutral facial expressions.

3.2. Method

3.2.1. Participants

One hundred and eighty-five 18 to 19 year olds (M = 18.45, SD = 0.50) took part in the study. Thirty-six participants were excluded as they had been diagnosed with or treated for a mental illness or developmental disorder, and one participant was excluded due to incorrect completion of a questionnaire. As the study included investigation of gender effects, one participant who described their gender as 'other' was excluded. The final sample therefore consisted of 147 participants (81 female). All participants were from the United Kingdom. Participants gave informed consent and were made aware that they could withdraw from the study at any time. The study was approved by the Department of Psychology Ethics Committee, University of Sheffield (#981). Thirty participants (recruited via www.prolific.ac) received £2.10 for completing the study; the remainder were offered entry to a £20 prize draw.

3.2.2. Materials

3.2.2.1. Face stimuli

Colour photographs of angry, happy and neutral facial expressions were taken from the 'FACES' database, a validated database of facial expressions (Ebner, Riediger, & Lindenberger, 2010). All of the colour photographs depict frontal views of the head, neck and upper shoulders of young (19 – 31 years) Caucasian individuals. Pilot testing indicated that inclusion of the full stimulus set (48 images depicting different individuals) in the survey would lead to attrition due to the length of time it would take to complete. Consequently, the full set was split into two sets of 24 images, and each participant was shown one of these two sets. The stimulus sets were each comprised of 12 male faces and 12 female faces, with four faces of each gender depicting each facial expression (angry, happy and neutral).

3.2.2.2. Questionnaires

Participants completed three questionnaires during the study. The first of these, the CATS (Sanders & Becker-Lausen, 1995), assesses a respondent's home environment during their childhood and adolescence,

and was used as a measure of ELS. The other two questionnaires, the STAI (Spielberger et al., 1983) and the HADS (Zigmond & Snaith, 1983) were used to measure anxiety and depression. Additional information about these questionnaires can be found in § 2.4.

3.2.3. Procedure

The study was carried out online via Qualtrics (www.qualtrics.com). After providing consent and demographic information, participants were shown one set of 24 images of male and female models depicting angry, happy and neutral facial expressions. Participants used four 'sliders' located below each image (Figure 3.1) to indicate, on a 100 point scale, the extent to which they would approach the person in the image, the extent to which they would avoid the person in the image, how angry they perceived the person to be, and how happy they perceived them to be. The order of the rating sliders was counterbalanced across participants. The task was presented across 24 web pages, with each page displaying one image positioned above the four sliders (Figure 3.1). The order of image presentation was randomised across participants. After completing this task, participants completed the questionnaires measuring levels of ELS, anxiety and depression. The order of these questionnaires was counterbalanced across participants.

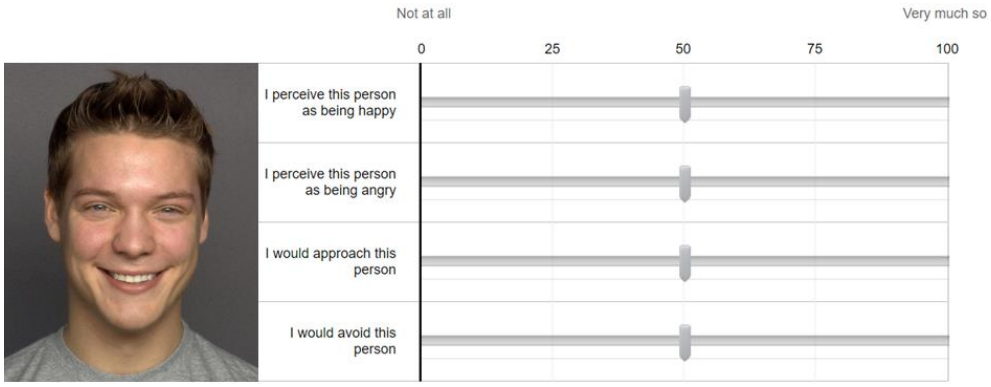

Figure 3.1. Example of a screen viewed by participants. Note in the actual task the image of the facial expression was positioned above the 'sliders'.

3.2.4. Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0. Several measures were non-normally distributed; thus, where appropriate, original *p* values are reported alongside bias-corrected and accelerated 95 % bootstrap confidence intervals based on 1000 samples. Bootstrapping was not applied to the regression analyses as linear regression does not rely on normal distribution of the input variables (Field, 2005).

The primary objective of the present research was to examine the effect of ELS on self-reported responses to emotional facial expressions, whilst controlling for additional variables that could also affect responding. These additional variables were participant gender, depression, anxiety and face set. Face set was included in the model in order to control for the effect of any differences between the two sets, given that each participant viewed one of two sets of stimuli rather than every stimulus. In order to avoid problems of multicollinearity, only one of the three measures of anxiety (STAI-T; STAI-S; HADS-A) which were completed by participants was included in the regression model. STAI-T was selected for entry into the regression model as it is one of the most widely used measures of anxiety across research studies (Julian, 2011). HADS-D scores were used as the measure of depression.

Therefore, the hierarchical linear regression model included participant gender, depression scores (HADS-D), anxiety scores (STAI-T) and face set in Step 1, and ELS scores (CATS) in Step 2. This regression model was used to predict (a) self-reported approach and avoidance of each of the six categories of face stimulus (angry, happy and neutral male and female faces) and (b) identification of emotions (anger and happiness) in these facial expressions. This resulted in a total of 24 hierarchical linear regression analyses. The Benjamini-Hochberg procedure was used to control for multiple comparisons (Benjamini & Hochberg, 1995). The present study is one of the first to investigate the effects of ELS on processing of facial expressions in mentally healthy adults, and is therefore exploratory in nature. Consequently, a false discovery rate (FDR) of 0.1 was chosen to allow for the detection of any findings which might warrant

further investigation in future work. In cases where the R^2 value of a regression model remained significant after controlling for multiple comparisons, the beta weights for the variables of interest were examined individually, using an alpha level of $p < .05$.

3.3. Results

3.3.1. Demographics

Mean scores on measures of ELS (CATS), depression (HADS-D) and anxiety (STAI-T; STAI-S; HADS-A) for male and female participants are presented in Table 3.1. The relationship between ELS (CATS), and scores on measures of depression (HADS-D) and anxiety (STAI-T) were examined using partial correlations. Due to the significant difference between male and female participants' depression scores (Table 3.1), correlations were performed separately for each gender. Given the strong positive correlation between depression and anxiety scores in both male ($r(64) = .62$, $p < .001$, 95% CI [.46, .77]) and female participants ($r(79) = .77$, $p < .001$, 95% CI [.67, .84]), anxiety and depression were included as control variables in the respective analyses. When controlling for anxiety, ELS was significantly associated with depression scores in both male ($r(63) = .39$, $p = .001$, 95% CI [.19, .60]) and female ($r(78) = .30$, $p = .007$, 95% CI [.05, .49]) participants. When controlling for depression, ELS was significantly associated with anxiety in male participants ($r(63) = .33$, $p = .008$, 95% CI [.09, .55]), but not in female participants ($r(78) = .12$, $p = .30$, 95% CI [-.14, .36]).

Table 3.1

Means, standard deviations (in brackets) and comparisons between male and female participants for ELS, depression and anxiety scores

Variable	Participants			*p*	95% CI
	All (n = 147)	**Male** (n = 66)	**Female** (n = 81)		
CATS	24.85 (16.15)	25.11 (13.60)	24.64 (18.04)	.86	-4.70, 4.90
HADS-D	3.79 (3.09)	4.53 (3.34)	3.19 (2.74)	.01*	0.37, 2.31
HADS-A	7.96 (3.99)	7.79 (3.86)	8.10 (4.10)	.64	-1.61, 0.96
STAI-T	44.49 (12.08)	44.20 (13.03)	44.73 (11.32)	.79	-4.14, 3.04
STAI-S	38.26 (11.84)	39.00 (12.51)	37.65 (11.32)	.50	-2.36, 5.14

Note. CATS = Child Abuse and Trauma Scale; HADS-D = Hospital Anxiety and Depression Scale – Depression; HADS-A = Hospital Anxiety and Depression Scale – Anxiety; STAI-T = Spielberger State Trait Anxiety Inventory – Trait; STAI-S = Spielberger State Trait Anxiety Inventory – State. Independent *t*-tests used for comparison of means between male and female participants. * = p <.05

3.3.2. Task performance

Mean responses (approach, avoidance, identification of anger, identification of happiness) towards the three facial expressions are presented in Figure 3.2. Four 2-factor mixed model ANOVAs were carried out in order to examine the effect of emotional facial expression on participants' responses. Facial expression (angry, happy, neutral) was entered as a repeated measures factor while face set (1,2) was entered as a between groups factor. There were significant effects of facial expression on approach ($F(1.64, 237.08) = 409.27$, $p < .001$) and avoidance responses ($F(1.75,253.74) = 455.53$, $p < .001$), as well as on identification of anger ($F(1.71, 248.43) = 670.50$, $p < .001$) and happiness ($F(1.57, 226.91) = 1059.77$, $p < .001$). Of the three facial expressions, participants were most likely to approach happy expressions ($M = 72.58$, $SD = 19.30$) and least likely to approach angry expressions ($M = 26.56$, $SD = 15.32$). Similarly, they were most likely to avoid angry expressions ($M = 65.57$, $SD = 16.74$) and least likely to avoid happy expressions ($M = 19.10$, $SD = 14.98$). Angry expressions were perceived to be the most angry ($M = 72.06$, $SD = 15.06$) while happy expressions were perceived to be the least angry ($M = 10.82$, $SD = 10.99$). Happy facial expressions were perceived to be the most happy ($M = 85.88$, $SD = 11.47$) while angry expressions were perceived to be the least happy ($M = 18.90$, $SD = 14.70$). Pairwise comparisons indicated significant differences between each pair of facial expressions on each response scale (Figure 3.2).

There was a significant effect of face set on approach responses ($F(1, 145) = 5.69$, $p = .02$), and the interaction between expression and face set had a significant effect on approach ($F(1.64, 237.08) = 7.97$, $p = .001$) and avoidance responses ($F(1.75, 253.74) = 8.96$, $p < .001$), and on identification of happiness ($F(1.57, 226.91) = 5.38$, $p = .01$). Consequently, face set was included as a covariate in all subsequent analyses.

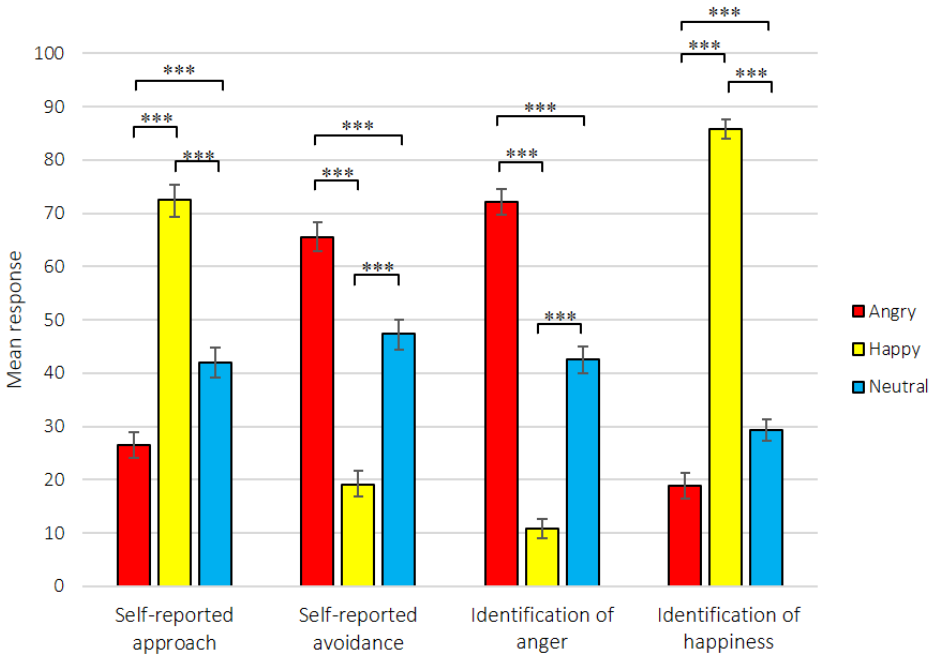

Figure 3.2. Mean responses on ratings scales for approach, avoidance and identification of anger and happiness for angry, happy and neutral facial expressions. Error bars represent 95% bias corrected and accelerated confidence intervals. Differences between facial expressions were calculated using pairwise comparisons with Bonferroni correction for multiple comparisons; *** $p < .001$.

3.3.3. Early life stress and participant gender predict approach and avoidance responses towards angry facial expressions

Hierarchical multiple regression analyses were used to examine the effect of ELS on approach and avoidance responses to angry facial expressions (Table 3.2), and on identification of anger and happiness in angry facial expressions (Table 3.3). A two-step hierarchical regression model was used to predict participants' responses to male and female angry facial expressions, with participant gender, depression scores, anxiety scores and face set entered in Step 1, and ELS entered in Step 2. The regression model explained a significant amount of the variance in participants' approach and avoidance responses to male and female angry facial expressions (Table 3.2), as well as a significant amount of the variance in participants' identification of anger and happiness in male and female angry facial expressions (Table 3.3).

Examination of the beta weights within these regression analyses showed that higher levels of ELS were significantly associated with increased approach of male and female angry facial expressions, and with decreased avoidance of female angry expressions. In addition, higher levels of ELS were significantly associated with reduced identification of anger in female angry facial expressions. Regarding participant gender, female participants were significantly less likely than male participants to approach male and female angry expressions, and significantly more likely than male participants to avoid male and female angry expressions. Additionally, female participants were significantly more likely than male participants to identify anger in male and female angry expressions. Female participants were significantly less likely than male participants to perceive happiness in female angry expressions. Neither depression nor anxiety scores were significantly associated with participants' responses to angry facial expressions.

Table 3.2

Hierarchical linear regression analyses examining the effect of ELS on approach and avoidance of male and female angry facial expressions

		Coefficients					
Response		**Participant gender**	**Depression**	**Anxiety**	**Face set**	**ELS**	R^2
Self-reported approach							
Angry male							
Model 1	*β*	-.19	.09	.01	.05		
	p	.03*	.44	.92	.55		
Model 2	*β*	-.21	.01	-.04	.04	.20	.09[a]
	p	.02*	.93	.75	.62	.04*	
Angry female							
Model 1	*β*	-.17	.07	-.05	-.28		
	p	.04*	.53	.65	.001**		
Model 2	*β*	-.19	-.01	-.10	-.29	.21	.13[a]
	p	.03*	.94	.37	< .001***	.04*	
Self-reported avoidance							
Angry male							
Model 1	*β*	.24	-.13	-.04	-.26		
	p	.004**	.24	.71	.001**		
Model 2	*β*	.25	-.07	-.01	-.26	-.14	.19[a]
	p	.002**	.52	.96	.001**	.14	
Angry female							
Model 1	*β*	.26	-.09	.03	.25		
	p	.003**	.45	.78	.002**		
Model 2	*β*	.27	.00	.08	.26	-.22	.16[a]
	p	.001**	.99	.44	.001**	.02*	

Note. Participant gender coded as 0 = male, 1 = female; Face set coded as 1 and 2. *** = $p < .001$, ** = $p < .01$, * = $p < .05$. [a]Model explains a significant amount of variance in the dependent variable, after correction for multiple (24) comparisons using an FDR threshold of 0.1.

Table 3.3

Hierarchical linear regression analyses examining the effect of ELS on identification of anger and happiness in male and female angry facial expressions

		Coefficients					
Response		**Participant gender**	**Depression**	**Anxiety**	**Face set**	**ELS**	R^2
Identification of anger							
Angry male							
Model 1	*β*	.16	-.16	-.02	-.16		
	p	.06	.16	.90	.05*		
Model 2	*β*	.17	-.12	.01	-.15	-.09	.10[a]
	p	.05*	.30	.95	.06	.35	
Angry female							
Model 1	*β*	.20	-.14	.07	.36		
	p	.01*	.19	.53	< .001***		
Model 2	*β*	.22	-.07	.11	.37	-.18	.20[a]
	p	.008**	.52	.30	< .001***	.05*	
Identification of happiness							
Angry male							
Model 1	*β*	-.14	.18	-.02	.02		
	p	.11	.13	.83	.82		
Model 2	*β*	-.15	.12	-.06	.01	.15	.07[a]
	p	.08	.33	.60	.88	.14	
Angry female							
Model 1	*β*	-.20	.15	-.00	-.16		
	p	.02*	.18	.99	.05*		
Model 2	*β*	-.21	.11	-.03	-.17	.11	.10[a]
	p	.02*	.37	.80	.04*	.25	

Note. Participant gender coded as 0 = male, 1 = female; Face set coded as 1 and 2. *** = $p < .001$, ** = $p < .01$, * = $p < .05$. [a]Model explains a significant amount of variance in the dependent variable, after correction for multiple (24) comparisons using an FDR threshold of 0.1.

3.3.4. Higher depression scores predict reduced identification of happiness in happy facial expressions

Hierarchical multiple regression analyses were used to examine the effects of ELS on approach and avoidance responses to male and female happy facial expressions (Table 3.4), and on identification of anger and happiness in these happy facial expressions (Table 3.5). As above, a two-step hierarchical regression model was used to predict participants' responses to male and female happy facial expressions, with participant gender, depression scores, anxiety scores and face set entered in Step 1, and ELS entered in Step 2. The regression model explained a significant amount of the variance in participants' approach and avoidance responses to male and female happy facial expressions (Table 3.4), as well as a significant amount of the variance in participants' identification of anger and happiness in male and female happy facial expressions (Table 3.5).

Examination of the beta weights revealed that ELS scores were not significantly associated with approach or avoidance of happy facial expressions, nor were they associated with identification of anger or happiness in these facial expressions. Though ELS scores were not associated with responses to happy facial expressions, higher depression scores were significantly associated with reduced identification of happiness in both male and female happy facial expressions. Higher depression scores were also associated with reduced self-reported approach and increased self-reported avoidance of female happy expressions. Neither anxiety scores nor participant gender predicted responding to happy facial expressions.

Table 3.4

Hierarchical linear regression analyses examining the effect of ELS on approach and avoidance of male and female happy facial expressions

		Coefficients					
Response		**Participant gender**	**Depression**	**Anxiety**	**Face set**	**ELS**	R^2
Self-reported approach							
Happy male							
Model 1	*β*	.11	-.20	.03	-.30		
	p	.17	.06	.79	<.001		
Model 2	*β*	.12	-.19	.04	-.30	-.03	.16[a]
	p	.16	.10	.75	< .001***	.79	
Happy female							
Model 1	*β*	.15	-.25	-.07	-.26		
	p	.06	.02*	.52	.001**		
Model 2	*β*	.15	-.24	-.06	-.26	-.02	21[a]
	p	.06	.04*	.57	.001**	.81	
Self-reported avoidance							
Happy male							
Model 1	*β*	-.05	.15	-.01	.24		
	p	.56	.20	.93	.004**		
Model 2	*β*	-.05	.12	-.02	.24	.05	.09[a]
	p	.54	.30	.84	.004**	.59	
Happy female							
Model 1	*β*	-.04	.28	.04	.23		
	p	.61	.01*	.71	.003**		
Model 2	*β*	-.04	.27	.04	.23	.02	16[a]
	p	.60	.02*	.75	.003**	.85	

Note. Participant gender coded as 0 = male, 1 = female; Face set coded as 1 and 2. *** = $p < .001$, ** = $p < .01$, * = $p < .05$. [a]Model explains a significant amount of variance in the dependent variable, after correction for multiple (24) comparisons using an FDR threshold of 0.1.

Table 3.5

Hierarchical linear regression analyses examining the effect of ELS on identification of anger and happiness in male and female happy facial expressions

		Coefficients					
Response		**Participant gender**	**Depression**	**Anxiety**	**Face set**	**ELS**	R^2
Identification of anger							
Happy male							
Model 1	*β*	-.07	.25	-.03	.07		
	p	.42	.03*	.77	.43		
Model 2	*β*	-.08	.21	-.06	.06	.10	.08[a]
	p	.38	.09	.62	.46	.34	
Happy female							
Model 1	*β*	-.03	.26	-.02	.11		
	p	.76	.03*	.86	.20		
Model 2	*β*	-.03	.21	-.05	.10	.11	.08[a]
	p	.69	.08	.68	.22	.26	
Identification of happiness							
Happy male							
Model 1	*β*	.08	-.37	.11	-.16		
	p	.35	.001**	.32	.05*		
Model 2	*β*	.08	-.37	.11	-.16	-.02	.15[a]
	p	.35	.002**	.32	.05	.88	
Happy female							
Model 1	*β*	.07	-.39	.13	-.17		
	p	.38	.001**	.23	.03*		
Model 2	*β*	.07	-.38	.13	-.17	-.03	.15[a]
	p	.37	.001**	.22	.03*	.77	

Note. Participant gender coded as 0 = male, 1 = female; Face set coded as 1 and 2. *** = $p < .001$, ** = $p < .01$, * = $p < .05$. [a]Model explains a significant amount of variance in the dependent variable, after correction for multiple comparisons using an FDR threshold of 0.1.

3.3.5. Early life stress does not predict identification of emotion in neutral facial expressions

The hierarchical regression model described in the previous section was used to examine the effects of ELS on approach and avoidance responses to male and female neutral facial expressions (Table 3.6), and on identification of anger and happiness in these neutral facial expressions (Table 3.7). The regression model explained a significant amount of the variance in participants' identification of happiness in male neutral facial expressions, but did not explain a significant amount of the variance in any other responses to male neutral facial expressions (approach, avoidance, identification of anger). Similarly, the regression model was unable to explain a significant amount of the variance in participants' approach or avoidance responses to female neutral expressions, or in participants' identification of anger or happiness in these facial expressions. Examination of the beta weights in the model predicting identification of happiness in male neutral expressions revealed that neither ELS nor any of the other variables of interest (participant gender, depression or anxiety) was significantly associated with identification of happiness in male neutral facial expressions.

3.3.6. Assessing assumptions of the regression analyses used to examine participant responses

As discussed in § 2.3.2, multiple linear regression makes a number of assumptions about the data. The following section addresses whether these assumptions were met for the regression analyses conducted within this chapter.

3.3.6.1. Outliers and influential points

Outliers (defined as residuals greater than +/- 3 *SD*) were present in two of the eight regression analyses used to examine responses to angry facial expressions. In each analysis two outliers were present. Cook's Distances were used to examine the extent to which these cases were influencing the analyses. In the analysis of angry ratings of male angry facial expressions, the two outliers had Cook's Distances of 0.09 and 0.08.

In the analysis of happy ratings of male angry facial expressions, the two outliers had Cook's Distances of 0.15 and 0.07. In all cases the Cook's Distances were well below the suggested cut-off value of 1 (Field, 2005), indicating that the outliers were not exerting an undue influence on the regression models.

All of the analyses used to predict participant responses to happy facial expressions contained outliers, though in each analysis the number of outliers was limited to either one or two cases. The Cook's Distances for these cases were examined in order to determine whether these outliers were having a substantial influence on the regression model. In all cases the Cook's Distances fell well below the cut-off value of 1, with the largest values across all analyses being 0.17 and 0.12. All other Cook's Distances fell below 0.1. Only one of the eight analyses used to predict participant responses to neutral facial expressions contained any outliers. This analysis, in which multiple regression was used to predict self-reported approach of male neutral expressions, contained one case with a standard deviation above 3. The Cook's Distance for this case was 0.07, indicating that the case was not exerting undue influence on the regression model.

3.3.6.2. Independence of residuals

The Durbin-Watson statistic was used to test the assumption of independence of residuals. Using the tables provided by Savin and White (1977), it was established that the upper bound for the Durbin-Watson value in the present regression analyses was 1.65, and the lower bound was 1.44. As discussed in § 2.3.2.2, values above the upper bound indicate that the assumption has been met, values below the lower bound indicate violation of the assumption, and values in between the two bounds indicate that the test is inconclusive. The Durbin-Watson statistic was above the upper bound of 1.65 for all of the analyses of participants' responses to angry facial expressions, indicating that the assumption of independence of residuals was met. With respect to the analysis of responses to happy facial expressions, the Durbin-Watson statistic was above the upper bound for all but two regression analyses. Similarly, with respect to the analysis of responses to neutral facial expressions, the Durbin-Watson statistic was

above the upper bound for all but two analyses. However, whilst there were four cases in which the Durbin-Watson statistic fell below the upper bound, it never fell below the lower bound. Therefore, although the test was inconclusive, it did not show that the assumption had been violated.

3.3.6.3. Presence of linearity

Multiple regression assumes a linear relationship between the dependent variable and each of the independent variables. This assumption was investigated by visual examination of the partial regression plots between the dependent variable and each independent variable. In all cases the pattern of data points suggested that the assumption of linearity had been met. In addition, the assumption of a linear relationship between the dependent variable and the independent variables collectively was tested via examination of scatterplots in which the studentised residuals were plotted against the unstandardised predicted values. These plots also showed that the assumption of linearity had been met.

3.3.6.4. Homoscedasticity of residuals

The assumption of homoscedasticity was tested by visual examination of the residual plots described in the previous section. In all analyses these plots showed a broadly random pattern of data points, indicating that the assumption of homoscedasticity had been met.

3.3.6.5. Absence of multicollinearity

The assumption of no multicollinearity was tested via examination of the correlations between the predictors and examination of the Tolerance values for each predictor. In all cases the correlations between predictors were below 0.8, with the largest correlation being that observed between BDI scores and STAI-T scores ($r(145) = 0.67$, $p < .001$). All Tolerance values fell well above the suggested cut-off value of 0.2 (Field, 2005), with the smallest Tolerance value (0.45) corresponding to the HADS-D predictor. These tests showed that although there was some correlation between the predictors, none of the correlations was large enough to violate the assumption of no multicollinearity.

3.3.6.6. Normal distribution of residuals

The assumption of normal distribution of residuals was tested via visual examination of histograms of the standardised residuals and probability plots in which the observed cumulative probability was plotted against the expected cumulative probability. In the majority of cases visual examination of these charts showed that the residuals were normally distributed. In a small number of cases the charts showed some non-normality, for example there was some positive skew in the histograms for angry ratings of happy facial expressions. However, in these cases the residuals still followed a broadly normal distribution, and given that regression analysis is relatively robust to non-normality, it was decided that transformation of the data was not necessary.

Table 3.6

Hierarchical linear regression analyses examining the effect of ELS on approach and avoidance of male and female neutral facial expressions

		Coefficients					
Response		**Participant gender**	**Depression**	**Anxiety**	**Face set**	**ELS**	R^2
Self-reported approach							
Neutral male							
Model 1	*β*	-.01	.00	-.03	-.00		
	p	.93	.98	.79	.97		
Model 2	*β*	-.00	.03	-.01	.00	-.07	.00
	p	.97	.81	.90	1.00	.52	
Neutral female							
Model 1	*β*	-.02	-.03	-.04	.04		
	p	.83	.81	.71	.65		
Model 2	*β*	-.02	-.05	-.05	.04	.05	.01
	p	.80	.71	.65	.67	.65	
Self-reported avoidance							
Neutral male							
Model 1	*β*	.10	-.07	.06	-.10		
	p	.27	.55	.57	.24		
Model 2	*β*	.10	-.07	.06	-.10	.01	.03
	p	.27	.57	.59	.25	.96	
Neutral female							
Model 1	*β*	.16	.01	.01	-.14		
	p	.07	.93	.91	.10		
Model 2	*β*	.17	.06	.04	-.13	-.12	.06
	p	.05	.64	.72	.12	.24	

Note. Participant gender coded as 0 = male, 1 = female; Face set coded as 1 and 2.

Table 3.7

Hierarchical linear regression analyses examining the effect of ELS on identification of anger and happiness in male and female neutral facial expressions

		Coefficients					
Response		**Participant gender**	**Depression**	**Anxiety**	**Face set**	**ELS**	R^2
Identification of anger							
Neutral male							
Model 1	*β*	-.06	-.15	.12	-.09		
	p	.48	.22	.29	.27		
Model 2	*β*	-.07	-.17	.11	-.10	.05	.02
	p	.45	.18	.35	.26	.61	
Neutral female							
Model 1	*β*	.13	.04	-.04	-.15		
	p	.15	.72	.71	.08		
Model 2	*β*	.13	.05	-.04	-.15	-.01	.04
	p	.15	.71	.73	.08	.92	
Identification of happiness							
Neutral male							
Model 1	*β*	-.07	.01	-.07	.31		
	p	.39	.90	.55	< .001***		
Model 2	*β*	-.07	.04	-.05	.31	-.06	.11[a]
	p	.42	.76	.65	< .001***	.56	
Neutral female							
Model 1	*β*	-.07	.18	-.25	.07		
	p	.41	.12	.03*	.40		
Model 2	*β*	-.07	.21	-.24	.07	-.06	.06
	p	.44	.09	.04*	.38	.56	

Note. Participant gender coded as 0 = male, 1 = female; Face set coded as 1 and 2. *** = $p < .001$, * = $p < .05$. [a]Model explains a significant amount of variance in the dependent variable, after correction for multiple comparisons using an FDR threshold of 0.1.

3.4. Discussion

This study investigated the effects of ELS on young adults' self-reported approach and avoidance tendencies towards photographs of angry, happy and neutral facial expressions, and their identification of anger and happiness in these facial expressions. Contrary to predictions, higher levels of ELS were associated with increased approach and reduced avoidance of angry facial expressions, and reduced identification of anger in female angry facial expressions. In addition, higher depression scores were associated with reduced identification of happiness in happy facial expressions, whilst female participants showed increased avoidance and reduced approach of angry facial expressions relative to male participants. Critically, both of these effects were independent of levels of ELS. Consistent with previous work (Heim, Shugart, Craighead, & Nemeroff, 2010), higher levels of ELS were associated with higher levels of depression and anxiety.

3.4.1. Early life stress and responses to angry facial expressions

In this study with young adults higher levels of ELS did not predict increased identification of anger in neutral facial expressions nor increased avoidance of angry facial expressions. This is in contrast to previous studies with children in which ELS was associated with increased identification of anger in neutral expressions (da Silva Ferreira et al., 2014), and appears to contradict the suggestion that ELS-related abnormalities in emotional face processing facilitate avoidance behaviour (Pollak et al., 2009). The absence of these predicted relationships may be due to differences in the severity and types of ELS experienced by the respective participant samples (McLaughlin, Sheridan, & Lambert, 2014), or to differences in the age at which the early stress was experienced (Andersen et al., 2008). The extent to which the type and timing of ELS can influence subsequent neurocognitive outcomes is discussed in detail in § 6.4.2.

Despite the absence of the predicted associations there was nevertheless strong evidence of atypical emotion processing in relation to ELS. Higher levels of ELS were associated with increased approach and reduced avoidance of male and female angry facial expressions. This relationship may be partially explained by reduced identification of anger,

as there was an association between higher levels of ELS and reduced identification of anger in female angry expressions. However, given that identification of anger in male angry expressions was not significantly associated with ELS, impaired identification of anger cannot fully explain the relationship between ELS and increased approach of both male and female angry facial expressions.

An alternative explanation lies in work demonstrating a relationship between ELS and active responses to threat (Perry & Sullivan, 2014). Consistent with the present findings, physical abuse in childhood has been associated with increased approach of threat in adulthood, specifically in terms of increased aggression (Malinosky-Rummell & Hansen, 1993; Nicholas & Bieber, 1996). Similarly, rodent models of abuse and neglect have found evidence for an association between high levels of ELS and increased approach of threat (Perry & Sullivan, 2014) as well as for a relationship between high levels of ELS and reduced avoidance of threat (Benetti et al., 2015; Kosten, Lee, et al., 2007; Toth et al., 2008). Therefore, whilst the present finding of increased approach and reduced avoidance of angry (threatening) facial expressions in young adults with high levels of ELS was unexpected, it is not without support in the broader literature. Potential explanations for the present findings are discussed further in the general discussion (Chapter 6).

In terms of the implications of the present findings, it is important to acknowledge that atypical or inappropriate approach-avoidance responses in either direction could have harmful social and emotional consequences. Inappropriate approach behaviour towards individuals displaying anger could lead to a heightened risk of interpersonal conflict, which could in turn increase an individual's vulnerability to the development of mental health problems (Stieglitz, Schniter, von Rueden, Kaplan, & Gurven, 2015). In this manner, the present findings could be conceptualised in light of the theory of latent vulnerability, which suggests that ELS is associated with neurocognitive alterations which increase vulnerability to future mental illness. However, this possibility cannot be assessed without the use of longitudinal paradigms which track participants across development (§ 6.5.4).

3.4.2. Distinct effects of participant gender and depression scores on approach and avoidance of emotional facial expressions

In this study there were also significant gender effects; female participants were more likely to avoid and less likely to approach angry facial expressions than male participants, an effect which was independent of levels of ELS. This is in partial accordance with Miller et al.'s (2013) finding that female participants kept a greater simulated distance between themselves and others than male participants did, irrespective of the emotional expression that was expressed by the other individual.

While ELS was selectively related to responses towards angry facial expressions, depression scores were selectively related to responses towards happy facial expressions. Higher depression scores were associated with reduced identification of happiness in happy facial expressions, and increased avoidance of female happy expressions. This supports previous evidence of a relationship between depressed affect and reduced identification of happiness in both clinical and non-clinical populations (Coupland et al., 2004; Joormann & Gotlib, 2006), and extends previous work which found that depression was associated with a non-specific increase in avoidance of emotional expressions (Derntl et al., 2011). Notably, while depression scores were highly positively correlated with ELS and anxiety scores, neither ELS nor anxiety was related to processing of happy expressions. These findings support previous research suggesting that atypical processing of happy facial expressions is a state feature of depressed mood, rather than a trait which remains following remission (Munkler et al., 2015; though see LeMoult, Joormann, Sherdell, Wright, & Gotlib, 2009).

3.4.3. Study limitations and future directions

The present study was limited by the use of a retrospective self-report measure of ELS and by its cross-sectional design. However, a review of the validity of adult retrospective reports by Hardt and Rutter (2004) concluded that, whilst not all adults will disclose abuse or neglect when asked, cases where abuse or neglect are disclosed are generally reliable.

Furthermore, both retrospective reports and cross-sectional designs play an important role in advancing knowledge about the pervasive long-term effects of ELS (e.g. Dannlowski et al., 2012; Edwards, Holden, Felitti, & Anda, 2003). An additional limitation of the present study concerns its lack of ecological validity; it is not known whether participants' self-reported approach and avoidance tendencies towards photographic stimuli reflect the responses they would make in real life situations.

In light of this, future work should utilise more ecologically valid paradigms in order to examine whether the relationship between ELS and atypical approach-avoidance tendencies towards individuals displaying anger can be seen in behavioural responses to 'real' individuals. An alternative direction for future studies concerns the use of implicit approach-avoidance tasks which do not rely on self-report measures of approach-avoidance. For example, work by Seidel et al. (2010) examined the effect of depression on implicit approach-avoidance tendencies using a task in which participants made an approach (joystick pull) response to emotional facial stimuli with a blue frame, and an avoidance (joystick push) response to emotional facial stimuli with a yellow frame. The researchers generated an implicit measure of each participant's dominant behavioural tendency towards each specific emotional expression by calculating the difference in reaction times during approach (blue frame) and avoidance (yellow frame) of these facial stimuli. This paradigm could be used in future studies to examine whether ELS is associated with atypical implicit approach and avoidance of angry facial expressions in mentally healthy young adults.

3.4.4. Conclusions

This study represents, to the author's knowledge, the first investigation of the relationship between ELS and self-reported approach-avoidance of emotional facial expressions. It was found that ELS was associated with increased approach and reduced avoidance of angry expressions, and with higher levels of depression and anxiety. In the context of the theory of latent vulnerability (McCrory & Viding, 2015), abnormal approach behaviour towards angry facial expressions could represent an ELS-related neurocognitive alteration which may increase the risk of mental

illness during young adulthood, a sensitive period of social and neurodevelopmental change (Arnett, 1994; Lebel & Beaulieu, 2011; Lebel et al., 2008). This possibility should be investigated in future work through the use of a longitudinal approach.

Chapter 4. High levels of early life stress are associated with changes in early perceptual responses to emotional facial expressions

Abstract

The present study aimed to examine the effects of ELS on mentally healthy young adults' early visual responses to emotional facial expressions. Sixty-two female participants (age 18 to 25 years) were recruited to either a low ELS group or a high ELS group, based on their scores on a measure of ELS. Participants viewed images of male and female angry, happy and neutral facial expressions whilst EEG was recorded. It was found that the high ELS group showed significantly smaller N170 peak amplitudes in response to angry, happy and neutral facial expressions relative to the low ELS group. These effects of ELS group on the N170 response were independent of scores on measures of depression and anxiety. In addition, it was found that higher levels of depression were significantly associated with larger N170 peak amplitudes to angry, happy and neutral facial expressions, and higher levels of anxiety were significantly associated with smaller N170 peak amplitudes to angry and neutral facial expressions, and to happy facial expressions at a trend level of significance. The findings suggest that ELS is associated with changes in early perceptual processing of emotional facial expressions and that, in contrast to the behavioural findings reported in Chapter 3, these changes are not specific to angry facial expressions but occur in response to happy and neutral expressions as well.

4.1. Introduction

The aim of the present study was to build on the findings of the previous behavioural study (Chapter 3) by using EEG to examine the relationship between ELS and early perceptual responses to emotional facial expressions. The previous study found that high levels of ELS were associated with atypical self-reported approach and avoidance responses towards angry facial expressions, and with reduced identification of anger in angry facial expressions displayed by female individuals. These findings were in partial accordance with other behavioural studies which found ELS-related alterations in the processing of angry facial expressions (da Silva Ferreira et al., 2014; Gibb et al., 2009). In addition to behavioural studies, there is now a growing body of work which seeks to examine the neural correlates of atypical responding to emotional facial expressions in those who experienced high levels of ELS (Dannlowski et al., 2013; Hein & Monk, 2017; McCrory et al., 2013).

The majority of this work to date has used fMRI to examine functional changes in specific brain regions during processing of emotional facial expressions. Taken together, the findings from these studies suggest that adults who experienced high levels of ELS show increased amygdala activation to emotional facial expressions relative to adults with low levels of ELS (Dannlowski et al., 2012; Redlich et al., 2015; van Harmelen et al., 2013). However, whilst the high spatial resolution of fMRI provides a clear picture of ELS-related changes in the activity of specific brain regions, its low temporal resolution makes it difficult to examine the time course of these alterations, or to identify where in the face processing stream these 'pathological' changes are expressed. Changes which occur early in the processing stream could have a knock-on effect on subsequent processing (Portella et al., 2012), and could reduce the effectiveness of interventions which take a cognitive, explicit approach to supporting those who experienced high levels of ELS.

In light of this, the present study used EEG, a neuroimaging technique with a high temporal resolution, to examine the effect of ELS on young adults' early implicit processing of angry, happy and neutral emotional facial expressions posed by male and female individuals.

Previous work using EEG has identified a specific ERP which is sensitive to images of faces, the N170. The N170 is an early visual-evoked potential which occurs at a latency of approximately 170 ms over lateral occipital-temporal sites (Section 2.1.3; Eimer, 2011b). There is ongoing debate in the literature as to whether the N170 is modulated by the emotion displayed by the facial stimulus (Hinojosa, Mercado, & Carretie, 2015), though convincing evidence in favour of this modulation is provided by a recent meta-analysis which found both global and specific effects of emotional expression on the N170 response (Hinojosa et al., 2015). Hinojosa et al. (2015) found that N170 peak amplitudes were significantly larger (more negative) to angry, happy and fearful facial expressions than to neutral facial expressions, with the greatest increase in amplitude occurring in response to angry facial expressions. Given its face-specificity and modulation by emotion, the N170 is an excellent candidate for investigating the neural processes which may underlie the atypical behavioural responses to emotional expressions amongst adults who experienced ELS.

Previous research examining atypical N170 responses to emotional facial expressions in adult participants has focussed not on ELS but on mental illness, with inconsistent results (Feuerriegel, Churches, Hofmann, & Keage, 2015). Studies have reported a relationship between higher depression levels and both blunted (Chen et al., 2014) and potentiated (Noll, Mayes, & Rutherford, 2012) N170 amplitudes in response to emotional facial expressions. In addition, a number of studies with participants with depression have found emotion-specific effects, reporting a pattern of enhanced N170 amplitudes to sad facial expressions alongside blunted N170 amplitudes to neutral and happy facial expressions (Chen et al., 2014; Wu et al., 2016; Zhang, He, Chen, & Wei, 2016). However, there are also a large number of studies which have found no effect of depression or anxiety levels on N170 amplitude to emotional facial expressions (Aarts & Pourtois, 2012; Camfield, Mills, Kornfeld, & Croft, 2016; He et al., 2012; Jaworska, Blier, Fusee, & Knott, 2012; Maurage et al., 2008; Morel, George, Foucher, Chammat, & Dubal, 2014; Walentowska & Wronka, 2012; Yoon, Shim, Kim, & Lee, 2016).

Despite consistent reports of higher levels of ELS in clinical samples than in control samples (Alvarez et al., 2011; Negele et al., 2015), and behavioural research highlighting ELS-related alterations in face processing (Ferreira et al., 2014; Pollak et al., 2009; Pollak & Sinha, 2002), only one of the aforementioned studies which examined the relationship between mental illness and N170 amplitudes controlled for ELS (Noll et al., 2012). This calls into question the conclusions of the aforementioned studies, as the clinical groups are likely to have experienced higher rates of ELS than the control groups. In their systematic review of the effect of mental illness on the N170 response to emotional facial expressions, Feuerriegel et al. (2015) found blunted N170 responses across a range of clinical conditions. In light of this, they suggest that blunted N170 responses represent a cross-diagnostic effect of mental illness on neural responding to emotional facial expressions. Given that ELS is associated with an increased risk for all common mental health conditions (McCrory & Viding, 2015), it is possible that ELS is a driving factor in these cross-diagnostic changes in the N170 response to emotional facial expressions. Studies with mentally healthy, medication-free participants that control for subclinical anxiety and depression are required in order to determine whether ELS is a contributing factor in the N170 alterations associated with mental health conditions.

To date, a small number of studies have examined the effect of ELS, rather than mental illness, on the N170 response to emotional facial expressions. The majority of these studies were carried out with children who had been abused or neglected. Curtis and Cicchetti (2011) found that children who had been maltreated (aged 42 months) showed blunted N170 peak amplitudes to emotional facial expressions (angry, happy and neutral) relative to children who had not been maltreated. Similarly, Moulson et al. (2009) reported blunted right hemisphere N170 amplitudes to emotional facial expressions in a cohort of infants (age 5 months to 31 months) who had experienced neglect as a result of early institutionalisation. Interestingly, however, this effect was no longer present when the researchers tested the same participants later, at 30 months (mean age) and again at 42 months (mean age), by which time some of the previously institutionalised children were living in foster care. Further studies with the

same sample of children, carried out when they were 8 years old and 12 years old, also reported no effect of ELS on N170 amplitude in response to emotional facial expressions (Nelson et al., 2013; Young et al., 2017). These findings were supported by a study with a different sample of infants aged 15 months, which found no effect of maltreatment on the N220, a component seen in infants which is thought to be analogous to the N170 seen in older individuals (Curtis & Cicchetti, 2013). Whilst studies examining the effect of ELS on children's N170 responses are relevant to the present research, it is important to acknowledge that the N170 ERP component undergoes a protracted course of development which lasts until adulthood (Batty & Taylor, 2006). Consequently, ELS-related effects observed in N170 amplitudes amongst child participants may differ from potential ELS-related effects that could occur in adult participants. Therefore, the present study sought to examine whether ELS-related alterations in the N170 response to emotional facial expressions can be observed in a sample of young adults.

To the author's knowledge, only one study has examined the effect of ELS on mentally healthy adults' N170 responses to emotional facial expressions. Chu et al. (2016) presented emotional face stimuli in two ways, consciously for 1200 ms and non-consciously for 10 ms with a 150 ms neutral face mask. They then examined the difference in the N170 response to angry facial expressions relative to happy facial expressions. Chu et al. (2016) used the Early Life Stress Questionnaire (ELSQ; McFarlane et al., 2005) to measure how many types of childhood interpersonal trauma each participant had experienced. They then divided the data into five groups based on the severity of the ELS that was encountered, and selected the top and bottom quintiles for analysis. Participants in the lowest quintile had experienced none of the seven forms of childhood interpersonal trauma measured by the ELSQ, whilst participants in the highest quintile had the most severe experiences of ELS relative to the rest of the sample. In the non-conscious condition only, adults in the lowest quintile of ELS experience showed a significantly lower N170 peak amplitude in response to happy facial expressions relative to angry facial expressions, whilst adults in the highest quintile of ELS experience showed no difference in N170

amplitude to happy relative to angry facial expressions. The authors interpreted this pattern as a lack of differentiation between angry and happy expressions in adults who experienced high levels of ELS, such that they showed a heightened N170 response to both threatening and non-threatening facial stimuli. This finding was apparent in the right hemisphere only, highlighting potential laterality effects in the relationship between ELS and the N170 response to facial expressions. However, it should be noted that, though the groups showed different patterns of responding, the low and high ELS groups were not significantly different from each other in their N170 peak amplitudes to either angry or happy facial expressions. Whilst these findings provide initial insight into the potential effect of ELS on the N170 response to facial expressions, the study did not examine face gender, instead collapsing male and female faces of the same expression together for analysis.

As a consequence of collapsing across gender, Chu et al. (2016) may have missed key effects; the findings presented in Chapter 3 showed that ELS was associated with reduced identification of anger in angry female faces but not in angry male faces, and evidence from the wider literature suggests that participants respond differently to emotional facial expressions displayed by male and female individuals (Miller et al., 2013; Seidel et al., 2010). In addition, though Chu et al. (2016) excluded participants with clinically significant mental health problems, they did not control for subclinical levels of anxiety or depression in their ANOVA analysis, despite their finding that experience of ELS was associated with higher levels of subclinical psychological distress in their sample of participants.

Therefore, in the present study EEG was used to examine the effects of ELS on peak N170 amplitudes in response to male and female angry, happy and neutral facial expressions. In order to examine the effects of ELS independently of mental health status, only participants who had no current or historical diagnosis of mental illness were recruited. In addition, scores on questionnaire measures of depression and anxiety were included as co-variates in the analyses, in order to control for any effects of these measures on the N170 response to emotional facial expressions. Participants were recruited if they reported either high or low levels of ELS on the CATS,

based on cut-off values derived from the top and bottom third of scores from respondents in the previous study (Chapter 3). This resulted in a low and a high ELS group. Full details of the procedure for participant recruitment can be found in § 2.2.1.2.

Studies examining the neural sequelae of ELS in female populations are particularly important, as research suggests that women may be more vulnerable than men to the neuropsychological effects of maltreatment (Cooke & Weathington, 2014). Indeed, relative to men, women in the UK experience higher rates of common mental disorders such as depression and anxiety (McManus et al., 2016), both of which are positively associated with ELS (Heim & Nemeroff, 2001). In light of this, a female sample of participants was recruited for this first exploratory study into the effects of ELS on the N170 response to emotional facial expressions.

Based on previous findings with child participants, it was hypothesised that the high ELS group would show blunted N170 amplitudes in response to facial expressions in general (angry, happy and neutral expressions). However, given the inconsistent nature of previous findings in the literature, no specific predictions were made regarding the effect of ELS group on N170 peak amplitude to specific emotional expressions. In addition, following previous work highlighting a relationship between mental health status and blunted N170 amplitudes (Chen, 2014; Feuerriegel et al., 2015), it was predicted that N170 amplitude would decrease as anxiety and depression scores increased.

4.2. Method

4.2.1. Participants

Full details of participant recruitment are presented in § 2.2.1.1. Briefly, prior to recruitment, the data collected in Chapter 3 was divided into three equal groups according to CATS scores (Sanders & Becker-Lausen, 1995), with the group boundaries used as cut-off values for a 'low' and a 'high' ELS group . Participants in the present study were recruited to the low group if they scored less than 16 on the CATS, and the high group if they scored more than 24 on the CATS. Individuals who scored between 16 and 24 on the CATS were not invited to participate in the present study. Additionally, individuals were only invited to participate if they met the following screening criteria: they were female; they grew up in the UK; they were right handed; they were aged between 18 and 25 years old; they were free from any disorders of consciousness; they had not had any significant head injuries; they had never been diagnosed with a mental illness; they were not receiving treatment for mental illness; and they were not taking any psychoactive medications.

Sixty-two participants met the screening criteria and took part in the study. All participants provided informed consent prior to data collection. Due to a problem with the EEG recording, one participant did not have any useable EEG data, and therefore was not included in the analyses. An additional three participants were excluded from the analyses as it was not possible to obtain a peak amplitude measurement for the N170 in at least one condition. Two of the excluded participants were in the low ELS group and two were in the high ELS group. The final sample was therefore comprised of 58 participants, with 26 in the low ELS group and 32 in the high ELS group. As expected, the high ELS group (M = 42.16, SD = 11.72) had significantly higher CATS scores than the low ELS group (M = 10.42, SD = 2.56; U = 0, p < .001). The mean age of the final sample was 19.88 (SD = 2.15). The high ELS group was significantly older (M = 20.50, SD = 2.34) than the low ELS group (M = 19.12, SD = 1.63; U = 267.50, p = .02). In light of this, age was controlled for in subsequent analyses, along with other variables on which the two groups differed significantly. Details of

these variables and how they were controlled for are described in the Statistical analysis section below (§ 4.2.8).

Table 4.1

Means, standard deviations (in parentheses), medians (in italics), ranges [in square brackets] and comparisons between ELS groups on age, early life stress scores, mental health measures and psychological measures

Variable	All participants (*n* = 58)	Low ELS (*n* = 26)	High ELS (*n* = 32)	Difference between ELS groups, *p* value
CATS	27.93 (2.15) *28.00* [5-70]	10.42 (2.56) *11.00* [5-15]	42.16 (11.72) *40.50* [25-70]	< .001***
Age	19.88 (2.15) *19.00* [18-25]	19.12 (1.63) *18.00* [18-23]	20.50 (2.34) *20.00* [18-25]	.02*
Mental health variables				
HADS-A	8.38 (3.38) *8.00* [1-20]	7.69 (3.70) *7.50* [1-20]	8.94 (3.05) *9.00* [3-14]	.08
HADS-D	3.86 (2.94) *3.00* [0-11]	3.04 (2.74) *2.00* [0-10]	4.53 (2.96) *4.00* [0-11]	.02*
STAI-S	40.17 (11.83) *39.00* [22-71]	37.12 (12.17) *37.50* [22-71]	42.66 (11.13) *46.50* [22-60]	.05
STAI-T	45.97 (10.91) *43.50* [28-73]	41.69 (10.04) *40.00* [28-66]	49.44 (10.49) *50.00* [31-73]	.01*
BDI-II	12.67 (8.77) *11.00* [1-43]	9.23 (6.04) *8.00* [1-26]	15.47 (9.69) *15.50* [1-43]	.01*
BAI	13.26 (8.79) *13.00* [0-35]	11.65 (7.92) *10.50* [0-28]	14.56 (9.69) *13.50* [0-35]	.27
Psychological variables				
SPSRQ: Punishment	14.05 (5.10) *14.00* [4-24]	12.65 (5.18) *12.50* [4-22]	15.19 (4.82) *16.00* [5-24]	.06
SPSRQ: Reward	10.47 (3.93) *10.50* [2-19]	10.31 (3.10) *10.00* [2-15]	10.59 (4.54) *11.00* [3-19]	.93
BAS: Drive	10.64 (2.13) *11.00* [6-15]	10.65 (1.88) *11.00* [6-14]	10.63 (2.35) *11.00* [6-15]	.82

Variable	All participants (*n* = 58)	Low ELS (*n* = 26)	High ELS (*n* = 32)	Difference between ELS groups, *p* value
BAS: Fun seeking	11.81 (2.14) *12.00* [8-15]	11.62 (2.02) *12.00* [8-15]	11.97 (2.25) *12.00* [8-15]	.59
BAS: Reward	16.98 (2.15) *17.00* [11-20]	17.23 (1.63) *17.00* [14-20]	16.78 (2.50) *17.00* [11-20]	.70
BIS	23.38 (3.19) *24.00* [15-28]	22.85 (3.28) *23.00* [15-28]	23.81 (3.10) *25.00* [16-28]	.21
PDS: Total	9.60 (4.12) *9.00* [1-19]	11.23 (3.93) *11.00* [5-19]	8.28 (3.84) *8.50* [1-18]	.01*
PDS: SDE	1.53 (1.83) *1.00* [0-8]	1.69 (1.85) *1.00* [0-6]	1.41 (1.83) *1.00* [0-8]	.43
PDS: IM	8.07 (3.44) *8.00* [1-17]	9.54 (3.30) *9.00* [4-17]	6.87 (3.12) *7.00* [1-14]	.003*

Note. CATS = Child Abuse and Trauma Scale; HADS-A = Hospital Anxiety and Depression Scale – Anxiety; HADS-D = Hospital Anxiety and Depression Scale – Depression; STAI-S = State Trait Anxiety Inventory – State; STAI-T = State Trait Anxiety Inventory – Trait; BDI-II = Beck Depression Inventory II; BAI = Beck Anxiety Inventory; SPSRQ = Sensitivity to Punishment and Reward Questionnaire; BAS = Behavioral Activation Scale; BIS = Behavioral Inhibition Scale; PDS: Total = Paulhus Deception Scales; PDS: SDE = Paulhus Deception Scales: Self-deceptive enhancement; PDS: IM = Paulhus Deception Scales: Impression Management. *$p < .05$ after correction for multiple comparisons using Benjamini-Hochberg procedure with an FDR threshold of 0.1 (16 comparisons including age, but excluding CATS, as difference scores between groups on this measure were built into the design of the study).

4.2.2. General procedure

The study received ethical approval from the Department of Psychology Ethics Committee, University of Sheffield (#1104). Participants who met the screening criteria were invited to take part in the study. After providing informed consent, participants were asked to fill in a number of questionnaires online. The order of the questionnaires was counterbalanced across participants. Details of these questionnaires can be found in § 4.2.3 of the present chapter, and in § 2.4. After completing the questionnaires in their own time, participants attended the University of Sheffield for the EEG recording session. After once again providing informed consent, participants were connected up to the EEG system. Full details of the EEG apparatus and recording can be found in Chapter 2. Once the EEG signal was stable, participants performed two separate experimental tasks. The order of the tasks was counterbalanced across participants. These tasks were an emotional face processing task, discussed below, and an active and passive avoidance task, presented in Chapter 5. Following completion of these tasks, the EEG cap was removed and the participant was directed to a different room in which they were asked to complete three additional questionnaires. Again the order of the questionnaires was counterbalanced across participants.

4.2.3. Questionnaires

Participants completed a battery of questionnaires: the Child Abuse and Trauma Scale (CATS; Kent & Waller, 1998; Sanders & Becker-Lausen, 1995), the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983), the Beck Depression Inventory (BDI-II; Beck et al., 1996) the Beck Anxiety Inventory (BAI; Beck et al., 1988), the State-Trait Anxiety Inventory (STAI; Spielberger et al., 1983), the Sensitivity to Punishment/Sensitivity to Reward Questionnaire (SPSRQ; Torrubia et al., 2001), the Behavioural Inhibition System/Behavioural Activation System scales (BIS/BAS; Carver & White, 1994), and the Paulhus Deception Scales (PDS; Paulhus, 1998). Full details of these questionnaires and the conditions under which they were completed can be found in Chapter 2. Means, standard deviations and comparisons between the two ELS groups for

scores on these questionnaire measures are reported in Table 4.1. A number of variables were non-normally distributed. Therefore, Mann-Whitney-U tests were used to examine group differences on the variables of interest.

4.2.4. Emotional face processing task

This task was one of two individual experiments carried out during the EEG recording session. The other task was the active and passive avoidance task, presented in Chapter 5. The order of the tasks was counterbalanced across participants. Full details of the procedure for the EEG recording session can be found in Chapter 2.

4.2.4.1. Stimuli

Images of angry, happy and neutral facial expressions were taken from the 'FACES' database (Ebner et al., 2010), a validated database of facial expressions. Given that the participants in the present study were aged 18 to 25, only faces from Ebner et al.'s (2010) 'younger' group (models aged 19 to 31) were used as stimuli. A total of 42 unique colour photographs of facial expressions were used in the study, with each image depicting a different person. Of these, 14 images depicted angry facial expressions, 14 depicted happy expressions and 14 depicted neutral expressions. Within each of the expression categories, seven faces were male and seven were female. Each expression/gender pair was considered to be one stimulus category (e.g. angry male; neutral female), resulting in a total of six stimulus categories. Each image depicted the head and shoulders of a single individual in front of a grey background. All individuals were wearing a standard grey T-shirt and were looking straight at the camera. The images were matched for brightness (Ebner et al., 2010). Examples of the facial stimuli are presented in Figure 4.1. In addition to the facial stimuli, the stimulus set included four unique colour photographs of houses, taken from the 'Pasadena Houses 2000' collection provided by the Computational Vision Group at the California Institute of Technology (www.vision.caltech.edu/archive). Each image was 11 cm by 8.8 cm and was presented on a black background. The total stimulus set consisted of 46 unique images. Each individual image was presented 8 times across the

course of the experiment, resulting in a total of 368 stimulus presentations. The experiment was divided into four blocks of equal length. Each unique stimulus was presented twice per block. The stimuli were presented in a pseudorandom order such that were no clear patterns in stimulus presentation, the same face gender did not appear more than three times in a row, and the same facial expression did not appear more than twice in a row. Each block consisted of 92 stimulus presentations in total.

Figure 4.1. Examples of facial expression stimuli: happy male and neutral female.

4.2.4.2. Procedure

During the task participants viewed images of facial expressions and houses. Participants were informed by the experimenter prior to beginning the task that they would see images of faces and houses, and that they should press the space bar when they saw an image of a house. The task was preceded by a series of instruction screens which participants could read at their own pace, pressing the space bar to move onto the next screen. The instructions began by informing the participant that they would see lots of pictures of faces, and that it was important that they attended to the screen at all times. They were then informed that they would also occasionally see pictures of houses to make sure they were paying attention, and that they should press the space bar immediately whenever they saw a picture of a

house. The instructions informed the participants to use their right hand to press the space bar. Participants were informed that there would be four blocks in the experiment, and that they would have the opportunity to take a break between blocks. The final instruction screen gave participants the opportunity to ask any questions they may have. Participants then pressed the space bar to begin the experiment.

Each block lasted approximately three and a half minutes. At the end of each block, participants were given the opportunity to take a break. Once they were ready, they could continue with the task by pressing the space bar. Pilot testing indicated that there was a risk that participants would see the break screen and press the space bar immediately, due to identifying the image as 'not a face' and reacting by pressing the space bar. Therefore, two break screens were included in the paradigm in order to prevent the participants from accidentally starting the next block before they had taken a break. If participants did respond to the break screen with a key press, they were simply taken to the second break screen. The two break screens were very similar in nature, with the only difference being that the first screen included the words 'Press the space bar to continue' and the second included the words 'Press the space bar when you are ready to continue with the task.'

Each trial consisted of a black screen which was presented for a pseudorandom length of time (inter-trial-interval; ITI), followed by the presentation of the stimulus for 200 ms, and then another black screen for 1000 ms (Figure 4.2). The length of the ITI varied across trials, with each ITI lasting either 500 ms, 800 ms, 1100 ms or 1400 ms. The order of the ITIs was pseudorandom, such that the same ITI never occurred more than twice in a row.

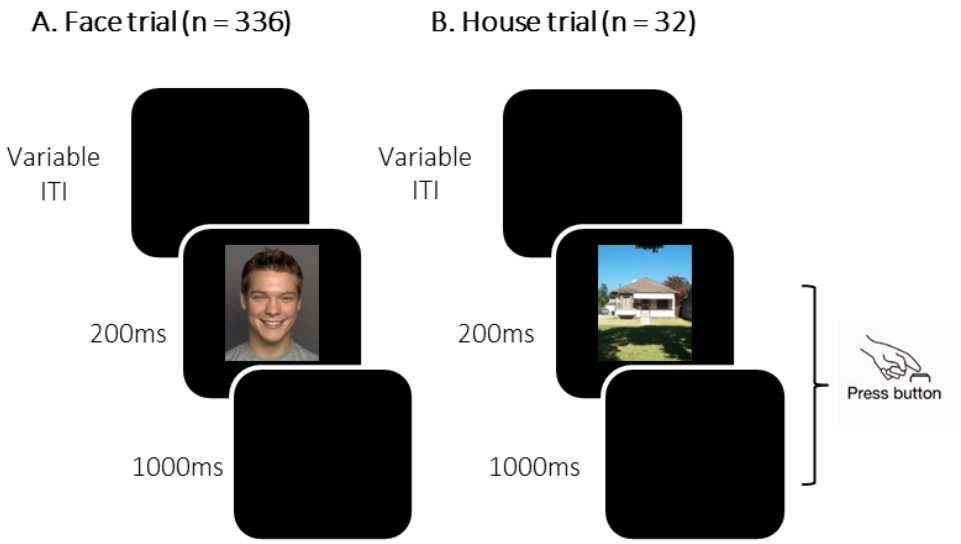

Figure 4.2. Structure of the trials in the emotional facial expressions task. During the task participants were presented with faces displaying either happy, as in the example shown (A), angry or neutral facial expressions. To make sure the participants were paying attention the task also included occasional (*n* = 32) catch trials in which houses were presented (B). Participants were required to make a key press when they saw an image of a house.

4.2.5. Apparatus

Full details of the apparatus used in the current experiment are reported in § 2.2.2.1.

4.2.6. EEG recording

Full details of the EEG recording procedure are reported in § 2.2.2.2.

4.2.7. EEG pre-processing

As the hypotheses were focussed on ERP responses to emotional facial expressions, and the house stimuli were presented only to maintain participants' attention, trials in which a house stimulus was presented were removed prior to pre-processing of the EEG data. Trials in which participants inaccurately made a response (pressed the space bar) following the presentation of a facial stimulus were also removed prior to pre-processing of the EEG data. Accuracy rates on these face trials were very high, at 99.83 % across the whole sample of participants.

Pre-processing of the EEG data is described in detail in § 2.2.3. Briefly, the EEG pre-processing consisted of: removing trials in which a blink occurred during the first 200 ms post stimulus-onset, referencing the data to Cz, filtering the EEG data from 0.1 Hz to 30 Hz, dividing the data into epochs from -200 ms pre-stimulus presentation to 800 ms post-stimulus presentation, removing bad channels, performing ICA and removing components representing blinks and lateral eye movements, performing baseline correction of the data, and finally removing epochs containing voltage fluctuations greater than +/- 150 μV.

The total number of trials for each stimulus category was 56. The mean number of trials excluded during EEG pre-processing for each stimulus category was as follows: male angry expressions (*M* = 5.49, *SD* = 4.98); female angry expressions (*M* = 4.41, *SD* = 4.11); male happy expressions (*M* = 4.26, *SD* = 4.27); female happy expressions (*M* = 5.08, *SD* = 4.84); male neutral expressions (*M* = 5.20, *SD* = 4.65); female neutral expressions (*M* = 4.62, *SD* = 4.76).

Once the data had been pre-processed, grand average waveforms were generated for each participant in each stimulus category. The event to which the epochs were locked was the presentation of the facial stimulus. In order to examine the N170 ERP component, an average of the signal was taken from two occipital-temporal electrodes over the left hemisphere (P7 and P9), and from the two corresponding occipital-temporal electrodes over the right hemisphere (P8 and P10). The peak amplitude of the N170 in each hemisphere and in each task condition was recorded using the measurement tool in ERPLAB. This resulted in twelve N170 amplitude measurements per participant. Full details regarding the measurement of the N170 response can be found in § 2.2.4.4. Participant data were excluded from subsequent analyses in cases where the measurement tool was unable to detect a value for the peak amplitude of the N170 in at least one condition. As a result, data from three participants were excluded from subsequent analyses, leaving a final sample of 58 participants.

4.2.8. Statistical analysis

Hierarchical regression analyses were used to examine the effect of ELS on the N170 peak amplitude in each stimulus category, with separate analyses for each hemisphere (e.g. male angry left hemisphere; female happy right hemisphere). This resulted in a total of 12 hierarchical regression analyses. Each hierarchical regression model contained the same independent variables but differed in its dependent variable. Each model contained two steps, with the first step including all the control variables (age, PDS: Impression Management, BDI-II and STAI-T) and the second step including the variable of interest, ELS group. Regression models were considered to be significant if they retained significance after correction for multiple comparisons. Correction for multiple comparisons was performed using the Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995) with an FDR threshold of 0.1. For the purposes of these analyses, analyses within one hemisphere were considered to be one 'family' of six tests, with the correction for multiple comparisons being applied separately to each family (i.e. correction for multiple comparisons was performed separately for each hemisphere). Further information regarding the Benjamini-Hochberg procedure can be found in § 2.3.1.1.

4.2.8.1. Selection of control variables

The two ELS groups differed in their mean age and on a number of psychological measures (Table 4.1). In light of this, it was necessary to control for these variables within the analyses. To determine which of these variables should be included as control variables, those which differed significantly between the two groups were identified. The Benjamini-Hochberg procedure with an FDR threshold of 0.1 was then used to correct for multiple comparisons (in this case the family of tests included 16 comparisons altogether; Table 4.1). The Benjamini-Hochberg correction procedure was chosen as the Bonferroni correction would be too conservative for the size of the sample. After correction for multiple comparisons using this procedure, six variables emerged as significantly different between the two ELS groups: age, PDS: Total, PDS: Impression Management, BDI-II, HADS-D and STAI-T.

Though both BDI-II and HADS-D differed significantly between the groups, it was decided that only one should be included in the regression model, given that both questionnaires are designed to measure the same construct (depression). As the difference between the ELS groups was larger for BDI-II scores than for HADS-D scores, BDI-II was retained as a variable in the regression model and HADS-D was removed. Examination of the regression model showed that there was a high level of collinearity between two of the independent variables, PDS: Total and PDS: Impression Management. This was not surprising given that impression management is a subscale of the PDS: Total scale. Examination of the Mann-Whitney U tests of between-group differences on each variable showed that the difference between the two ELS groups was larger for the PDS: Impression Management subscale than for the PDS: Total scale. Therefore the PDS: Total scale was removed from the regression models, and the PDS: Impression Management scale was retained. This left a total of four independent variables which were entered into the regression model in Step 1: age, PDS: Impression Management, BDI-II and STAI-T.

4.3. Results

4.3.1. Task performance

To ensure that participants had been paying attention to the stimuli, the number of misses (failure to make a button press) in response to house stimuli ('catch trials') were examined. Error rates on the catch trials were low, occurring on only 0.97 % of trials. The mean error rate for the low ELS group (M = 0.27, SD = 0.72) did not differ from the mean error rate for the high ELS group (M = 0.34, SD = 0.60; U = 369.00, p = .31).

4.3.2. N170 scalp topography

The scalp distributions of the neural response to male and female angry, happy and neutral facial expressions for the low and high ELS groups are shown in Figures 4.3, 4.4 and 4.5, respectively. In addition, the right hand side of each figure shows the topographical distribution of the difference in activation between the two ELS groups. All topographical plots show the distribution of activity (in μV) at the time at which the peak of the N170 response was maximal (162 ms). This peak was derived from the mean of the N170 response across all stimulus categories, both ELS groups and both hemispheres in the electrode clusters of interest (P7 and P9 in the left hemisphere and P8 and P10 in the right hemisphere).

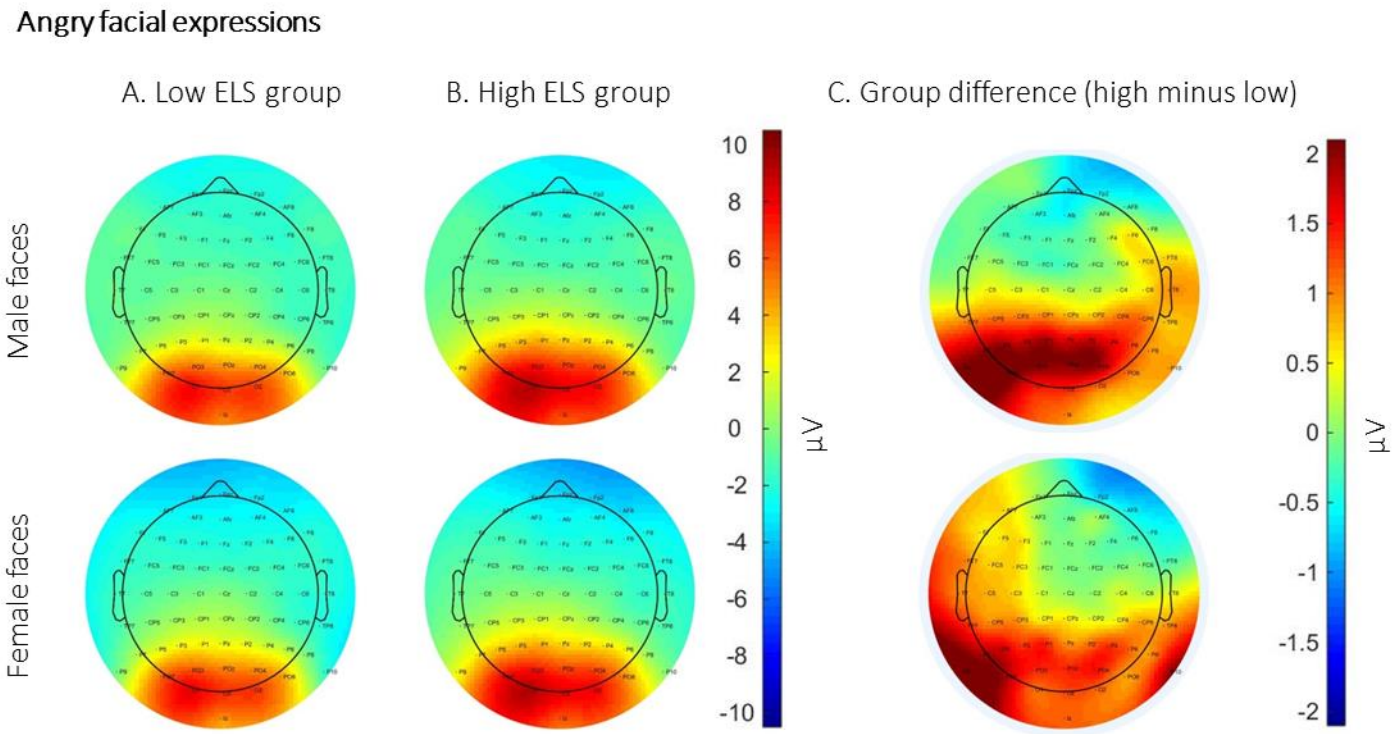

Figure 4.3. Scalp distribution of the neural response to male (top row) and female (bottom row) angry facial expressions at 162 ms post-stimulus onset (the time at which the grand average peak amplitude of the N170 occurred) for the low (A) and high (B) ELS groups. Column C shows the difference in activation between the low and high ELS groups (high minus low), also at a latency of 162 ms. Note the voltage scale for the activity in each condition ranges from -10 μV to 10 μV, whilst the scale for the activity between groups (right-hand column) ranges from -2 μV to 2 μV.

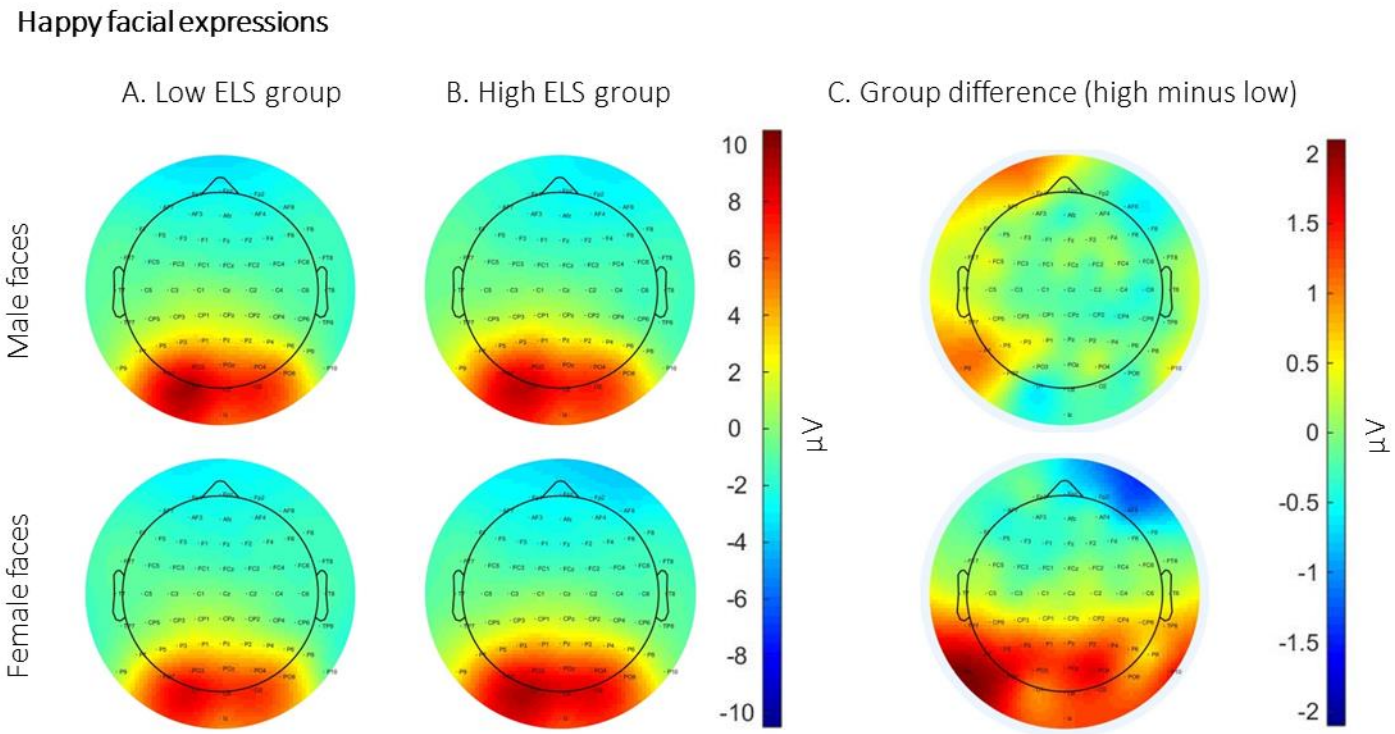

Figure 4.4. Scalp distribution of the neural response to male (top row) and female (bottom row) happy facial expressions at 162 ms post-stimulus onset (the time at which the grand average peak amplitude of the N170 occurred) for the low (A) and high (B) ELS groups. Column C shows the difference in activation between the low and high ELS groups (high minus low), also at a latency of 162 ms. Note the voltage scale for the activity in each condition ranges from -10 µV to 10 µV, whilst the scale for the activity between groups (right-hand column) ranges from -2 µV to 2 µV.

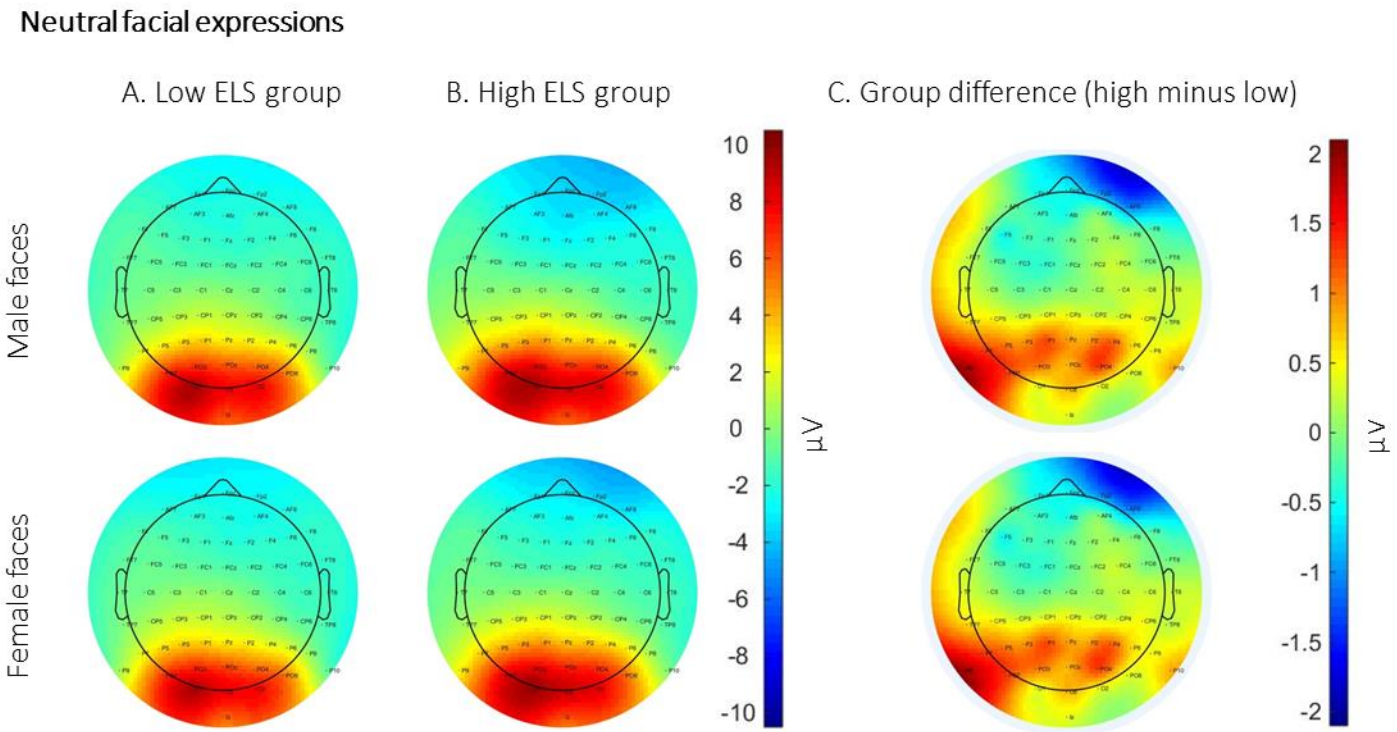

Figure 4.5. Scalp distribution of the neural response to male (top row) and female (bottom row) neutral facial expressions at 162 ms post-stimulus onset (the time at which the grand average peak amplitude of the N170 occurred) for the low (A) and high (B) ELS groups. Column C shows the difference in activation between the low and high ELS groups (high minus low), also at a latency of 162 ms. Note the voltage scale for the activity in each condition ranges from -10 μV to 10 μV, whilst the scale for the activity between groups (right-hand column) ranges from -2 μV to 2 μV.

4.3.3. N170 peak amplitude

Figures 4.6 to 4.9 display the time course of the N170 response to male and female angry facial expressions in the left and right hemispheres. In each figure, the waveform for each ELS group is presented (A). Each figure also includes two bar charts illustrating the mean value for the peak of the P1 (B) and N170 (C) in each ELS group. Figures 4.10 to 4.13 illustrate the corresponding data for the neural response to male and female happy facial expressions, whilst Figures 4.14 to 4.17 illustrate the neural response to male and female neutral facial expressions.

Multiple hierarchical regression analyses were used to examine the effect of ELS on N170 peak amplitude to each stimulus category. Separate sets of analyses were carried out for each hemisphere. A two-step model was used with the control variables (age, impression management, depression and anxiety) entered in the first step and the variable of ELS group entered in the second step. In this way the contribution of ELS group to the variance in N170 amplitudes over and above the effect of the control variables could be examined.

Table 4.2

Means and standard deviations of the N170 peak amplitude to each facial expression by stimulus category, hemisphere and ELS group

N170 amplitude (mean, μV)	Low ELS group	High ELS group
Left hemisphere		
Angry male	-.47 (4.16)	1.63 (5.00)
Angry female	-1.11 (2.76)	1.44 (5.46)
Happy male	.35 (3.48)	1.36 (4.55)
Happy female	-.62 (3.66)	1.51 (5.23)
Neutral male	.11 (2.90)	1.63 (5.49)
Neutral female	-.38 (3.63)	1.61 (4.94)
Right hemisphere		
Angry male	-1.69 (6.50)	-.19 (4.87)
Angry female	-2.28 (5.91)	-.28 (5.59)
Happy male	-1.02 (6.14)	-.61 (4.74)
Happy female	-1.13 (6.27)	.04 (5.35)
Neutral male	-1.28 (6.48)	-.35 (5.33)
Neutral female	-1.61 (5.96)	-.49 (4.52)

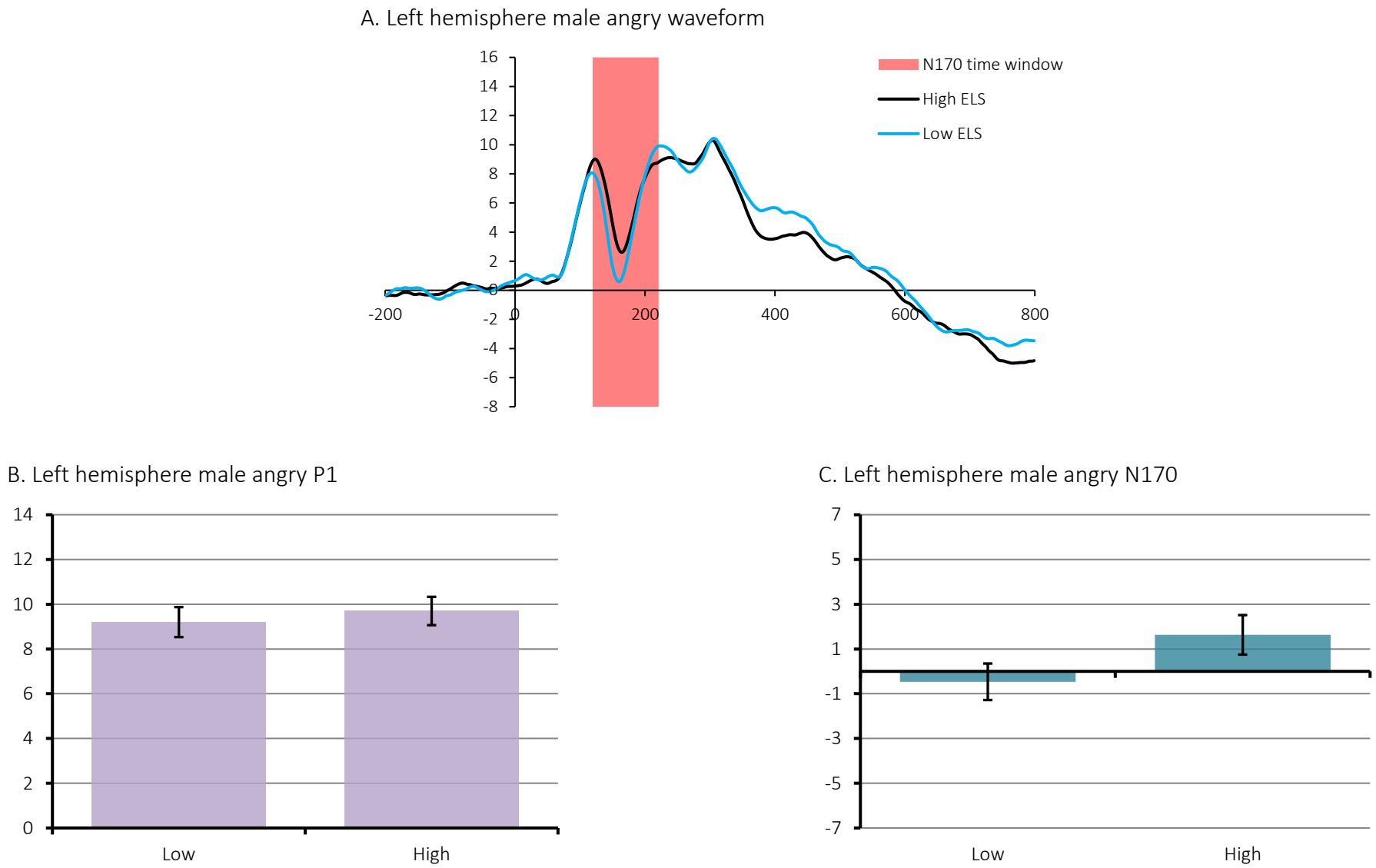

Figure 4.6. Left hemispheric neural responses to male angry facial expressions by early life stress group. Responses depicted as a grand average waveform (A) and as bar charts displaying the mean of the peak amplitudes for the P1 (B) and N170 (C) components. Error bars represent the standard error of the mean.

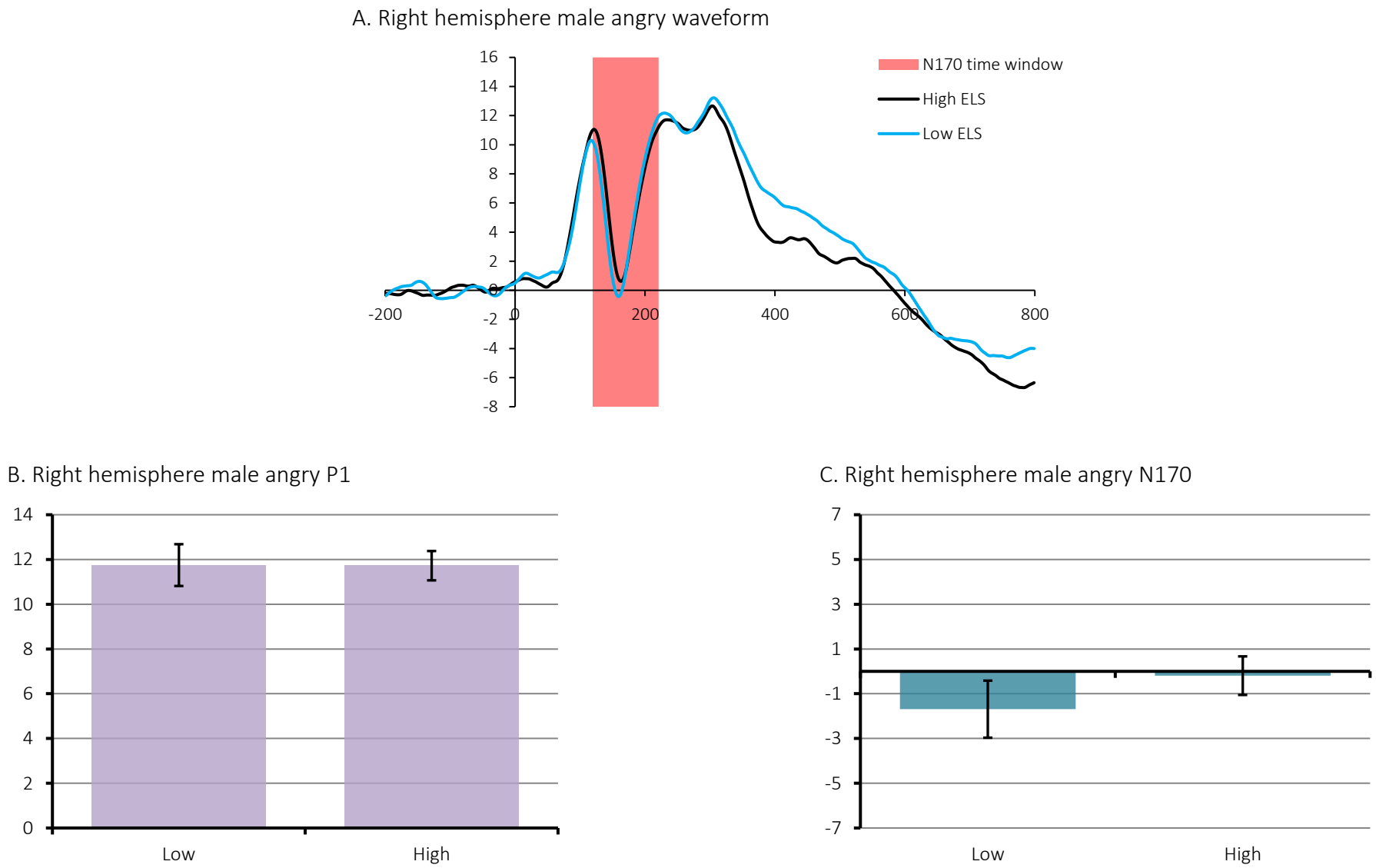

Figure 4.7. Right hemispheric neural responses to male angry facial expressions by early life stress group. Responses depicted as a grand average waveform (A) and as bar charts displaying the mean of the peak amplitudes for the P1 (B) and N170 (C) components. Error bars represent the standard error of the mean.

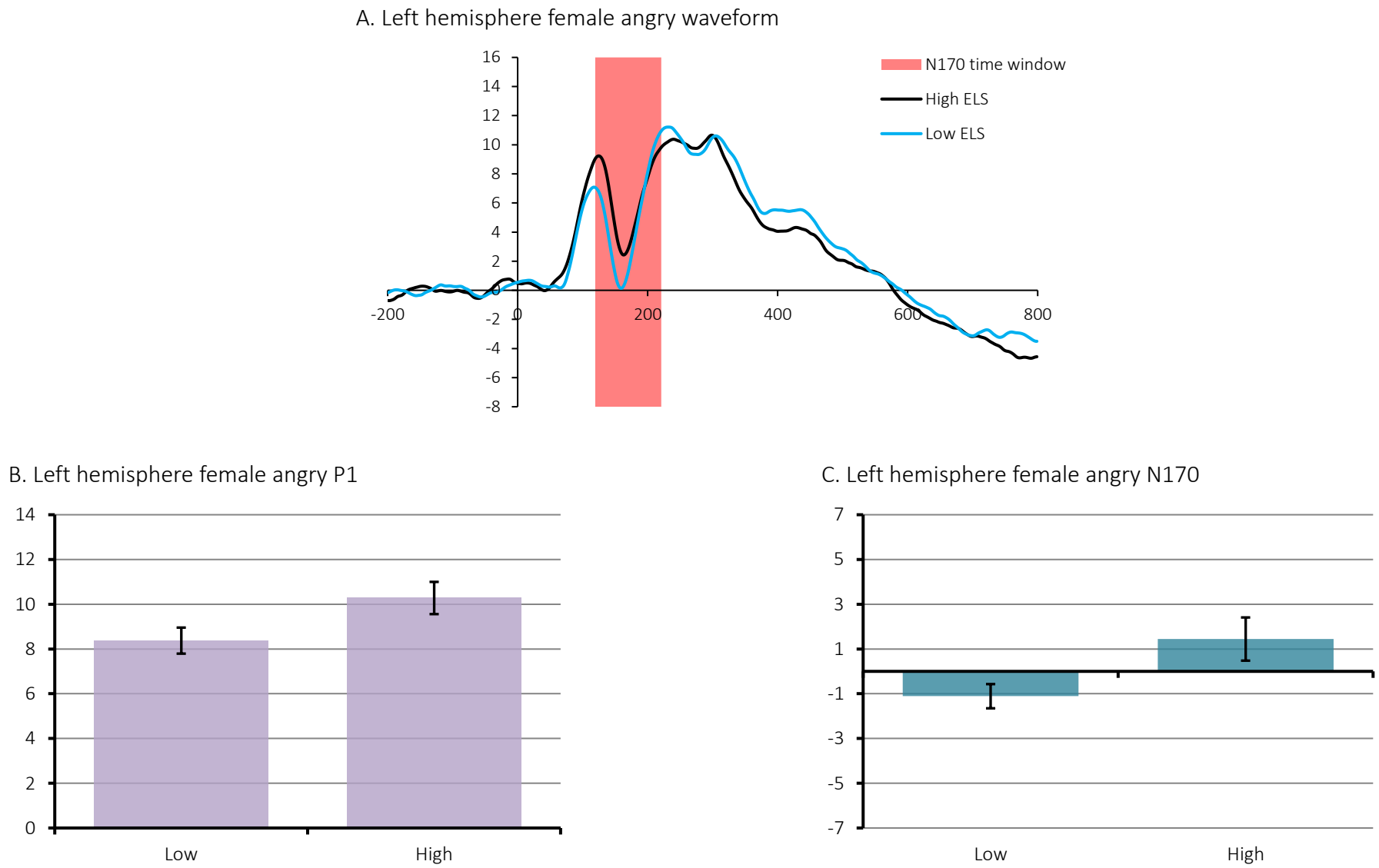

Figure 4.8. Left hemispheric neural responses to female angry facial expressions by early life stress group. Responses depicted as a grand average waveform (A) and as bar charts displaying the mean of the peak amplitudes for the P1 (B) and N170 (C) components. Error bars represent the standard error of the mean.

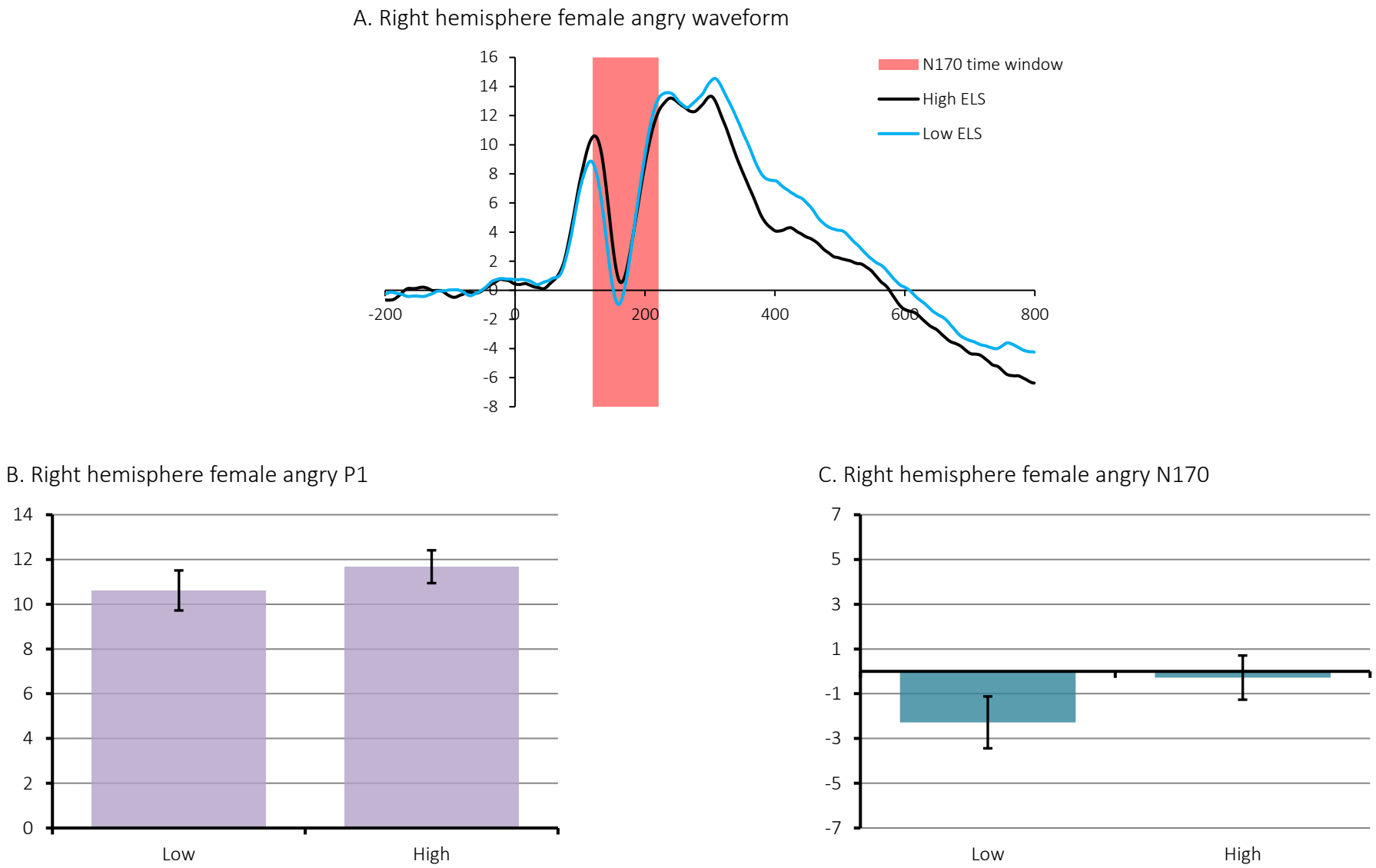

Figure 4.9. Right hemispheric neural responses to female angry facial expressions by early life stress group. Responses depicted as a grand average waveform (A) and as bar charts displaying the mean of the peak amplitudes for the P1 (B) and N170 (C) components. Error bars represent the standard error of the mean.

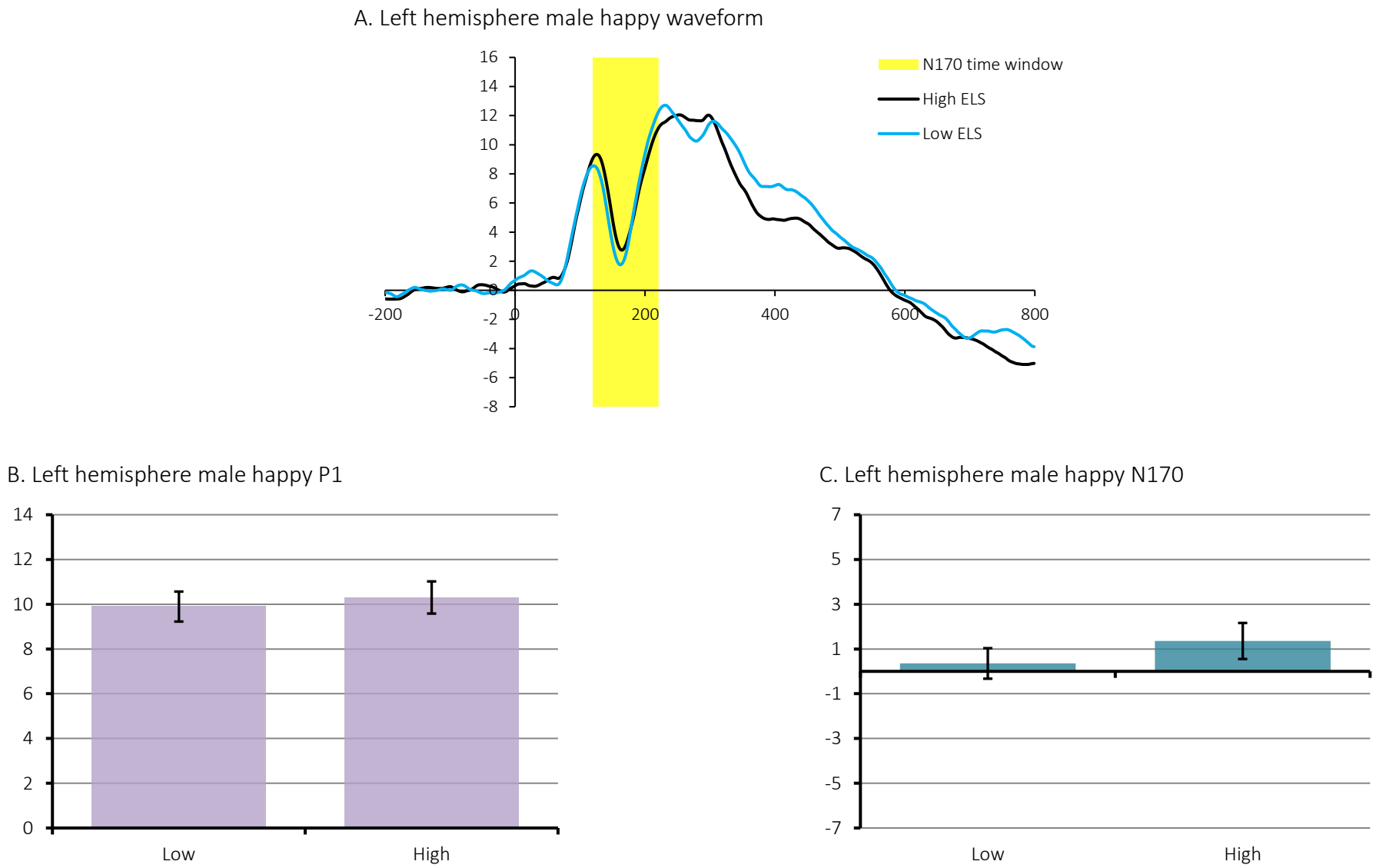

Figure 4.10. Left hemispheric neural responses to male happy facial expressions by early life stress group. Responses depicted as a grand average waveform (A) and as bar charts displaying the mean of the peak amplitudes for the P1 (B) and N170 (C) components. Error bars represent the standard error of the mean.

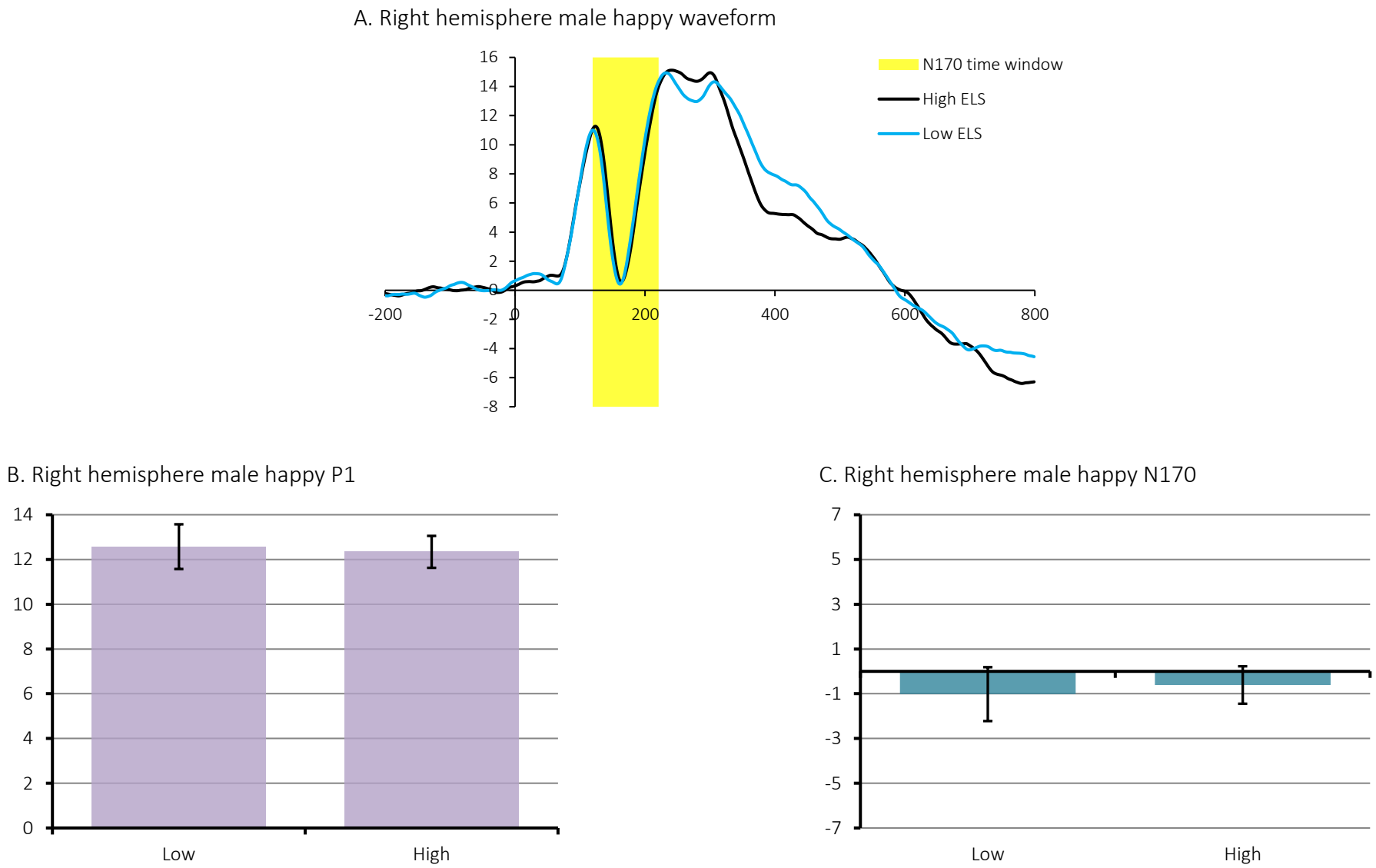

Figure 4.11. Right hemispheric neural responses to male happy facial expressions by early life stress group. Responses depicted as a grand average waveform (A) and as bar charts displaying the mean of the peak amplitudes for the P1 (B) and N170 (C) components. Error bars represent the standard error of the mean.

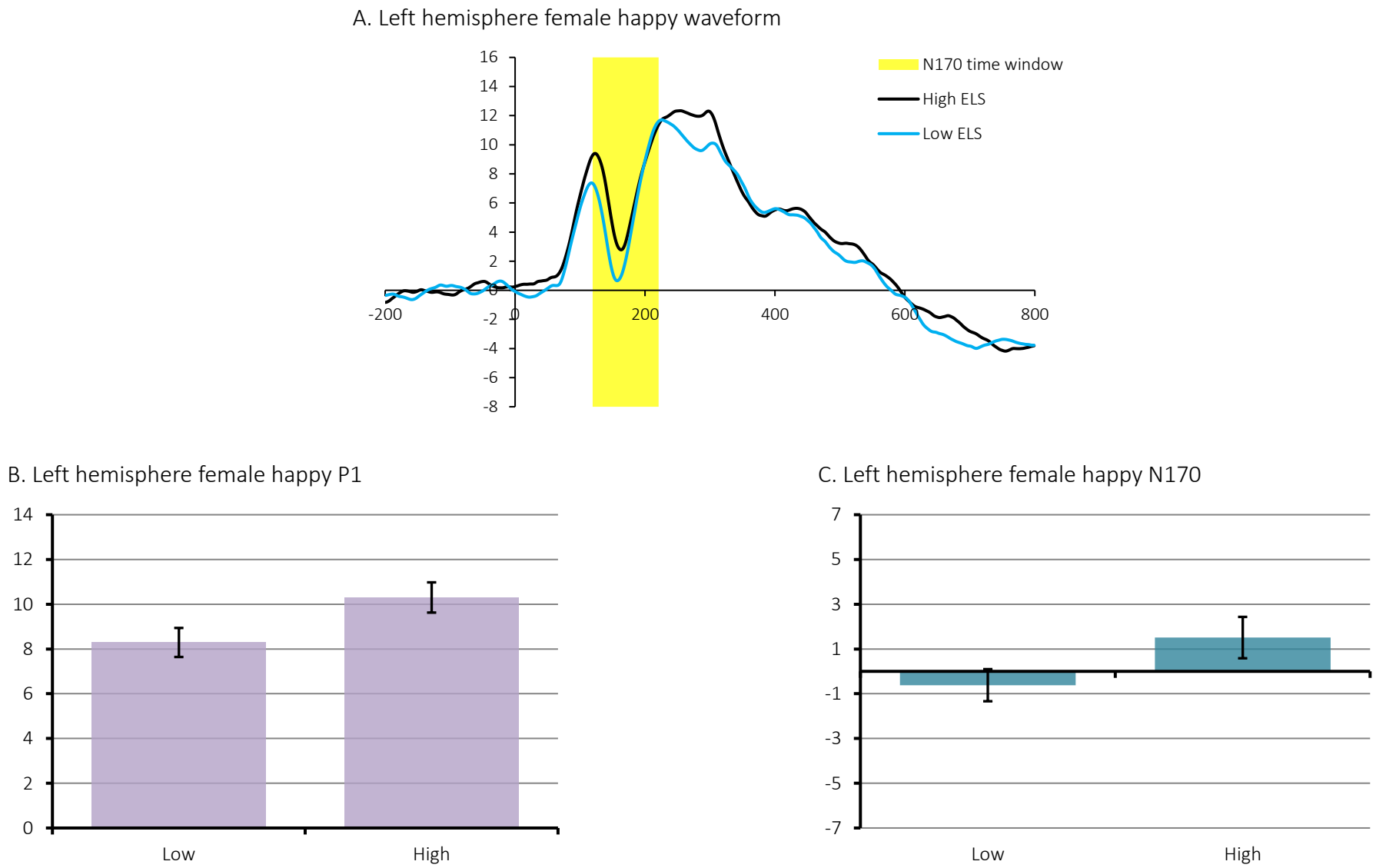

Figure 4.12. Left hemispheric neural responses to female happy facial expressions by early life stress group. Responses depicted as a grand average waveform (A) and as bar charts displaying the mean of the peak amplitudes for the P1 (B) and N170 (C) components. Error bars represent the standard error of the mean.

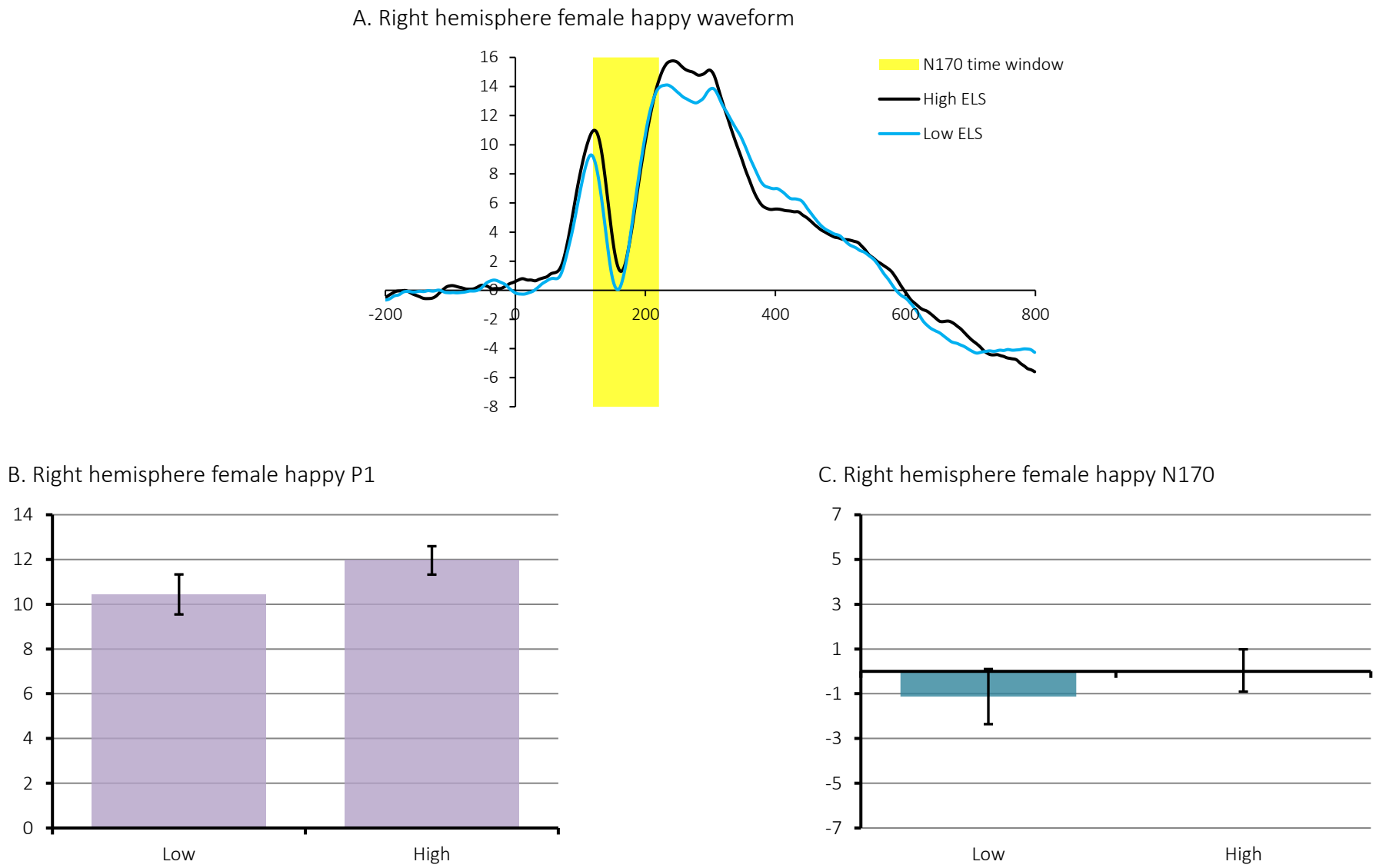

Figure 4.13. Right hemispheric neural responses to female happy facial expressions by early life stress group. Responses depicted as a grand average waveform (A) and as bar charts displaying the mean of the peak amplitudes for the P1 (B) and N170 (C) components. Error bars represent the standard error of the mean.

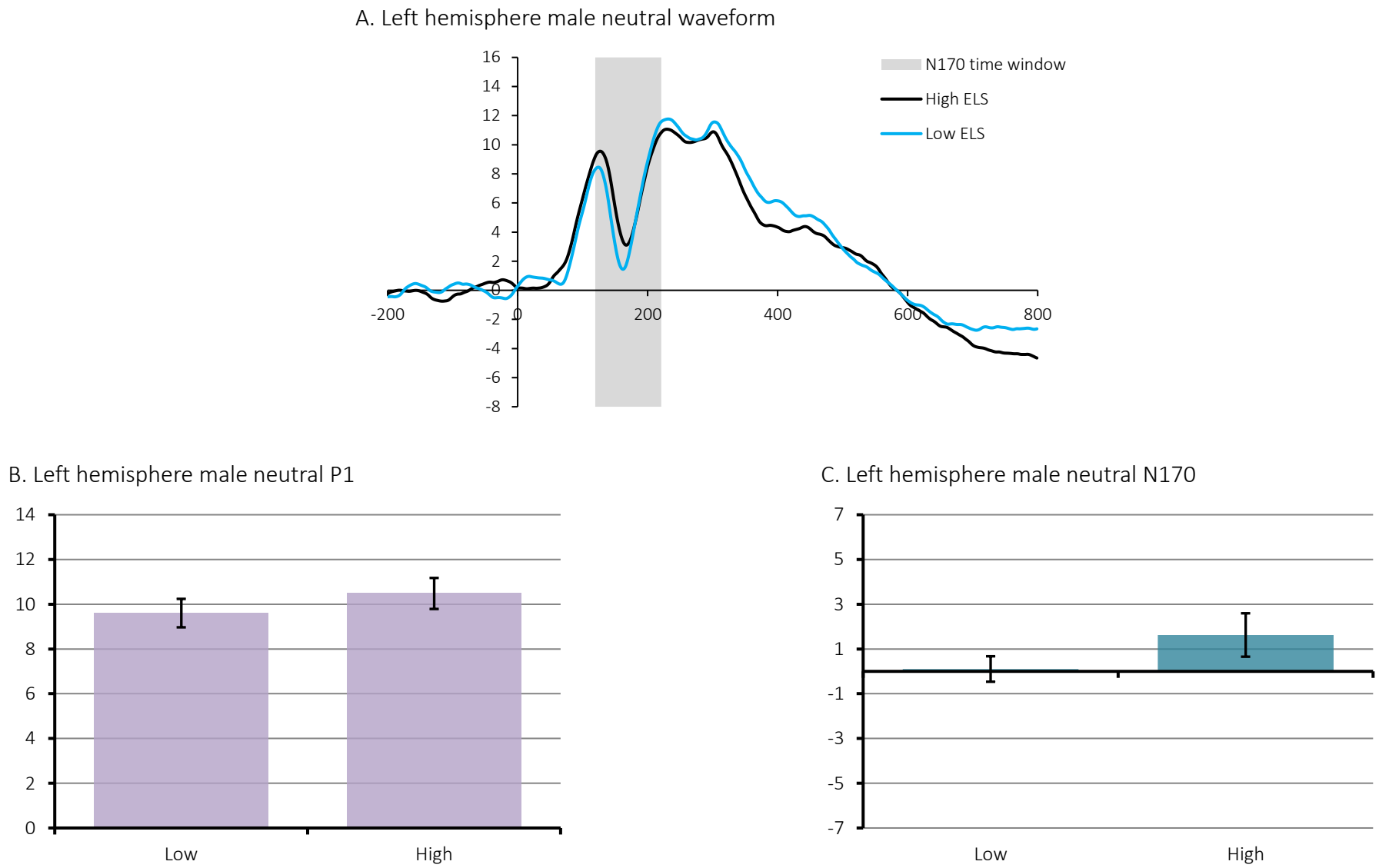

Figure 4.14. Left hemispheric neural responses to male neutral facial expressions by early life stress group. Responses depicted as a grand average waveform (A) and as bar charts displaying the mean of the peak amplitudes for the P1 (B) and N170 (C) components. Error bars represent the standard error of the mean.

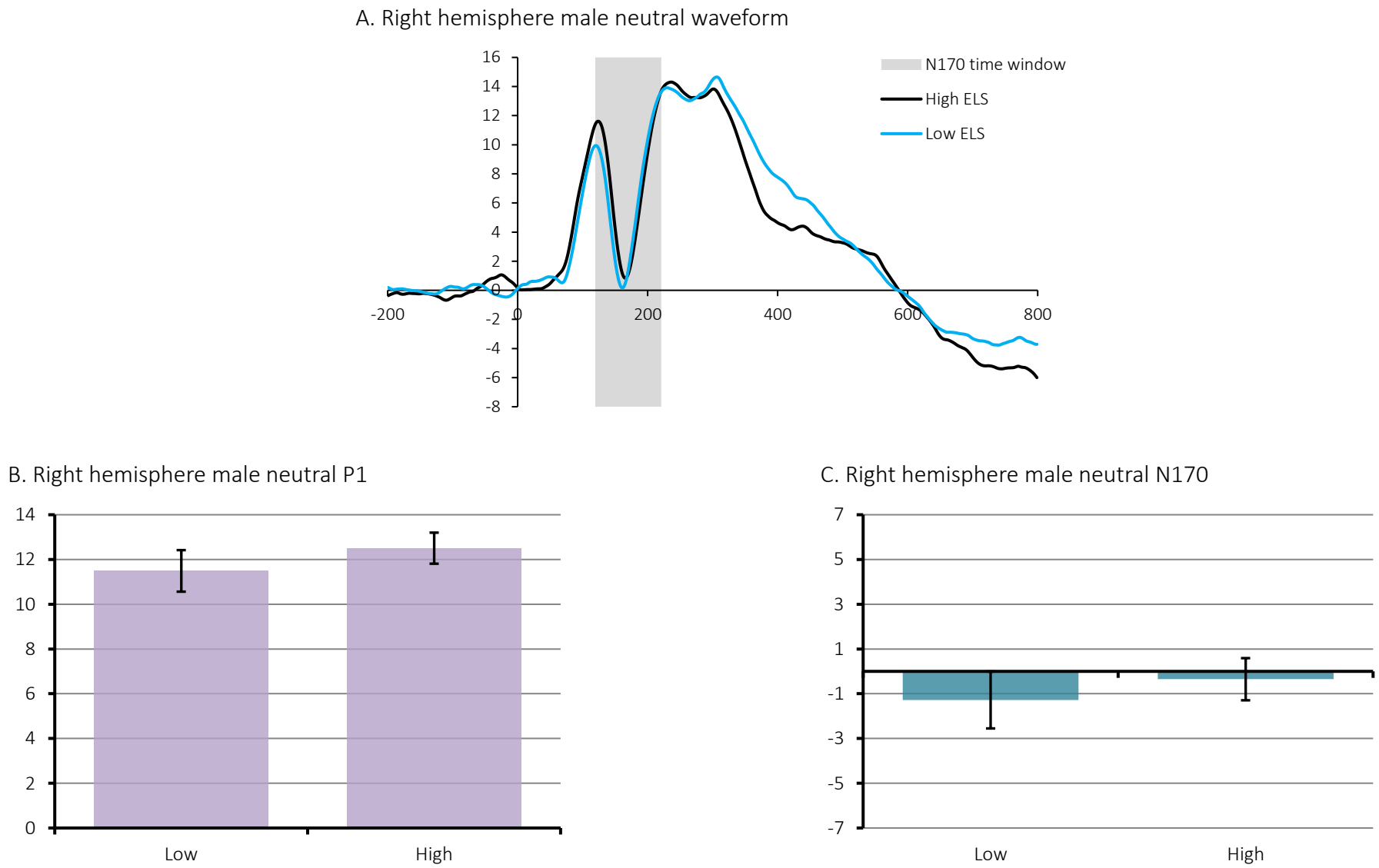

Figure 4.15. Right hemispheric neural responses to male neutral facial expressions by early life stress group. Responses depicted as a grand average waveform (A) and as bar charts displaying the mean of the peak amplitudes for the P1 (B) and N170 (C) components. Error bars represent the standard error of the mean.

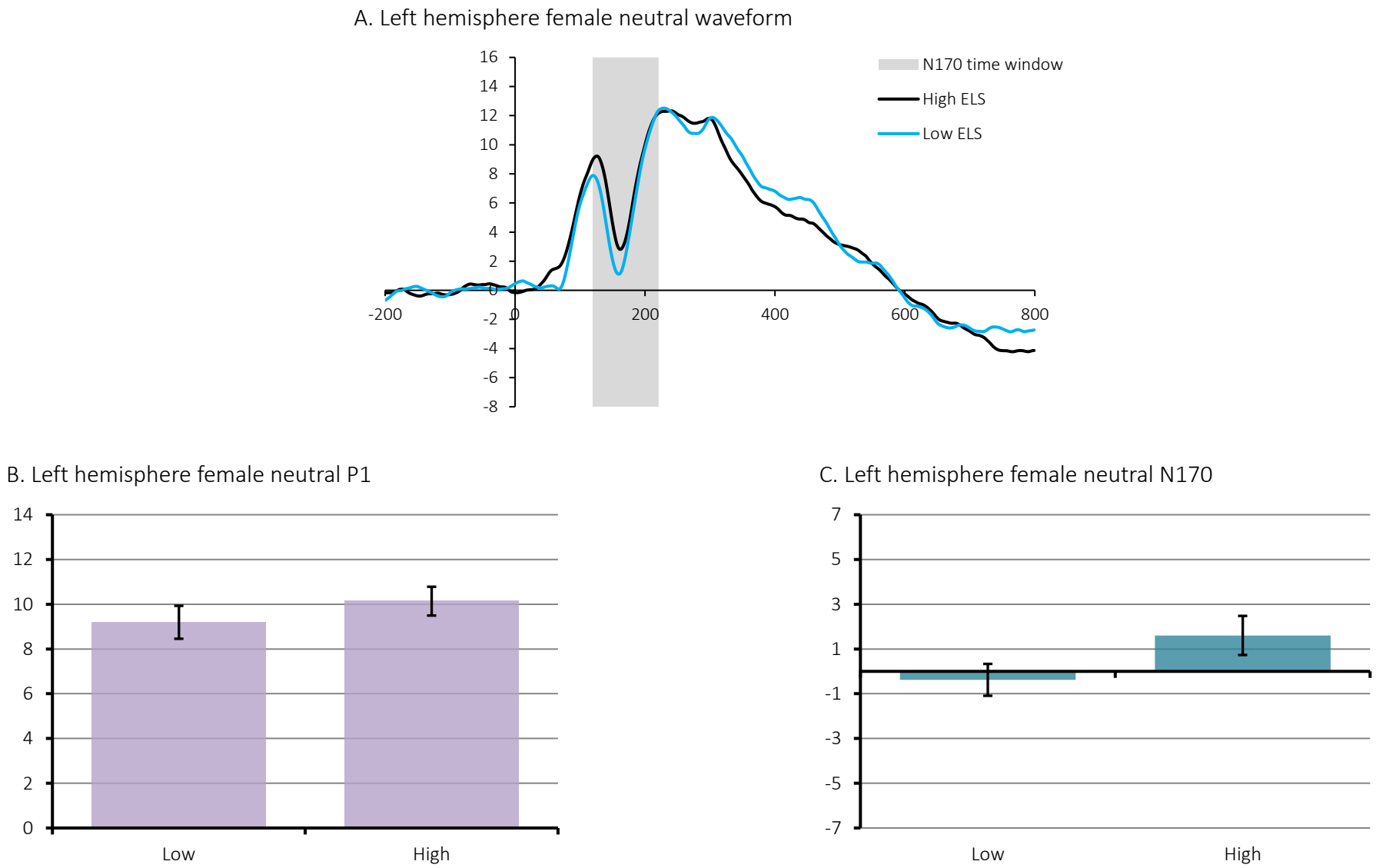

Figure 4.16. Left hemispheric neural responses to female neutral facial expressions by early life stress group. Responses depicted as a grand average waveform (A) and as bar charts displaying the mean of the peak amplitudes for the P1 (B) and N170 (C) components. Error bars represent the standard error of the mean.

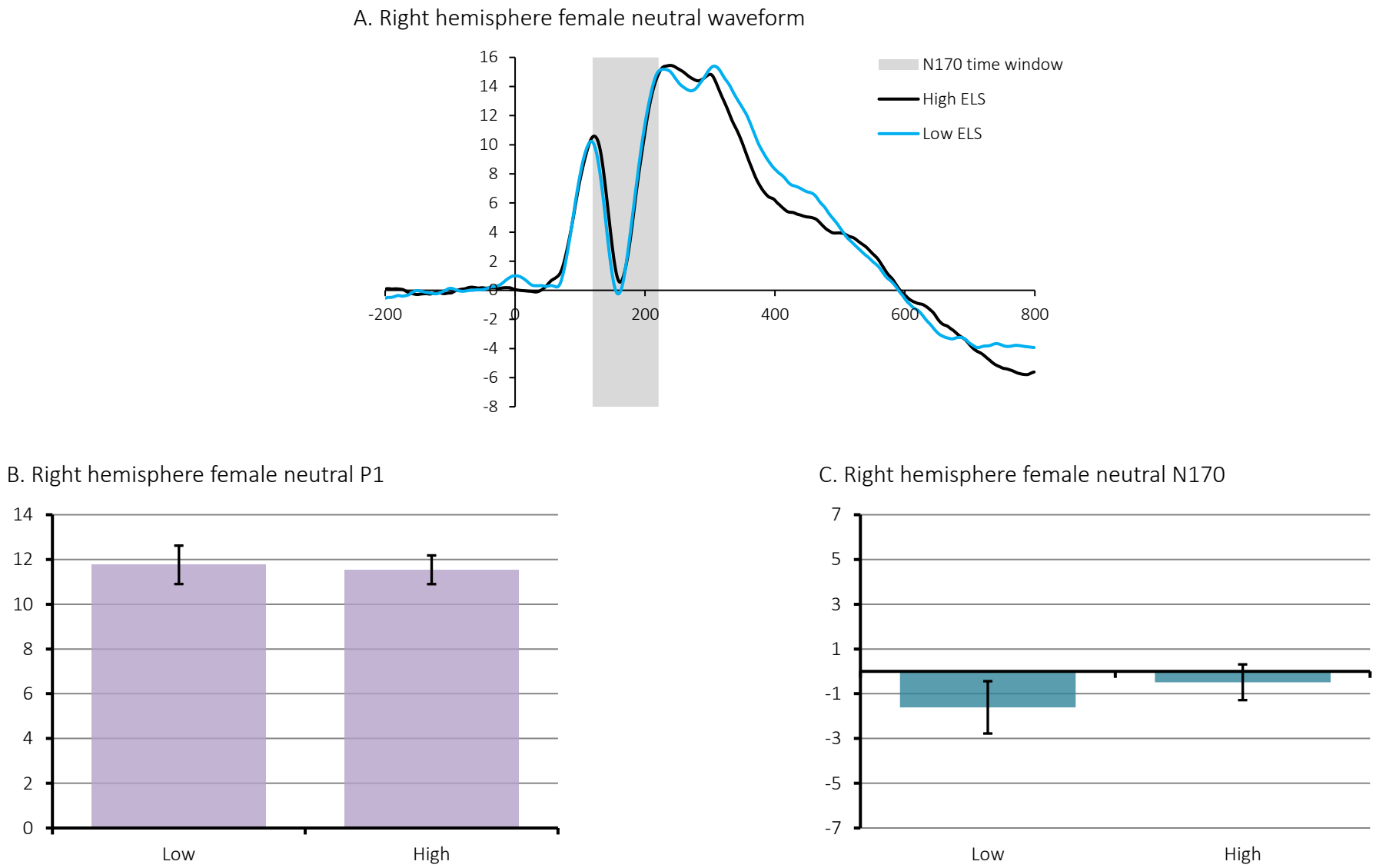

Figure 4.17. Right hemispheric neural responses to female neutral facial expressions by early life stress group. Responses depicted as a grand average waveform (A) and as bar charts displaying the mean of the peak amplitudes for the P1 (B) and N170 (C) components. Error bars represent the standard error of the mean.

4.3.4. Participants with high levels of early life stress show blunted left hemisphere N170 peak amplitudes to emotional facial expressions

Six multiple hierarchical regression analyses were used to examine whether the two ELS groups differed in left hemisphere N170 peak amplitudes to male and female angry, happy and neutral facial expressions. Four control variables (age, PDS: Impression Management, BDI-II, STAI-T) were entered in the first step of the analysis, and ELS group was entered in the second step of the analysis. The final regression model explained a significant proportion of the variance in left hemisphere N170 peak amplitude to five of the six stimulus categories (Table 4.3). These categories were: male angry expressions, female angry expressions, female happy expressions, male neutral expressions and female neutral expressions. These analyses remained significant after correction for multiple comparisons using the Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995) with an FDR threshold of 0.1 (§ 2.3.1.1). In each of these five analyses the entry of ELS group in Step 2 explained a significant additional amount of variance in N170 peak amplitude to the stimulus category ($p < .05$).

Examination of the beta weights across all five significant analyses showed that ELS group was significantly positively associated with the peak amplitude of the N170 response to angry and neutral facial expressions displayed by both male and female individuals, and to happy facial expressions displayed by female individuals. Therefore, for all five stimulus categories, the high ELS group showed blunted N170 peak amplitudes relative to the low ELS group. In addition to ELS group, depression scores and anxiety scores were also significantly related to N170 peak amplitudes to emotional facial expressions. Specifically, higher depression scores were significantly associated with greater (more negative) N170 responses to angry and neutral facial expressions displayed by both male and female individuals, and to happy facial expressions displayed by female individuals. Higher anxiety scores, on the other hand, were significantly associated with blunted (less negative) N170 responses to male angry facial expressions and male and female neutral facial expressions. Higher anxiety scores were also associated with blunted N170 responses to female angry and happy facial expressions at a trend level of significance ($p = .06$).

Neither age nor impression management scores were significantly associated with N170 peak amplitude to any facial expression.

4.3.5. Early life stress is not related to right hemisphere N170 peak amplitudes to emotional facial expressions

Following analysis of the effect of ELS on left hemisphere N170 peak amplitudes, six multiple hierarchical regression analyses were used to examine whether the two ELS groups differed in right hemisphere N170 peak amplitudes to male and female angry, happy and neutral facial expressions. As with the previous set of analyses, the independent variables were entered in two steps, with the four control variables (age, PDS: Impression Management, BDI-II, STAI-T) entered in the first step of the analysis, and ELS group entered in the second step of the analysis. In contrast to the findings in the left hemisphere, the regression model did not predict a significant amount of the variance in right hemisphere N170 peak amplitudes to any of the stimulus categories (Table 4.4).

Table 4.3

Hierarchical regression models examining the effect of age, impression management, depression, anxiety (Step 1) and ELS (Step 2) on the N170 peak amplitude to facial expressions in the left hemisphere

N170 peak amplitude (μV)		**Coefficients**					ΔR^2	R^2
Left hemisphere		**Age**	**Impression management**	**Depression**	**Anxiety**	**ELS group**		
Angry male								
Model 1	*β*	-.16	-.07	-.44	.46			
	p	.30	.63	.02*	.03*			
Model 2	*β*	-.30	.06	-.53	.51	.35	.08	.20
	p	.06	.70	.006**	.01*	.03*	.03*	.03[a]
Angry female								
Model 1	*β*	-.05	-.08	-.37	.33			
	p	.75	.61	.06	.12			
Model 2	*β*	-.21	.08	-.47	.39	.41	.11	.19
	p	.18	.64	.01*	.06	.01*	.01*	.05[a]
Happy male								
Model 1	*β*	-.08	.01	-.45	.50			
	p	.58	.93	.02*	.02*			
Model 2	*β*	-.16	.09	-.50	.52	.20	.03	.15
	p	.31	.58	.01*	.01*	.20	.20	.12
Happy female								
Model 1	*β*	-.03	-.09	-.42	.34			
	p	.83	.58	.03*	.11			
Model 2	*β*	-.17	.05	-.51	.39	.35	.08	.18
	p	.28	.77	.008**	.06	.03*	.03*	.07[a]

N170 peak amplitude (μV)		Coefficients					ΔR^2	R^2
Left hemisphere		**Age**	**Impression management**	**Depression**	**Anxiety**	**ELS group**		
Neutral male								
Model 1	*β*	-.08	.08	-.50	.53			
	p	.59	.59	.008**	.01*			
Model 2	*β*	-.21	.21	-.58	.57	.32	.07	.22
	p	.18	.20	.002**	.006**	.04*	.04*	.02[a]
Neutral female								
Model 1	*β*	-.11	.10	-.45	.45			
	p	.48	.53	.02*	.03*			
Model 2	*β*	-.28	.27	-.56	.51	.44	.13	.24
	p	.07	.09	.003**	.01*	.004**	.004**	.01[a]

Note. ELS group coded as low = 0 and high = 1. * p < .05, ** p < .01, [a]Model explains a significant amount of variance after correction for multiple comparisons.

Table 4.4

Hierarchical regression models examining the effect of age, impression management, depression, anxiety (Step 1) and ELS (Step 2) on the N170 peak amplitude to emotional facial expressions in the right hemisphere

N170 peak amplitude		**Coefficients**					ΔR^2	R^2
Right hemisphere		**Age**	**Impression management**	**Depression**	**Anxiety**	**ELS group**		
Angry male								
Model 1	*β*	-.12	-.13	-.36	.39			
	p	.44	.41	.06	.07			
Model 2	*β*	-.18	-.07	-.41	.41	.17	.02	.12
	p	.27	.70	.04*	.06	.30	.30	.24
Angry female								
Model 1	*β*	-.03	-.03	-.21	.30			
	p	.86	.87	.29	.16			
Model 2	*β*	-.11	.05	-.26	.33	.20	.03	.08
	p	.52	.76	.19	.13	.22	.22	.52
Happy male								
Model 1	*β*	-.03	-.03	-.36	.38			
	p	.85	.85	.06	.08			
Model 2	*β*	-.05	-.02	-.37	.39	.04	.00	.08
	p	.78	.93	.07	.08	.80	.80	.46
Happy female								
Model 1	*β*	-.06	-.09	-.34	.35			
	p	.70	.57	.08	.10			
Model 2	*β*	-.11	-.04	-.37	.37	.12	.01	.09
	p	.52	.80	.06	.09	.45	.45	.43

N170 peak amplitude		**Coefficients**					ΔR^2	R^2
Right hemisphere		**Age**	**Impression management**	**Depression**	**Anxiety**	**ELS group**		
Neutral male								
Model 1	β	-.09	-.02	-.47	.47			
	p	.56	.88	.01*	.03*			
Model 2	β	-.15	.03	-.51	.49	.15	.01	.14
	p	.37	.84	.01*	.02*	.34	.36	.16
Neutral female								
Model 1	β	-.07	-.04	-.39	.37			
	p	.67	.78	.04*	.08			
Model 2	β	-.14	.02	-.44	.40	.18	.02	.11
	p	.41	.89	.03*	.07	.28	.28	.31

Note. ELS group coded as low = 0 and high = 1. * $p < .05$.

4.3.6. P1 peak amplitude is not related to early life stress

Visual examination of the N170 waveforms (Figures 4.6 to 4.17) raised the possibility that the peak amplitude of the P1 to emotional facial expressions differed between the high and low ELS groups. The implication of this possibility is that significant between-group differences in the P1 could, at least in part, explain the significant between-group differences in the N170. In light of this, the ERPLAB measurement tool was used to extract a value for the peak amplitude of the P1 to each stimulus category. The parameters of the measurement tool were set to find a positive local peak over a latency of 65 ms to 165 ms. Using this tool, a value for the peak amplitude of the P1 was extracted for all but one of the participants whose data were included in the analysis of N170 peak amplitudes. The case where no local peak could be found was removed from subsequent analyses. The final sample for the P1 analyses therefore contained 57 participants, with 25 participants in the low ELS group and 32 in the high ELS group.

The effects of ELS on P1 peak amplitudes to emotional facial expressions were examined using hierarchical regression analysis. As in the regression analyses used to examine the N170 peak amplitudes, the regression model consisted of four control variables entered in Step 1 (age, PDS: Impression Management, BDI-II, STAI-T) and the variable of interest, ELS group, entered in Step 2. The regression model did not explain a significant amount of the variance in the peak amplitude of the P1 to any of the stimulus categories in either the left hemisphere (Table 4.5) or the right hemisphere (Table 4.6). This suggests that the effect of ELS group on N170 peak amplitudes to emotional facial expressions cannot be explained by differences between the two ELS groups in the peak amplitude of the P1.

Table 4.5

Hierarchical regression models examining the effect of age, impression management, depression, anxiety (Step 1) and ELS (Step 2) on the P1 peak amplitude to facial expressions in the left hemisphere

P1 peak amplitude		**Coefficients**					**ΔR^2**	**R^2**
Left hemisphere		**Age**	**Impression management**	**Depression**	**Anxiety**	**ELS group**		
Angry male								
Model 1	*β*	.03	-.04	-.14	-.06			
	p	.83	.80	.49	.80			
Model 2	*β*	-.04	.02	-.18	-.04	.17	.02	.05
	p	.83	.90	.38	.85	.31	.31	.77
Angry female								
Model 1	*β*	.24	-.12	-.15	.03			
	p	.12	.45	.45	.90			
Model 2	*β*	.14	-.03	-.21	.05	.25	.04	.11
	p	.42	.88	.30	.82	.12	.12	.28
Happy male								
Model 1	*β*	.13	.03	-.26	.21			
	p	.39	.83	.19	.35			
Model 2	*β*	.11	.05	-.27	.21	.05	.00	.07
	p	.51	.76	.18	.34	.76	.76	.56
Happy female								
Model 1	*β*	.29	-.19	-.09	-.20			
	p	.06	.23	.65	.35			
Model 2	*β*	.17	-.08	-.16	-.18	.31	.06	.15
	p	.31	.65	.41	.41	.06	.06	.12

P1 peak amplitude		**Coefficients**					ΔR^2	R^2
Left hemisphere		**Age**	**Impression management**	**Depression**	**Anxiety**	**ELS group**		
Neutral male								
Model 1	β	.06	.10	-.21	.23			
	p	.71	.52	.29	.30			
Model 2	β	-.02	.18	-.26	.25	.19	.03	.07
	p	.90	.31	.21	.26	.25	.25	.54
Neutral female								
Model 1	β	.02	.11	-.14	.17			
	p	.93	.52	.47	.44			
Model 2	β	-.08	.19	-.20	.19	.23	.03	.06
	p	.65	.28	.33	.39	.18	.18	.67

Table 4.6

Hierarchical regression models examining the effect of age, impression management, depression, anxiety (Step 1) and ELS (Step 2) on the P1 peak amplitude to facial expressions in the right hemisphere

P1 peak amplitude		**Coefficients**					ΔR^2	R^2
Right hemisphere		**Age**	**Impression management**	**Depression**	**Anxiety**	**ELS group**		
Angry male								
Model 1	*β*	.04	-.27	-.35	.00			
	p	.80	.09	.07	.99			
Model 2	*β*	.04	-.27	-.35	.00	.00	.00	.11
	p	.82	.12	.08	.99	.98	.98	.29
Angry female								
Model 1	*β*	.16	-.29	-.18	-.06			
	p	.31	.07	.36	.77			
Model 2	*β*	.13	-.27	-.20	-.06	.07	.00	.08
	p	.44	.13	.33	.79	.69	.69	.48
Happy male								
Model 1	*β*	.06	-.26	-.35	.13			
	p	.68	.11	.07	.55			
Model 2	*β*	.11	-.30	-.32	.12	-.11	.01	.11
	p	.52	.09	.10	.58	.51	.51	.32
Happy female								
Model 1	*β*	.23	-.33	-.27	-.07			
	p	.13	.03*	.16	.73			
Model 2	*β*	.17	-.28	-.31	-.06	.15	.02	.15
	p	.31	.10	.12	.78	.33	.33	.13

P1 peak amplitude		**Coefficients**					**ΔR^2**	**R^2**
Right hemisphere		**Age**	**Impression management**	**Depression**	**Anxiety**	**ELS group**		
Neutral male								
Model 1	β	.12	-.29	-.38	.11			
	p	.42	.06	.05	.59			
Model 2	β	.09	-.26	-.40	.12	.09	.01	.13
	p	.60	.12	.04*	.57	.60	.60	.19
Neutral female								
Model 1	β	.03	-.17	-.37	.23			
	p	.86	.29	.06	.28			
Model 2	β	.06	-.20	-.35	.23	-.09	.01	.09
	p	.71	.24	.08	.30	.59	.59	.42

Note. * $p < .05$.

4.3.7. Testing assumptions of multiple regression analyses

As discussed in § 2.3.2, multiple linear regression makes a number of assumptions about the data. The following section addresses whether these assumptions were met for the regression analyses conducted within this chapter.

4.3.7.1. Outliers and influential points

Across the 12 regression analyses used to predict the N170 response to emotional facial expressions, two analyses contained outliers in which the standardised residuals were greater than +/- 3 *SD*. The remaining 10 analyses showed no outliers. The two analyses which contained outliers were the prediction of the left hemisphere N170 response to female angry facial expressions, and the left hemisphere N170 response to female happy facial expressions. In both analyses only one outlier emerged, and in both cases this outlier was generated by the same participant (43). After confirming that these outliers were not a consequence of an error in data entry, Cook's Distances were computed to examine the extent to which the cases were influencing their respective analyses. The Cook's Distances were 0.27 in the analysis of female angry facial expressions and 0.25 in the analysis of female happy facial expressions. In both cases this value was below 1, suggesting that the outliers were not exerting an undue influence on the regression models (Field, 2005). There were no outliers in the analyses of the P1 response to any of the emotional facial expressions.

4.3.7.2. Independence of residuals

The Durbin-Watson statistic was used to test the assumption of independence of residuals. Using the tables provided by Savin and White (1977), it was established that the upper bound for the Durbin-Watson value in the present regression analyses was 1.59, and the lower bound was 1.21. As discussed in § 2.3.2.2, values above the upper bound indicate that the assumption has been met, values below the lower bound indicate violation of the assumption, and values in between the two bounds indicate that the test is inconclusive. The Durbin-Watson statistic fell above the upper bound

for all 12 analyses of the N170 response to emotional facial expressions, indicating that the assumption of independence of residuals was met.

Regarding the 12 analyses of the P1 response to emotional facial expressions, there were seven cases in which the Durbin-Watson statistic fell above the upper bound, and five cases in which it fell between the two bounds (left hemisphere male angry, left and right hemisphere male happy, and left and right hemisphere female neutral). However, none of the values fell below the lower bound. Therefore, although the test was inconclusive, it did not show that the assumption had been violated.

4.3.7.3. Presence of linearity

Multiple regression assumes a linear relationship between the dependent variable and each of the independent variables. This assumption was investigated by visual examination of the partial regression plots between the dependent variable and each independent variable. In all cases the pattern of data points suggested that the assumption of linearity had been met. In addition, the assumption of a linear relationship between the dependent variable and the independent variables collectively was tested via examination of scatterplots in which the studentised residuals were plotted against the unstandardised predicted values. These plots also showed that the assumption of linearity had been met.

4.3.7.4. Homoscedasticity of residuals

The assumption of homoscedasticity was tested by visual examination of the residual plots described in the previous section. In all analyses these plots showed a broadly random pattern of data points, indicating that the assumption of homoscedasticity had been met.

4.3.7.5. Absence of multicollinearity

The assumption of no multicollinearity was tested via examination of the correlations between the predictors and examination of the Tolerance values for each predictor. In all cases the correlations between predictors were below 0.8, with the largest correlation being that observed between BDI scores and STAI-T scores ($r(56) = 0.69$, $p < .001$). All Tolerance

values fell well above the suggested cut-off value of 0.2 (Field, 2005), with the smallest Tolerance value (0.39) corresponding to the STAI-T predictor. These tests showed that although there was some correlation between the predictors, none of the correlations was large enough to violate the assumption of no multicollinearity.

4.3.7.6. Normal distribution of residuals

The assumption of normal distribution of residuals was tested via visual examination of histograms of the standardised residuals and probability plots in which the observed cumulative probability was plotted against the expected cumulative probability. These plots indicated that the assumption had been met for all analyses.

4.4. Discussion

This study aimed to examine the impact of early life stress (ELS) on young adults' early visual processing of facial expressions as measured by the N170, an early visual ERP observed over occipital-temporal regions. ELS-specific effects were found in the left hemisphere but not the right hemisphere. When controlling for participants' age and scores on measures of depression, anxiety and impression management (deception), it was found that in the left hemisphere only, the high ELS group showed significantly smaller N170 peak amplitudes than the low ELS group in response to male and female angry and neutral facial expressions, and to female happy facial expressions. Notably, also in the left hemisphere but in contrast to the effects of ELS, higher depression scores were significantly associated with greater N170 peak amplitudes to these emotional facial expressions (male and female angry and neutral expressions, and female happy expressions). In addition, higher anxiety scores were significantly associated with blunted left hemisphere N170 peak amplitudes to female angry expressions and male and female neutral expressions, and with blunted left hemisphere N170 peak amplitudes to male angry facial expressions and female happy facial expressions at a trend level of significance.

4.4.1. Early life stress is related to blunted left hemisphere N170 peak amplitudes to emotional facial expressions

In line with the tentative prediction, it was found that high levels of ELS were associated with reduced N170 peak amplitudes to facial emotional expressions. This finding accords with the findings from two previous studies of young children's ERP responses to emotional facial expressions. Curtis and Cicchetti (2011) presented maltreated and non-maltreated children (M = 42 months) with angry, happy and neutral facial expressions and found that maltreatment was associated with an overall reduction in N170 peak amplitude to these facial stimuli. Similarly, Moulson et al. (2009) found blunted N170 peak amplitudes to angry, happy, fearful and sad facial expressions in a sample of infants (age 5 to 31 months) who had been institutionalised. However, this effect was present in

the right hemisphere, in contrast to the present finding in the left hemisphere, and was no longer apparent when the sample was tested later, at a mean age of 30 months and again at 42 months. Indeed, whilst there is some evidence for a relationship between ELS and blunted N170 peak amplitudes to emotional facial expressions, other studies with children have found no effect of ELS on N170 peak amplitudes (Curtis & Cicchetti, 2013; Nelson et al., 2013; Young et al., 2017). In a recent paper which discussed ERP responses to emotional facial expressions in children who had lived in institutions, the research group who carried out many of the aforementioned studies (Moulson et al., 2009; Nelson et al., 2013; Young et al., 2017), suggest that N170 responding to emotional facial expressions reflects a mechanism that is 'spared' from the effects of ELS, that is, it is not affected by early institutionalisation (Young et al., 2017).

A possible reason for the discrepancy between the present findings and the conclusions drawn by Young et al. (2017) concerns the development of the N170 itself. Batty and Taylor (2006) suggest that the morphology and neural generators of the N170 component change across childhood. Similarly, its functional significance appears to shift over time, with evidence for a shift to emotion-sensitivity around the age of 14 to 15 years (Batty & Taylor, 2006). Therefore, given that the N170 component is likely to index different neural mechanisms across development, it is perhaps unsurprising that the present findings with adult participants differed from previous findings with child participants.

Having said this, it should be acknowledged that the only other study, to the author's knowledge, which has examined the effect of ELS on N170 peak amplitudes to emotional facial expressions did not find between-group differences in the peak amplitude of the N170 to either angry or happy facial expressions (Chu et al., 2016). This was in contrast to the present findings which showed a significant effect of ELS group on the N170 peak amplitude to male and female angry facial expressions, and to female happy facial expressions. There are a number of methodological differences between the present study and the study carried out by Chu et al. (2016) which could explain this discrepancy in findings. Firstly, Chu et al. (2016) presented the stimuli for only 10 ms, whilst the present study

presented the stimuli for 200 ms. Furthermore, the stimuli in Chu et al.'s (2016) study were followed by a neutral face mask, whilst the stimuli in the present study were followed by a black background. As a result, the neural response to the stimuli may have varied between studies. In addition, Chu et al. (2016) assessed male and female participants aged 18 to 70 years, whilst the present study assessed female participants aged 18 to 25 years. Therefore, the two participant samples differed markedly in their neurodevelopmental stage and social context. In contrast to the participant sample recruited by Chu et al. (2016), the majority of the participants in the present study were university students who were in a transitional and socially demanding stage of life, and whose brains would have been still undergoing final maturational processes (Lebel et al., 2008; Sowell et al., 1999). As a result, the neural mechanisms involved in processing emotional information could be more vulnerable to potential ELS-related effects in the present sample than in the sample assessed by Chu et al. (2016).

The present study found that ELS was related to alterations in early neural processing of angry, happy and neutral facial expressions. This finding appears to be at odds with the findings of the previous study (Chapter 3), which found that the effects of ELS on behavioural responses to emotional facial expressions were specific to angry facial expressions, and did not occur in response to happy or neutral facial expressions. This dissociation is also present in the wider literature on emotional face processing in people who have experienced ELS. Behavioural studies typically show a specific relationship between ELS and responses to angry facial expressions (Gibb et al., 2009; Pollak et al., 2009), whilst numerous fMRI studies have found evidence for a relationship between ELS and increased amygdala activation during processing of emotional facial expressions in general (Dannlowski et al., 2012; McCrory et al., 2013; Redlich et al., 2015; van Harmelen et al., 2013). It is possible that ELS is associated with atypical early neural responses to facial or emotional stimuli in general, irrespective of the specific emotion displayed, but that later compensatory neural mechanisms act to prevent the early atypical response from affecting subsequent behavioural responding to happy and neutral facial expressions. Additional discussion of the dissociation between the

behavioural and neural effects reported in the present research can be found in § 6.2.2.

The present study found that the effect of ELS on N170 peak amplitude to emotional facial expressions was specific to the left hemisphere, and did not occur in the right hemisphere. An intriguing potential explanation for this left hemisphere specificity can be found in the wider neuroimaging literature. A growing body of work has reported reduced left hemispheric white matter integrity in individuals who experienced ELS (Choi et al., 2012; Choi et al., 2009; Lu et al., 2013; Teicher & Samson, 2016). White matter consists of the fibre tracts which connect populations of neurons (Daniels, Lamke, Gaebler, Walter, & Scheel, 2013), and reductions in the integrity of these tracts have been associated with neurological and psychiatric disorders, as well as disruption in cognitive function (Chanraud, Zahr, Sullivan, & Pfefferbaum, 2010). Of particular interest to the present discussion are reports of ELS-related alterations in white matter integrity within the left fusiform gyrus (Lu et al., 2013), and in the left inferior longitudinal fasciculus, a tract which connects the fusiform gyrus to the amygdala (Choi et al., 2012; Herrington, Taylor, Grupe, Curby, & Schultz, 2011). Given that the fusiform gyrus is thought to be involved in the generation of the N170 (Eimer, 2011a), reduced white matter integrity in this region could explain the reduced N170 response shown by the high ELS group in the present study. Future work should examine whether changes in the white matter integrity of face processing regions mediate the relationship between ELS and reduced N170 peak amplitudes to emotional facial expressions.

A key finding of the present study is that ELS-related changes in early perceptual responses to emotional facial expressions were observed in a sample of young adults without any diagnosed mental health conditions. This adds to previous work which suggests that some of the neural effects of ELS may occur in the absence of clinically significant mental health problems (Chaney et al., 2014; Dannlowski et al., 2012; Teicher & Samson, 2016; van Harmelen et al., 2013). The present findings therefore have important implications for our broader understanding of the effects of ELS, as they suggest that people who experienced high levels of ELS, but have

not been diagnosed with a mental illness, may nevertheless process social-emotional cues differently to those who experienced low levels of ELS. Given the importance of social cues such as emotional facial expressions for successful social interaction, it is possible that differences in the way these cues are processed could have an effect on individuals' interpersonal relationships, potentially increasing their vulnerability to mental illness in the future (McCrory et al., 2017).

4.4.2. Anxiety and depression scores have differential effects on N170 peak amplitudes to emotional facial expressions

To the author's knowledge, the present findings are the first to show differential, independent effects of ELS, depression scores and anxiety scores on the N170 response to emotional facial expressions in a sample of mentally healthy adults. Specifically, as predicted, both ELS and anxiety levels were independently associated with blunted N170 amplitudes to angry, happy and neutral facial expressions in the left hemisphere. In contrast, and contrary to the prediction of a relationship between higher depression scores and blunted N170 responses to emotional facial expressions, depression scores were associated with potentiated N170 peak amplitudes to angry, happy and neutral facial expressions, again in the left hemisphere.

At first glance, this finding of increased N170 peak amplitudes in participants with higher depression scores is at odds with the majority of previous research, which has typically found no effect of depression on the N170 response to emotional facial expressions (Camfield et al., 2016; Jaworska et al., 2012; Maurage et al., 2008; Riwkes, Goldstein, & Gilboa-Schechtman, 2015). However, the present findings do not necessarily contradict previous research. Given the close association between ELS and adult depression (Kessler et al., 2010), and the over-representation of people with ELS in clinical samples (Alvarez et al., 2011; Negele et al., 2015; Teicher & Samson, 2016), it is likely that the depressed groups in these studies experienced higher levels of ELS than the control groups. As these studies did not control for ELS, the depressed groups might show both a potentiation of N170 amplitudes (associated with depression scores), and a

blunting of N170 amplitudes (associated with ELS scores). As a result, the two factors (depression and ELS) could 'cancel each other out', giving the impression that depression had no effect on the N170 response to emotional facial expressions. Though speculative, this explanation is supported by the fact that a study by Noll et al. (2012), which did control for ELS (via the exclusion of individuals who reported experiencing current or historical trauma), found that depression scores were associated with increased N170 amplitudes to images of infants displaying emotional facial expressions.

Whilst depression scores were associated with potentiated N170 amplitudes, anxiety scores were associated with blunted N170 amplitudes. This relationship between higher anxiety scores and reduced N170 amplitudes in response to emotional facial expressions is not supported by previous research, which has typically found no effects of anxiety on the N170 response to emotional facial expressions (Aarts & Pourtois, 2012; Morel et al., 2014; Rossignol, Philippot, Douilliez, Crommelinck, & Campanella, 2005; Walentowska & Wronka, 2012; Yoon et al., 2016). However, despite the positive association between anxiety and depression (Brown, Campbell, Lehman, Grisham, & Mancill, 2001), only one of the five studies (Yoon et al., 2016) controlled for depression scores in their analyses. Therefore, the failure of the other four studies to find an effect of anxiety may have been due to the potentiating effect of depression on the N170 'cancelling out' the blunting effect of anxiety on the N170.

The discrepancy between the present findings and those of Yoon et al. (2016), who did control for depression when examining the effect of anxiety on the N170 response to emotional facial expressions, may be due to differences in the samples used; whereas the present study recruited participants with no diagnoses of mental illness, Yoon et al. (2016) compared healthy controls to participants with diagnosed anxiety conditions. All participants in the anxiety group were taking anti-depressant medication, and the sample was heterogeneous in terms of the conditions experienced, such that it included people with panic disorder, generalised anxiety disorder and post-traumatic stress disorder (PTSD). Both of these factors could have reduced the likelihood of finding an effect of anxiety on the N170 response to emotional facial expressions.

The discrepancy between the findings of the aforementioned studies and the present findings may also be related to the paradigms that were used. In the present study participants were required to make a response if they saw an image of a house, but not if they saw an image of a facial expression. In contrast, two of the previous studies required participants to make a judgement about the facial expression depicted (Morel et al., 2014; Rossignol et al., 2005), and a further study used facial expressions as feedback in a go/no-go task (Aarts & Pourtois, 2012). In these paradigms the facial stimuli took on task-specific salience. Indeed, it is known that the N170 response to a stimulus can be modulated by pairing the stimulus with a specific outcome (Levita et al., 2015), and is therefore subject to task-specific influences. It is possible that the effect of anxiety on the N170 to facial expressions is only present when the facial expressions are presented as passive stimuli which do not have any additional task-specific salience. However, this explanation is not supported by the two remaining aforementioned studies, which did not find an effect of anxiety on the N170 despite using passive-viewing paradigms.

Another difference between the present study and the previous studies concerns the presentation time of the stimuli. In the present study the stimuli were presented for 200 ms, a substantially longer period of time than the presentation time of 16 ms used by one of the five aforementioned studies (Walentowska & Wronka, 2012), and a substantially shorter period of time than the presentation times of 500 ms and 1000 ms used by the remaining four studies (Yoon et al., 2016; Aarts & Purtois, 2012; Rossignol et al., 2015; Morel et al., 2014). Previous research has shown that at the behavioural level, negative facial expressions which are presented for 200ms are rated as more negative than those presented for 500ms (Vassilopoulos, 2011), and attentional bias for fearful faces is modulated by stimulus duration (Leung, Drevets, Furey, & Mah, 2010). It is therefore possible that the effect of anxiety on the N170 differs according to the length of time that the facial expression is presented.

4.4.3. Study limitations and future directions

The present study had a number of limitations. Firstly, whilst none of the participants had received a diagnosis of a mental health condition (as measured by self-report), some of them did score highly on questionnaire measures of anxiety and depression, and therefore it cannot be assumed that the sample as a whole were entirely free of mental health problems. This limitation is discussed in detail in § 6.4.1.3. In addition, the present study may have been limited by its sample size. For example, whilst the regression model was unable to predict a significant amount of variance in the left hemisphere N170 peak amplitude to male happy facial expressions, there were the beginnings of a trend towards significance (p = .12), and the pattern of effects across the beta weights was comparable to the pattern observed in the beta weights of the other, significant, regression analyses (i.e. negative beta weights for depression and positive beta weights for anxiety and ELS). Therefore, it is possible that the regression model would have explained a significant amount of variance in the N170 peak amplitude to male happy facial expressions had the analysis included a greater number of participants.

There were also limitations within the pre-processing of the EEG data. The use of both artefact rejection (removal of epochs containing blinks within 200 ms post stimulus onset) and artefact correction (removal of ICA components representing ocular artefacts) was unnecessary; only one or the other was required. In addition, the output produced by the ICA decomposition in the present research was unclear for two reasons: firstly, 'bad' or noisy portions of data were not removed prior to the running of the ICA (Luck, 2014), and secondly the high pass filter that was used (0.1 Hz) was unsuitable for ICA decomposition. A high pass filter of 1 Hz is more appropriate in cases where ICA is applied to the data (Winkler, Debener, Müller & Tangermann, 2015). In light of this, any future research which uses this paradigm should use either artefact rejection or artefact correction, rather than both procedures. If ICA is used to correct for artefacts, it should be preceded by the removal of bad portions of data and the application of a high pass filter set to 1 Hz.

Similarly, visual examination of the grand average waveforms (Figures 4.6 to 4.17) revealed a possible effect of ELS group on the peak amplitude of the P1 component. However, analyses of the P1 peak amplitudes did not reveal any significant differences between the groups. It is possible that a significant effect of ELS group on the P1 might emerge if a larger group of participants was recruited. Future work with more participants could examine this possibility whilst also seeking to validate the present finding of a significant effect of ELS on the peak amplitude of the left hemisphere N170 response to emotional facial expressions.

It is important to acknowledge that the analytical methods used in the present study were not capable of partialling out any effects of the P1 component on the N170 component. That is, it remains unclear whether the blunted N170 component seen in the high ELS group was influenced by the presence of higher P1 peaks within this group. One way to examine this further would be to use ICA to extract components representing the P1 and the N170. As discussed above, the parameters used in the processing of the present data were not well suited to the use of ICA. As a consequence, the ICA components produced were noisy, and rarely represented a single neural component (such as the P1). Re-processing the data using appropriate removal of noise prior to running ICA could allow for the identification of individual neural components. This in turn would help to clarify whether the P1 was influencing the amplitude of the N170, or whether the ELS group differences in the N170 occurred independently of any possible group differences in the P1.

One strength of the present study was its focus on the investigation of a priori hypotheses that were based on the small amount of previous research available. However, given the rich nature of the data that were acquired during the present research, other more exploratory analytical approaches could have led to additional findings of interest. The effects of ELS on the brain are complex and wide-ranging, and it is possible that by focusing on early perceptual ERPs, higher-order differences between the two ELS groups may have been missed. For example, as discussed in § 1.2.2.4, previous work has found effects of ELS on the P3b component (Pollak et al., 2001; Shackman & Pollak, 2014; Shackman et al., 2007),

which occurs after 350 ms and is thought to represent allocation of attention (Nelson & McCleery, 2008). Indeed, visual examination of the waveforms depicted in the present chapter suggests that there could be group differences in later processes. This is particularly evident around 250 – 350 ms in the grand average responses to the happy facial expressions, and from approximately 400 ms in the grand average responses to all the emotional expressions presented. Further investigation of these possible group differences could yield additional findings of interest.

The study presented in this chapter used a passive task to measure the N170 response to emotional facial expressions. It therefore remains unclear whether similar effects of ELS would be seen in an active paradigm, for example, during a task in which participants make a button press to indicate the gender of the face. This work would be particularly interesting as it could begin to address the question of whether the present finding of a relationship between ELS and blunted N170 responses to emotional facial expressions represents a general ELS-related change in emotional face processing that occurs across different experimental contexts, or alternatively whether the effect of ELS on the N170 is selectively related to the passive viewing of emotional facial expressions.

4.4.4. Conclusions

The current study examined the effect of ELS on young adults' N170 responses to male and female angry, happy and neutral facial expressions. Relative to participants in the low ELS group, participants in the high ELS group showed blunted left hemisphere N170 peak amplitudes to angry, happy and neutral facial expressions. These findings suggest that even in young adults with no diagnosed mental health problems, past experiences of ELS may influence early neural processing of important social-emotional cues.

Chapter 5. Early life stress is not related to responses to learned danger signals during active or passive avoidance

Abstract

Work with animals suggests that ELS is associated with alterations in avoidance learning and behaviour. However, very few studies have investigated whether humans who have experienced ELS also show changes in avoidance learning and behaviour. To that end, the present study used EEG to examine early perceptual responses to warning stimuli during an active and passive avoidance task. In this task, participants with high or low levels of ELS were required to either emit or omit a response in order to avoid an aversive outcome. Fifty-two female participants aged 18 to 25 (*M* = 19.85 years) with no past or present diagnoses of mental health problems took part in the study. It was found that, in the left hemisphere, the N170 ERP component was potentiated to the warning stimuli relative to the control stimuli, but this effect was not modulated by ELS. However, higher depression scores were associated with greater learning-dependent potentiation of the N170 over the right hemisphere during active but not passive avoidance. These findings could suggest that ELS is not associated with alterations in processing of non-social danger signals during active or passive avoidance in human participants. Alternatively, the lack of ELS-related alterations in the present study could be explained by the absence of extreme levels of ELS in the sample of individuals who took part.

5.1. Introduction

This doctoral thesis focusses on two neurocognitive mechanisms which may be altered in adults who experienced high levels of ELS: emotional face processing and avoidance of threat. The study presented in this chapter focussed on the latter of these two mechanisms, avoidance of threat, building on the findings of the first study (Chapter 3) which showed that high levels of ELS were associated with atypical avoidance of social cues of threat (angry facial expressions). The findings presented in Chapter 3 suggest that avoidance responding may be altered in young adults who experienced high levels of ELS. However, it remains unclear whether this altered pattern of avoidance is specific to social cues of threat (angry facial expressions), or whether it reflects atypical avoidance of threat in general. Furthermore, as the study presented in Chapter 3 was behavioural, such that participants were required to indicate how much they would approach or avoid the angry facial expressions, it was not possible to determine whether the observed effects were related to changes in relatively early, implicit processing of the threatening stimuli or in later, explicit processing of these stimuli (§ 2.1.2). Indeed, the focus on behavioural and fMRI paradigms in the broader ELS literature means that very little is known about how ELS affects the time course of neural responding to specific stimuli. Clarification of which levels of processing are most affected by ELS is important not just for expanding our knowledge of the effects of ELS, but also for informing interventions which aim to reduce the risk of mental illness in those who experienced high levels of ELS (§ 1.2.2.3).

In light of these considerations, the present EEG study examined early perceptual responses, as measured by the N170 ERP component, to non-social learned cues of threat in adults with high or low levels of ELS using a previously validated active and passive avoidance task (Levita et al., 2012; Levita et al., 2015). As discussed in § 1.4.1, theories suggest that avoidance learning involves two stages: classical fear conditioning and instrumental responding (Krypotos et al., 2015). Work with rats has found that ELS is associated with changes in both of these associative learning processes (Kosten et al., 2012). Specifically, ELS has been frequently associated with abnormal classical fear conditioning in rats, though the

direction of the effects varies across studies, with reports of both enhanced and reduced classical fear conditioning (§1.4.5.2; Kosten et al., 2006; Kosten et al., 2005; Lehmann et al., 1999; Quinn et al., 2014).

The instrumental learning stage of avoidance responding can involve two different types of action; active or passive. In active avoidance the animal must make a response to the warning stimulus in order to avoid an aversive outcome (unconditioned stimulus, US), and in passive avoidance the animal must withhold a response to the warning stimulus in order to avoid an aversive outcome (US). Numerous studies have found that adult rats which experienced ELS show greater active avoidance responses to a warning stimulus which has been associated with an aversive US (Section 1.4.5.3; Abraham & Gruss, 2010; Catalani et al., 2002; Catalani et al., 2000; Nunez et al., 1995; Pryce et al., 2003; Rio-Alamos et al., 2015; Rio-Alamos et al., 2017; Schable et al., 2007). However, it is important to note that there is also evidence for a relationship between ELS and a reduction in the number of active avoidance responses made to a warning stimulus (Toth et al., 2008; Weiss et al., 2001). In contrast, the relationship between ELS and passive avoidance appears, at least from the existing literature, to be more consistent (Kosten et al., 2012). Specifically, passive avoidance has been found to be impaired in rats which experience ELS, as indicated by shorter latencies to enter an environment that has been previously paired with an aversive US (Section 1.4.6.5; Benetti et al., 2012; Benetti et al., 2015; Kosten, Karanian, et al., 2007; Kosten et al., 2012; Kosten, Lee, et al., 2007; Mello et al., 2009; Neves et al., 2015; Vivinetto et al., 2013; Zugno et al., 2013). In other words, compared to rats without experience of ELS, rats which have experienced ELS spend less time withholding a response to a warning stimulus which predicts an aversive outcome (US).

Whilst the relationship between ELS and avoidance learning has received attention in non-human animal work, there has been little investigation of this relationship in the human literature. This is surprising, given that avoidance of danger is thought to play a key role in the development of hyper-sensitivity to anger in children who have been abused (Pollak et al., 2009). In addition, brain regions involved in avoidance learning, such as the striatum and the amygdala (Levita et al., 2012), have

been found to show altered activation in people who experienced ELS (Dannlowski et al., 2012; Dillon et al., 2009; van Harmelen et al., 2013). Studies which have examined skin conductance responses (SCRs), a physiological measure of emotional arousal, have found that experience of trauma during childhood or adulthood may be associated with enhanced SCRs during fear conditioning (Bremner et al., 2005; Cacciaglia et al., 2017). Given that classical fear conditioning is thought to be an important component of avoidance learning, this provides some evidence for the possibility of a relationship between ELS and changes in avoidance learning.

It is important to acknowledge that a small body of work has examined the relationship between ELS and attentional avoidance using attentional bias paradigms (§ 1.3.1). However, findings from these studies are inconsistent, with some reporting a relationship between high levels of ELS and attentional bias away from angry facial expressions (attentional avoidance; Kelly et al., 2015; Pine et al., 2005) and others reporting a relationship between high levels of ELS and attentional bias towards angry facial expressions (Gibb et al., 2009; Pollak & Tolley-Schell, 2003). Furthermore, these findings do not have direct relevance to the present work as attentional bias paradigms are designed to examine participants' pre-existing stimulus-response associations (such as biases towards or away from facial expressions), whilst the present study was designed to examine new learning about novel warning stimuli.

The present study is the first, to the author's knowledge, to investigate the effect of ELS on avoidance learning and behaviour in human participants. The study employed a previously validated paradigm (Levita et al., 2012; Levita et al., 2015) in which participants learn to make (active avoidance) or withhold (passive avoidance) a response in order to avoid an aversive outcome, a loud tone. The task involved the presentation of two warning stimuli which were associated with the aversive outcome, and two control stimuli which were never associated with the aversive outcome. Participants could avoid the aversive outcome by making a response (button press) to one of the warning stimuli (the active warning stimulus) and withholding a button press response to the other warning stimulus (the

passive warning stimulus). Participants were also required to either make or withhold a response to the active and passive control stimuli, but in this case, there was no aversive outcome, even if the participant made an incorrect response. The inclusion of two control stimuli with the same response contingencies as the two warning stimuli was necessary in order to ensure that any neural changes associated with differences in active and passive avoidance of threat could not simply be attributed to differences in the neural mechanisms underlying the emission or omission of a response. A recent EEG study using this paradigm found significant potentiation of an early visual response, as measured by the N170 component, to the warning stimuli (learned danger signals) compared to the control stimuli (Levita et al., 2015).

Following on from that study, the present study was designed to examine whether learning-dependent potentiation to learned danger cues, as measured by greater N170 peak amplitudes to warning stimuli (relative to control stimuli) in an active and passive avoidance task, is altered in individuals with high levels of ELS. In doing so, this study aimed to examine whether human participants would show ELS-related alterations in their avoidance of danger signals, an effect which has been widely reported in rat models of ELS (§ 1.4.5). In previous work, potentiation of the N170 to a warning stimulus occurred irrespective of whether this stimulus required an active or passive avoidance response (Levita et al., 2015). However, as discussed above and in § 1.4.5.3, work with rats has shown that ELS may have differential effects depending upon the type of avoidance required; specifically, experience of ELS in rats has been frequently associated with increased active avoidance (Abraham & Gruss, 2010; Nunez et al., 1995; Pryce et al., 2003; though see Toth et al., 2008), yet studies of passive avoidance have generally found reduced passive avoidance in rats which experienced ELS (Kosten, Karanian, et al., 2007; Neves et al., 2015; Vivinetto et al., 2013). Therefore, it was tentatively predicted that the effect of ELS on the potentiation of the N170 would vary depending upon the type of avoidance (active or passive) that was required. Specifically, it was predicted that, relative to the low ELS group, participants in the high ELS group would show greater learning-dependent potentiation of the N170 to

the active warning stimulus, and reduced learning-dependent potentiation of the N170 to the passive warning stimulus.

5.2. Method

5.2.1. Participants

Participants in the present study were taken from the sample described in Chapter 4. All individuals who participated in the study reported in Chapter 4 also participated in the present study. Recruitment of these participants is described in detail in § 4.2.1 and in § 2.2.1.2. Briefly, women aged 18 to 25 with no history of mental illness who scored either below 16 ('low' ELS group) or above 24 ('high' ELS group) on the CATS (Sanders & Becker-Lausen, 1995) were invited to take part in the study. Sixty-two participants met the screening criteria and took part in the study. All participants provided informed consent prior to data collection. Due to a problem with the EEG recording, one participant did not have any useable EEG data, and was not included in the analyses. An additional eight participants were excluded from the analyses as it was not possible to obtain a peak amplitude measurement for the N170 in at least one condition, and one participant was excluded because, by chance, they were never exposed to the aversive tone (all their (non) responses to the warning stimuli were accurate). Five of the excluded participants were in the low ELS group and five were in the high ELS group. The final sample was comprised of 52 participants, with 23 in the low ELS group and 29 in the high ELS group. As expected, the high ELS group (M = 42.34, SD = 12.26) had significantly higher CATS scores than the low ELS group (M = 10.43, SD = 2.69; U = 0.00, $p < .001$). Means, standard deviations, medians and ranges for each of the demographic and psychological variables are presented in Table 5.1.

Table 5.1

Means, standard deviations (in parentheses), medians (in italics), range [in square brackets] and comparisons between ELS groups on mental health and psychological variables

Variable	All participants (*n* = 52)	Low ELS (*n* = 23)	High ELS (*n* = 29)	Difference between ELS groups, *p* value
CATS	28.23 (18.49) *28.00* [5-70]	10.43 (2.69) *11.00* [5-15]	42.34 (12.26) *41.00* [25-70]	< .001***
Age	19.85 (2.20) *19.00* [18-25]	19.00 (1.62) *18.00* [18-23]	20.52 (2.39) *20.00* [18-25]	.02*
Mental health variables				
HADS_A	8.42 (3.26) *8.00* [4-20]	7.83 (3.60) *7.00* [4-20]	8.90 (2.94) *9.00* [4-14]	.11
HADS_D	3.75 (2.74) *3.00* [0-10]	3.13 (2.82) *2.00* [0-10]	4.24 (2.61) *4.00* [0-10]	.07
STAI_S	40.06 (12.01) *38.50* [22-71]	37.09 (12.71) *37.00* [22-71]	42.41 (11.08) *47.00* [22-57]	.07
STAI_T	46.06 (10.41) *45.00* [28-70]	42.04 (10.16) *40.00* [28-66]	49.24 (9.62) *50.00* [31-70]	.01*
BDI	12.58 (7.98) *11.50* [1-31]	9.48 (6.22) *8.00* [1-26]	15.03 (8.46) *15.00* [1-31]	.02*
BAI	12.94 (8.43) *13.00* [0-35]	11.00 (7.51) *9.00* [0-27]	14.48 (8.93) *13.00* [0-35]	.18
Psychological variables				
SPSRQ: Punishment	14.08 (5.06) *15.00* [4-24]	12.78 (5.08) *12.00* [4-22]	15.10 (4.89) *16.00* [5-24]	.09
SPSRQ: Reward	10.06 (3.85) *10.00* [2-19]	9.96 (2.95) *10.00* [2-14]	10.14 (4.49) *10.00* [3-19]	.90
BAS: Drive	10.50 (2.14) *11.00* [6-15]	10.61 (1.99) *11.00* [6-14]	10.41 (2.28) *10.00* [6-15]	.56
BAS: Fun seeking	11.81 (2.21) *12.00* [8-15]	11.61 (2.04) *12.00* [8-15]	11.97 (2.35) *12.00* [8-15]	.58
BAS: Reward	16.77 (2.09) *17.00* [11-20]	17.04 (1.49) *17.00* [14-19]	16.55 (2.47) *16.00* [11-20]	.63

Variable	All participants (n = 52)	Low ELS (n = 23)	High ELS (n = 29)	Difference between ELS groups, p value
BIS	23.33 (3.22) *24.00* [15-28]	22.74 (3.41) *23.00* [15-28]	23.79 (3.03) *25.00* [16-28]	.19
PDS: Total	9.50 (3.97) *9.00* [1-19]	11.22 (3.92) *11.00* [5-19]	8.14 (3.51) *9.00* [1-14]	.01*
PDS: SDE	1.44 (1.64) *1.00* [0-6]	1.87 (1.89) *2.00* [0-6]	1.10 (1.35) *0.00* [0-4]	.15
PDS: IM	8.06 (3.39) *8.00* [1-16]	9.35 (3.10) *9.00* [4-16]	7.03 (3.31) *7.00* [1-14]	.01*

Note. CATS = Child Abuse and Trauma Scale; HADS-A = Hospital Anxiety and Depression Scale – Anxiety; HADS-D = Hospital Anxiety and Depression Scale – Depression; STAI-S = State Trait Anxiety Inventory – State; STAI-T = State Trait Anxiety Inventory – Trait; BDI-II = Beck Depression Inventory II; BAI = Beck Anxiety Inventory; SPSRQ = Sensitivity to Punishment and Reward Questionnaire; BAS = Behavioral Activation Scale; BIS = Behavioral Inhibition Scale; PDS: Total = Paulhus Deception Scales; PDS: SDE = Paulhus Deception Scales: Self-deceptive enhancement; PDS: IM = Paulhus Deception Scales: Impression Management. *p < .05 after correction for multiple comparisons using Benjamini-Hochberg procedure with an FDR threshold of 0.1 (16 comparisons including age, but excluding CATS, as difference scores between groups on this measure were built into the design of the study).

5.2.2. General procedure

The study received ethical approval from the Department of Psychology Ethics Committee, University of Sheffield (#1104). Participants who met the screening criteria were invited to take part in the study. After providing informed consent, participants were asked to fill in a number of questionnaires online. The order of the questionnaires was counterbalanced across participants. Details of these questionnaires can be found in § 5.2.3, and in § 2.4. After completing the questionnaires in their own time, participants attended the University of Sheffield for the EEG recording session. After once again providing informed consent, participants were connected up to the EEG system. See § 2.2.2 for full details of the EEG apparatus and recording. Once the EEG signal was stable, participants performed two separate experimental tasks. The order of the tasks was counterbalanced across participants. These tasks were an emotional face processing task (Chapter 4), and an active and passive avoidance task, discussed below. Following completion of these tasks, the EEG cap was removed and the participant was directed to a different room in which they were asked to complete three additional questionnaires. Again the order of the questionnaires was counterbalanced across participants.

5.2.3. Questionnaires

Questionnaires were presented using Qualtrics survey software (www.qualtrics.com). Participants completed a battery of questionnaires: the Child Abuse and Trauma Scale (CATS; Kent & Waller, 1998; Sanders & Becker-Lausen, 1995), the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983), the Beck Depression Inventory (BDI-II; Beck et al., 1996), the Beck Anxiety Inventory (BAI; Beck et al., 1988), the State-Trait Anxiety Inventory (STAI; Spielberger et al., 1983), the Sensitivity to Punishment/Sensitivity to Reward Questionnaire (SPSRQ; Torrubia et al., 2001), the Behavioural Inhibition System/Behavioural Activation System scales (BIS/BAS; Carver & White, 1994), and the Paulhus Deception Scales (PDS; Paulhus, 1998). Full details of these questionnaires and the conditions under which they were completed can be found in Chapter 2. Means, standard deviations, medians, ranges and

comparisons between the two ELS groups for scores on these questionnaire measures are reported in Table 5.1. A number of variables were non-normally distributed. Therefore, Mann-Whitney-U tests were used to examine group differences on the variables of interest.

5.2.4. Active and passive avoidance task

5.2.4.1. Stimuli

Four 'Greeble'-like images (Figure 5.1), which have been used with this task in previous studies, were presented as stimuli in the present study (Howsley & Levita, 2017; Levita et al., 2012; Levita et al., 2015). The stimuli were created by Scott Yu, and provided courtesy of Michael J. Tarr, Center for the Neural Basis of Cognition and Department of Psychology, Carnegie Mellon University (www.tarrlab.org). Each of the four stimuli was presented 76 times across the course of the experiment, resulting in a total of 304 stimulus presentations. The experiment was divided into four blocks of equal length with 19 presentations of each stimulus in each block. Stimuli were presented in a pseudorandom order.

Condition	Active avoid	Passive avoid	Control go	Control no-go
Stimulus				
	Active warning stimulus (learned danger signal)	Passive warning stimulus (learned danger signal)	Active control stimulus	Passive control stimulus
Response contingency	Emit action	Omit action	Emit action	Omit action
Outcome contingency	Aversive tone	Aversive tone	No outcome	No outcome

Figure 5.1. Stimulus contingencies for the active and passive avoidance task. This figure depicts one version of the task. In the full experiment, the contingencies for each condition remained the same but the 'Greeble' stimulus used for each condition was counterbalanced across participants.

5.2.4.2. Procedure

5.2.4.2.1. Participant instructions

The task began with instruction screens, which participants read at their own pace, pressing the space bar to move on to the next screen. The instruction screens showed an image of the two warning stimuli and informed participants that these stimuli were always followed by a loud sound. The instructions also informed the participants that they could avoid the aversive outcome by making or withholding a button press, and that they would have to learn by trial and error which stimulus required which response. Next, participants were presented with a screen showing the two control stimuli, and were informed that these stimuli were never followed by the loud sound, but that they were presented in order to ensure that the participants were paying attention. They were then shown which control stimulus required them to make a button press, and which control stimulus required them to withhold a button press. Participants were then presented with an illustration of the structure of the trial, which encompassed a stimulus, followed by a white cross, followed by a yellow cross, and finally another white cross. Participants were instructed to make or withhold their response when the yellow cross was presented.

5.2.4.2.2. Practice block

The instructions for the task were followed by a practice block. The practice block was designed to allow the participants to learn (by trial and error) which of the warning stimuli were associated with the aversive tone (outcome contingencies), and which response was required for each stimulus (response contingencies). Each practice block contained one presentation of each of the four stimuli (the two warning stimuli and the two control stimuli). If the participant responded incorrectly to more than one of the four stimuli, the practice block was automatically repeated. If the participant responded correctly to three or more of the four stimuli the practice block ended. Once a practice block had ended, the experimenter presented the participant with pictures of the four stimuli (printed on paper) and asked them to report the outcome and response contingencies for these four stimuli. If the participant was not confident in their knowledge of the

outcome and response contingencies, the practice block was repeated. The experimenter then spoke to the participant again and asked them to report the contingencies. This process was repeated until the participant was able to report the correct outcome and response contingencies for all of the four stimuli.

5.2.4.2.3. Experimental block

After the practice block, participants began the experimental task (Figure 5.2). The experimental task consisted of four blocks, each of which contained 76 trials and lasted approximately seven and a half minutes. In between blocks, participants were allowed to take a break. The break lasted until the participant pressed the space bar to continue the experiment. Each trial began with a white fixation cross presented for 1500 ms. This was then followed by the presentation of either a warning or control stimulus for 1000 ms. After this, the white fixation cross was presented for 1000 ms, followed by a yellow target cross for 1000 ms. The trial ended with the presentation of the white fixation cross for 1000 ms. All stimuli were presented on a black background. During the presentation of the yellow target cross participants were required to either make or withhold a response. If an incorrect response was made to the yellow cross which followed a warning stimulus, the loud aversive tone was presented (1000 ms). The tone was played at the same time as the presentation of the final white fixation cross. In control trials, and in experimental trials in which the participant correctly made or withheld a response, the white fixation cross was presented for 1000 ms (without simultaneous presentation of the aversive tone).

Despite the fact that the experimenter ensured that the participant could report the response contingencies verbally before the experimental trials began, a small number of participants showed a pattern of continuous incorrect responding to one or both of the control stimuli. This was unexpected given that it did not occur in previous studies that used this task (Levita et al., 2012; Levita et al., 2015). It is possible that the difficulty experienced by a small number of participants in the present study was an unexpected consequence of the decision to modify the paradigm so that all

the stimuli were yellow. In previous work, the control go stimulus was green and the control no-go stimulus was red. As the control stimuli in the present research could no longer be distinguished by colour, and given that they were never followed by the loud tone (even if the participant's response was incorrect), participants who made this error did not realise that their responding was inaccurate. On the rare occasions that a participant did make this error, the experimenter reminded them of the correct contingencies.

5.2.4.2.4. Aversion ratings and contingency awareness

After completion of the task, participants were asked to fill in a paper form (check-sheet) which contained a series of questions (Appendix B). The first question asked participants to indicate how aversive they found the loud sound by making a mark on a 10 cm line which ranged from 'Not at all aversive' to 'Very aversive'. Once the participant had marked the line, the distance from the start of the line was measured. The maximum score was 10 and the minimum score was 0. Mean aversion ratings for each ELS group are presented in § 5.3.1.1. After this, participants read a series of questions which were designed to determine whether they were aware of the outcome and response contingencies for the two warning stimuli (Appendix B). Participants were presented with an image of one of the warning stimuli and asked to respond in writing to three questions. These questions were: (1) 'Was this character ever followed by a loud sound?', (2) 'Could you avoid it?' and (3) 'If you could avoid it what action did you take?'. The same three questions were asked two times, once in relation to the active warning stimulus and once in relation to the passive warning stimulus. The order in which the stimuli were presented on the check-sheet was counterbalanced between participants.

Participants' written responses to these questions were examined. Note that the numbers presented in this paragraph refer to the sample of participants whose EEG data were included in the analyses (n = 52; § 5.2.1). Regarding the first question, 'Was this character ever followed by a loud sound?', two participants responded incorrectly for both warning stimuli (active and passive), one participant responded incorrectly to the warning

stimulus in the active avoid condition but correctly to the warning stimulus in the passive avoid condition, and 10 participants responded incorrectly to the warning stimulus in the passive avoid condition but correctly to the warning stimulus in the active avoid condition. The remaining 39 participants responded correctly to both warning stimuli (i.e., correctly stated that both warning stimuli were followed by the loud sound). Regarding question 2, 'Could you avoid it?', two participants responded inaccurately in relation to one of the warning stimuli, and the remaining 50 participants responded correctly in relation to both warning stimuli. Regarding Question 3, 'If you could avoid it what action did you take?' all but one of the participants responded accurately to both warning stimuli, such that they correctly identified which warning stimulus required a response and which did not.

Given that the aversive tone only occurred if a participant made an incorrect response, and given that the accuracy rates across the experimental blocks were very high (mean accuracy rates were 97.8 % in the active avoid condition and 99.1 % in the passive avoid condition), most presentations of the warning stimuli were not actually followed by the aversive tone. In light of this, it is possible that some of the participants who gave an incorrect response to Question 1, 'Was this character ever followed by a loud sound?', did so because they interpreted the question as asking whether the loud sound *actually did* occur following the given warning stimulus, rather than whether the loud sound *could* occur following this warning stimulus. Therefore, as it was not possible on the basis of their answers to determine whether a given participant was aware of the outcome contingencies or not, it was decided that participants would not be excluded from further analyses due to the presence of an incorrect response on the check-sheet.

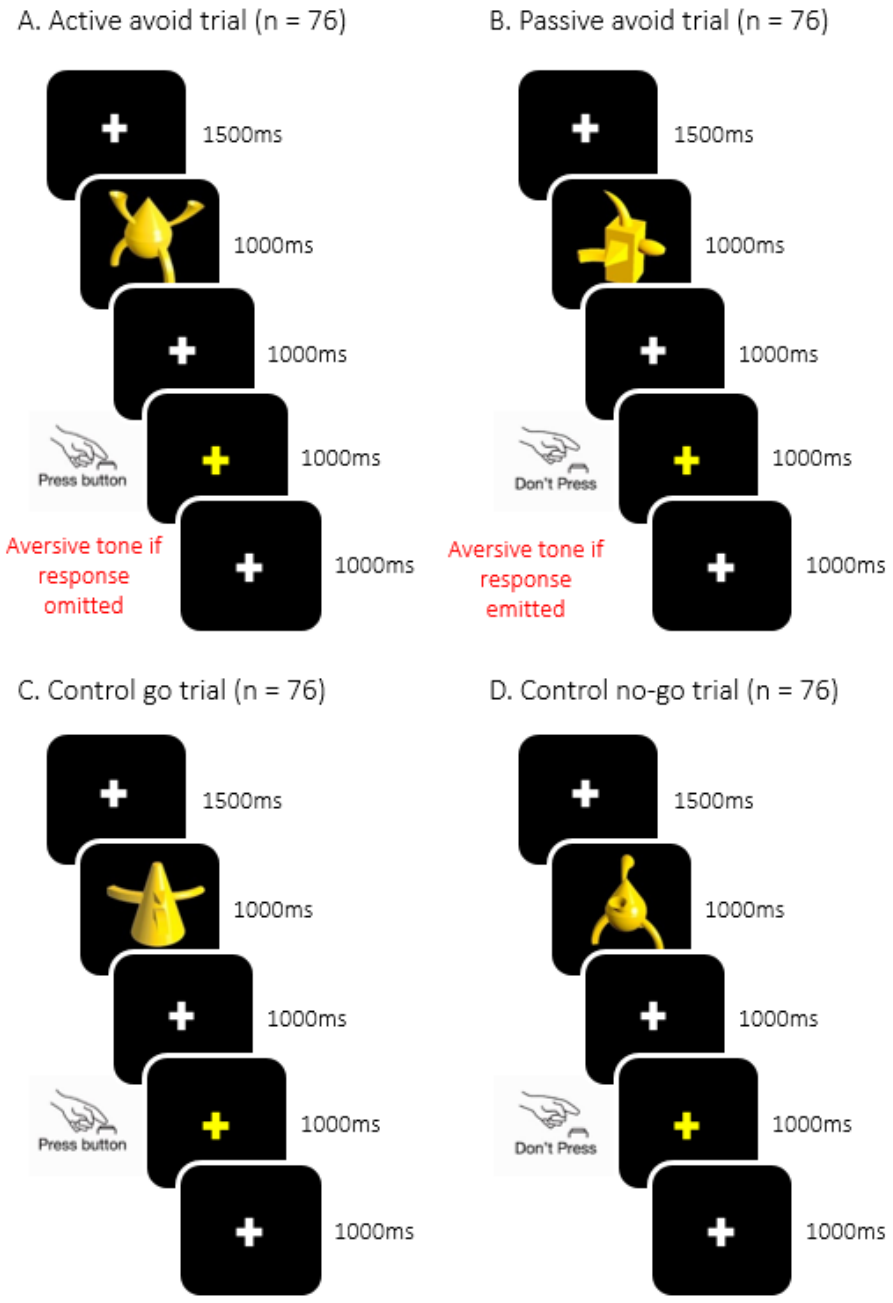

Figure 5.2. Structure of the trials in the active and passive avoidance task. During the task participants were presented with 'Greeble' stimuli. Two of these stimuli (A and B) were warning stimuli associated with an aversive outcome, whilst the other two (C and D) were control stimuli which were not associated with an aversive outcome. Participants were informed that they could learn to avoid the aversive outcome by either making or withholding a response (button press) when they saw the warning stimuli. Participants were informed that the control stimuli would never be associated with an aversive outcome, but that they should make a key press to the control stimulus depicted in C and withhold a key press to the control stimulus depicted in D. Participants were required to respond when they saw the yellow cross, rather than when they saw the stimulus itself.

5.2.5. Apparatus

Full details of the apparatus used in the current experiment are reported in § 2.2.2.1.

5.2.6. EEG recording

The procedure for the EEG recording is reported in § 2.2.2.2.

5.2.7. EEG pre-processing

Only data from the experimental blocks (and not from the practice block) were included in analyses. Incorrect trials were excluded from the analyses. Pre-processing of the EEG data is described in detail in § 2.2.3. Briefly, the EEG pre-processing consisted of: removing trials in which a blink occurred during the first 200 ms post stimulus-onset, referencing the data to Cz, filtering the EEG data from 0.1 Hz to 30 Hz, dividing the data into epochs from -200 ms pre-stimulus presentation to 800 ms post-stimulus presentation, removing bad channels, performing ICA and removing components representing blinks and lateral eye movements, performing baseline correction of the data, and finally removing epochs containing voltage fluctuations greater than +/- 150 μV.

The total number of trials in each condition was 76. The mean number of trials excluded during EEG pre-processing in each condition was as follows: active avoid (M = 6.95, SD = 6.18), passive avoid (M = 7.61, SD = 6.54), control go (M = 7.30, SD = 6.33), control no-go (M = 7.48, SD = 6.47).

Once the data had been pre-processed, grand average waveforms were generated for each participant in each task condition. The event to which the epochs were locked was the onset of the warning or control stimulus. The N170 component was examined over left and right occipital-temporal regions. Specifically, an average of the signal from P7 and P9 was taken from over left hemisphere, and an average of the signal from the corresponding right-hemisphere electrodes, P8 and P10, was taken from over the right hemisphere. Following this, the peak amplitude of the N170 was measured (ERPLAB) over each hemisphere and in each task condition.

Full details regarding the measurement of the N170 peak amplitudes can be found in § 2.2.4.

5.2.8. Statistical analysis

5.2.8.1. Analysis of behavioural data

Prior to analysis of the EEG data, the behavioural data were analysed in order to determine whether there were any behavioural differences between the low and high ELS groups in either how aversive they found the aversive tone, or in their task performance as measured by their error scores and reaction times. As the data were not normally distributed, Mann Whitney-U tests were used to examine whether the two ELS groups differed on their self-reported aversion to the tone. Mann-Whitney U tests were also used to examine the difference between the two ELS groups in the total number of errors and the number of errors by task condition. Two repeated measures ANOVAs, one per ELS group, were then used to determine whether the number of errors made differed between the four task conditions. Following this, reaction times in the two conditions which required a response, that is, the active avoidance condition and the control go condition, were examined. As the data were not normally distributed Mann Whitney-U tests were used to determine whether reaction times as a whole differed between the two ELS groups, and whether reaction times in each condition differed between the two ELS groups. Wilcoxon Signed Ranks analyses were then used to examine whether reaction times differed between the active and control conditions within either the low ELS group or the high ELS group. Faster reaction times in the active condition relative to the control go condition would indicate that the participants were more avoidant of the active warning stimulus (which was associated with the aversive outcome) than the active control stimulus (which was not associated with the aversive outcome).

5.2.8.2. Analysis of N170 peak amplitudes using Analysis of Variance (ANOVA)

In order to investigate the effect of ELS on the potentiation of early sensory processing of danger signals, differences in the N170 amplitude

across the four task conditions and between the two ELS groups were examined using a mixed model ANOVA. This ANOVA had three within-subject factors: Laterality (left hemisphere (P7 and P9) vs. right hemisphere (P8 and P10), Response (button press vs. no button press) and Danger (warning stimuli vs. control stimuli), and one between-groups factor: ELS group (high vs. low).

5.2.8.3. Analysis of N170 peak amplitudes using hierarchical regression

The use of an ANOVA allowed for comparison between the current findings and previous work which used the same paradigm (Levita et al., 2015). However, as discussed throughout this thesis, ELS is closely associated with anxiety and depression, and as a result analyses which examine the effect of ELS on neurocognitive processing should control for levels of anxiety and depression. In light of this, hierarchical regression analyses were also used to examine whether ELS was related to active or passive avoidance once the potential influence of anxiety and depression was taken into account. Specifically, hierarchical regression analyses were used to examine the effect of ELS on the difference between the N170 peak amplitude to the active and passive warning stimuli relative to their respective control stimuli. These analyses allowed for examination of the effect of ELS on the N170 response during active and passive avoidance processing once the impact of all other neural factors, such as those involved in the emission or omission of a motor action, were partialled out.

Hierarchical regression analyses were carried out separately for each hemisphere. This resulted in a total of four regression analyses. The same hierarchical regression model was used to predict each dependent variable. The model contained two steps, with the first step including all the control variables (age, PDS: Impression Management, BDI-II and STAI-T; for details on the selection of these control variables see § 5.2.8.4), and the second step including one categorical variable, ELS group. Regression models were considered to be significant if they retained significance after correction for multiple comparisons. Correction for multiple comparisons was carried out using the Benjamini-Hochberg procedure with an FDR

threshold of 0.1 (§ 2.3.1.1). Analyses within one hemisphere were considered to be one 'family' (i.e. the error rate was controlled separately for each hemisphere).

5.2.8.3.1. Selection of control variables

The two ELS groups differed in age and on a number of psychological measures (Table 5.1). In light of this, it was necessary to control for these variables within the regression analyses. To determine which of these variables should be included as control variables in the regression analyses, Mann-Whitney U tests were used to identify variables which differed significantly between the two groups. Variables which remained significant after correction for multiple comparisons were then selected for inclusion as independent variables in the first step of the hierarchical regression analysis. Correction for multiple comparisons was carried out using the Benjamini-Hochberg procedure with an FDR threshold of 0.1. The Benjamini-Hochberg correction procedure was chosen as a Bonferroni correction would be too conservative given the reasonably small sample size. After correction for multiple comparisons using this procedure, five variables emerged as significantly different between the two ELS groups: age, PDS: Total, PDS: Impression Management, BDI-II and STAI-T. Examination of the regression model showed that there was a high level of collinearity between two of the independent variables, PDS: Total and PDS: Impression Management. This was not surprising given that PDS: Impression Management is a subscale of the total PDS scale. In order to allow for comparisons between the results of the present analyses and the results of the hierarchical regression analyses computed in Chapter 4, PDS: Total score was removed from the regression model and PDS: Impression Management score was retained as an independent variable. This left a total of four independent variables which were entered into the regression model in Step 1: age, PDS: Impression Management, BDI-II and STAI-T.

5.3. Results

Three analysis strategies were used to examine the effect of ELS on active and passive avoidance. The first set of analyses examined behavioural avoidance responses in the two ELS groups during task performance (§ 5.3.1). The subsequent two analyses examined the effect of ELS on learning-dependent potentiation of the N170 to warning stimuli (learned danger signals). The first of these analyses used an ANOVA which allowed for comparison of the present data with previous research that used the same paradigm (Levita et al., 2015). The second of these analyses used hierarchical linear regression (§ 5.2.8.3). This allowed for examination of the effect of ELS group on potentiation of the N170 peak amplitude to learned danger signals whilst controlling for the effects of anxiety and depression. The scalp topography and time course of the N170 response to each stimulus for the high and low ELS groups are presented in § 5.3.2 and § 5.3.3, respectively.

5.3.1. High and low early life stress groups did not differ on how aversive they found the unconditioned stimulus or on task performance

5.3.1.1. Rating of the aversive unconditioned stimulus

After completion of the task participants received a paper rating scale on which they were asked to indicate how aversive they found the aversive tone (US) by making a mark on a 10 cm line which ranged from 'Not at all aversive' to 'Very aversive' (Appendix B). The maximum score was 10 and the minimum score was 0. The mean aversion score was 7.99 (SD = 1.63), indicating that the participants found the tone aversive. The high (M = 7.87, SD = 1.86) and low (M = 8.16, SD = 1.30) ELS groups did not differ on how aversive they perceived the tone to be (U = 306.00, p = .61).

5.3.1.2. Error rates

Participants' acquisition and performance of the task were assessed by examining the number of errors (unsuccessful avoidance of the aversive tone or incorrect responses to the control stimuli) they made during the task. The number of errors made across the task was low (Table 5.2). The low

ELS group made errors on only 1.43 % of trials (M = 4.35, SD = 4.03), whilst the high ELS group made errors on only 2.08 % of trials (M = 6.31, SD = 7.21). There was no significant difference between the two ELS groups on the total number of errors made during the experiment (U = 286.00, p = .38). Similarly, after correction for multiple comparisons, there were no significant differences between the low and high ELS groups for the number of errors made in any of the four task conditions (p values > .01).

Table 5.2

Means, standard deviations, medians and ranges for the number of errors made by the low and high ELS groups in each task condition

ELS group	**Errors**			
	Warning stimuli		**Control stimuli**	
	Active avoid	**Passive avoid**	**Control go**	**Control no-go**
Low	1.39 (1.53) *1.00* [0-5]	1.00 (1.17) *1.00* [0-5]	1.61 (1.85) *1.00* [0-8]	0.35 (0.71) *0.00* [0-3]
High	1.93 (2.96) *1.00* [0-14]	0.41 (0.57) *0.00* [0-5]	2.66 (2.50) *2.00* [0-9]	1.31 (2.94) *0.00* [0-13]

Error rates across task conditions were analysed in order to examine whether the participants' performance differed between conditions. A repeated measures ANOVA was used to examine the error rates between conditions in the low ELS group (n = 23). Mauchly's test indicated that the assumption of sphericity had been violated ($\chi^2(5) = 22.96$, $p < .001$), therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity. There was a significant main effect of condition on error rates ($F(1.82, 40.10) = 5.89$, p = .007). Wilcoxon Signed Ranks tests were used to examine the relationships between pairs of conditions. The mean number of errors made in the control no-go condition (M = 0.35, SD = 0.71) was significantly smaller than the mean number of errors made in the active avoid condition (M = 1.39, SD = 1.53; Z = -3.05, p = .002), the passive avoid condition (M = 1.00, SD = 1.17; Z = -3.10, p = .002) and the control go condition (M = 1.61, SD = 1.85; Z = -3.07, p = .002). There were

no differences between any other pairs of conditions in the mean number of errors made.

A repeated measures ANOVA was then used to examine the error rates across the task conditions in the high ELS group (n = 29). There was a significant main effect of condition on error rates ($F(3, 84) = 7.15$, $p < .001$). Therefore, Wilcoxon Signed Ranks tests were used to examine the relationships between pairs of conditions. The mean number of errors made in the passive avoid condition (M = 0.41, SD = 0.57) was significantly smaller than the mean number of errors made in the active avoid condition (M = 1.93, SD = 2.96; Z = -3.06, p = .002) and in the control go condition (M = 2.66, SD = 2.50; Z = -3.86, $p < .001$). There were no significant differences between the other pairs of variables after correction for multiple comparisons (p values > ..01).

In summary, both low and high ELS groups made more errors in passive conditions which did not require a response than in active conditions which did require a response. In the low ELS group, this was reflected in fewer errors in the control no-go condition than in any of the other conditions (active avoid, passive avoid and control go). In the high ELS group, this was reflected in fewer errors in the passive avoid condition than in the active avoid and control go conditions. Importantly, the two ELS groups did not differ in the number of errors made, either in individual conditions or across the task as a whole. Therefore, the low and high ELS groups did not differ in their performance of the task.

5.3.1.3. Reaction times

In this task, the warning stimuli predict an aversive outcome which participants are motivated to avoid by making or withholding a response, whilst the control stimuli never predict an aversive outcome, irrespective of the accuracy of the participant's response. Consequently, it would be expected that participants who were aware of the outcome contingencies would show faster reaction times when responding to the active warning stimulus than when responding to the active control stimulus. This effect was found in previous work which used the same experimental paradigm (Levita et al., 2015). Therefore, reaction times to the active warning and

control stimuli in the present study were examined in order to assess participants' acquisition of the outcome contingencies.

Reaction times in the active avoid condition were compared to reaction times in the control co condition in the low ELS group (n = 23). A Wilcoxon Signed Ranks test was used as the data were not normally distributed (Shapiro-Wilk). Reaction times were significantly faster in the active avoid condition (M = 338.51 ms, SD = 72.26 ms) than in the control go condition (M = 354.44 ms, SD = 80.73 ms; Z = -3.04, p = .002; Figure 5.3).

Reaction times in the active avoid condition were compared to reaction times in the control go condition in the high ELS group (n = 29). Although the data for the high ELS group were normally distributed, a Wilcoxon Signed Ranks test was used in order to allow for comparison with the analysis carried out with the low ELS group. Reaction times were significantly faster in the active avoid condition (M = 335.44 ms, SD = 57.73 ms) than in the control go condition (M = 350.87 ms, SD = 58.40 ms; Z = -3.69, p < .001; Figure 5.3).

Mann-Whitney U tests were used to compare reaction times between the high and low ELS groups. There were no significant differences between the two ELS groups in overall reaction time across conditions (low ELS M = 346.48 ms, SD = 75.45 ms; high ELS M = 343.15 ms, SD = 57.28 ms; U = 329.00, p = .93) nor within the active avoid condition (U = 324.00, p = .86) or the control go condition (U = 326.00, p = .89; Figure 5.3).

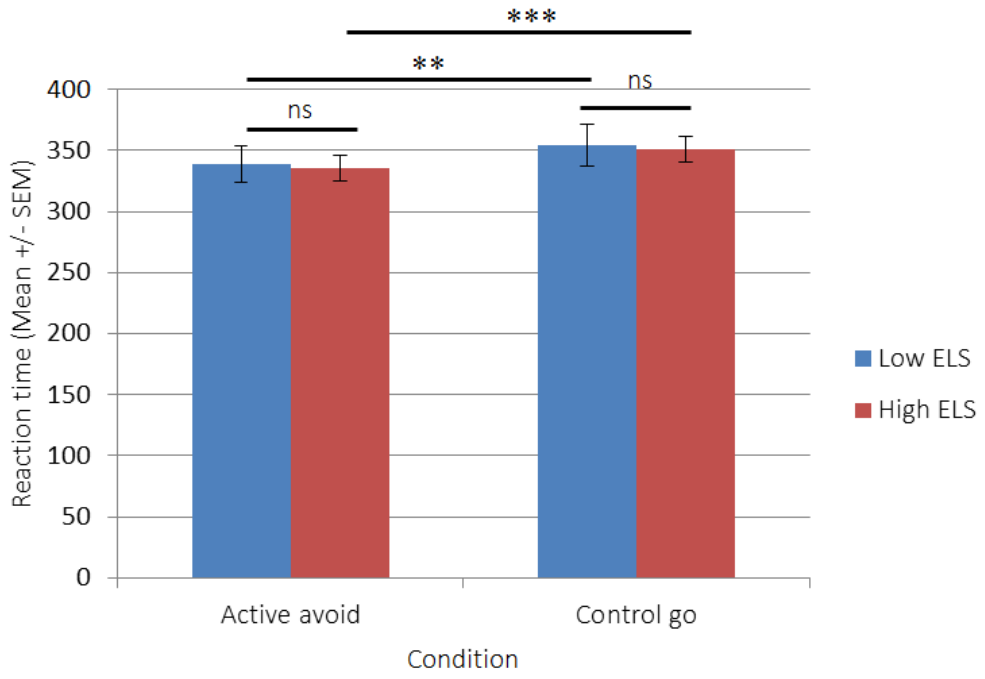

Figure 5.3. Mean reaction times in the active avoid and control go conditions by ELS group (low, high). There was no significant difference between the two ELS groups for reaction times in the active avoid or control go conditions. In both the low and high ELS groups, reaction times were significantly faster in the active avoid condition than in the control go condition ($p < .01$).

5.3.2. N170 scalp topography

The distribution of activation during the N170 response in each task condition (active avoid, passive avoid, control go and control no-go) for the low (A) and high (B) ELS groups are shown in Figure 5.4. The right-hand column in Figure 5.4 shows the scalp distribution unique to each of the two warning stimuli once the activation associated with their respective control stimulus was subtracted, i.e. active and passive avoidance. Each topographical map represents the distribution of activation (in μV) at a latency of 176 ms post-stimulus presentation. This latency was chosen as it represents the time at which the peak of the grand average N170 response occurred (mean of the N170 peak amplitudes across all task conditions for both ELS groups combined).

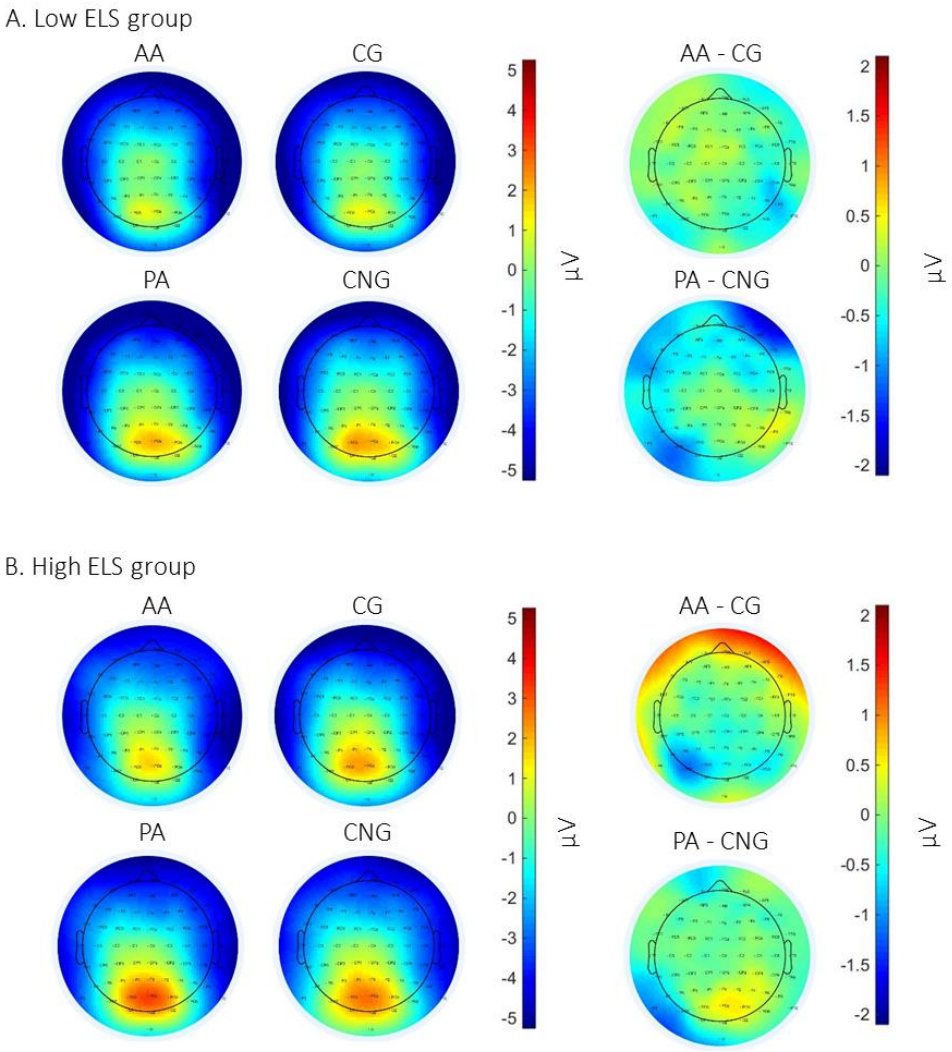

Figure 5.4. Scalp distributions for the peak amplitude of the N170 component. Each topographical map depicts the activation which occurred at 176 ms post-stimulus onset in the active avoid (AA), passive avoid (PA), control go (CG) and control no-go (CNG) conditions for the low (A) and high (B) ELS groups. Images in the right-hand column show the scalp distribution of the N170 response to the active and passive warning stimuli after subtraction of their respective control conditions (active and passive avoidance). Note the voltage scale for the activity in each condition ranges from -5 μV to 5 μV, whilst the scale for the activity between conditions (right-hand column) ranges from -2 μV to 2 μV.

5.3.3. N170 peak amplitude

As discussed in § 5.2.8, the effect of ELS on N170 peak amplitudes was analysed in two ways. Firstly, an ANOVA was used to examine the effect of ELS on the potentiation of the N170 peak amplitude to the warning stimuli. This approach was based on the analysis used in previous work which employed the same experimental paradigm and allowed for comparison of the results across studies (Levita et al., 2015). Secondly, hierarchical multiple regression analyses were used to examine the effect of ELS on potentiation of the N170 response during active and passive avoidance once anxiety and depression scores were taken into account. This latter analysis was necessary given the close relationship between ELS and mental illness, and given that both anxiety and depression could in themselves be associated with changes in the peak amplitude of the N170 (as demonstrated in Chapter 4). Although it would be possible to include anxiety and depression as covariates in an ANCOVA, this approach can only provide information on whether anxiety or depression have a significant effect on the N170 amplitude; unlike a regression-based approach, it cannot provide information on the direction of this relationship.

Figure 5.5 shows the grand-average ERP responses as a function of task condition in the left and right hemispheres for the low and high ELS groups. Mean values for the N170 peak amplitude in each task condition in the low and high ELS groups are presented in Table 5.3.

5.3.3.1. ANOVA analysis

In order to investigate the effect of ELS on learning-dependent potentiation of the N170 to danger signals, differences in the N170 amplitude to the warning and control stimuli were examined. A mixed design analysis of variance (ANOVA) was used with three within-subject factors of Laterality (left hemisphere (P7 and P9) vs. right hemisphere (P8 and P10), Response (key press vs. no key press) and Danger (warning stimuli vs. control stimuli). ELS group was entered as a between-groups factor (high vs. low).

There was no significant main effect of ELS group on N170 amplitude, nor were there any significant interactions between ELS and any of the other factors. However, there was a significant interaction between Danger and Laterality $F(1,50) = 3.89$, $p = .05$; Figure 5.6), such that in the left hemisphere, the N170 response to the warning stimuli ($M = -4.89$, $SD = 3.83$) was larger (more negative) than the N170 response to the control stimuli ($M = -4.36$, $SD = 3.67$; $t(51) = -2.18$, $p = .03$), whereas in the right hemisphere there was no significant difference in N170 response to the warning stimuli ($M = -5.07$, $SD = 4.41$) relative to the control stimuli ($M = -4.95$, $SD = 4.34$; $t(51) = -.44$, $p = .66$). There was also a significant main effect of Response on N170 peak amplitude ($F(1, 50) = 6.06$, $p = .02$; Figure 5.7), such that active conditions in which a response was required (active avoid and control go; $M = -5.29$, $SD = 4.09$) showed a larger (more negative) N170 peak amplitude than passive conditions in which a response was not required (passive avoid and control no-go; $M = -4.34$, $SD = 3.96$).

Therefore, the present findings show left hemisphere learning-dependent potentiation of the N170 response to warning stimuli relative to control stimuli. The high and low ELS groups did not differ in the degree of learning-dependent potentiation to the warning stimuli.

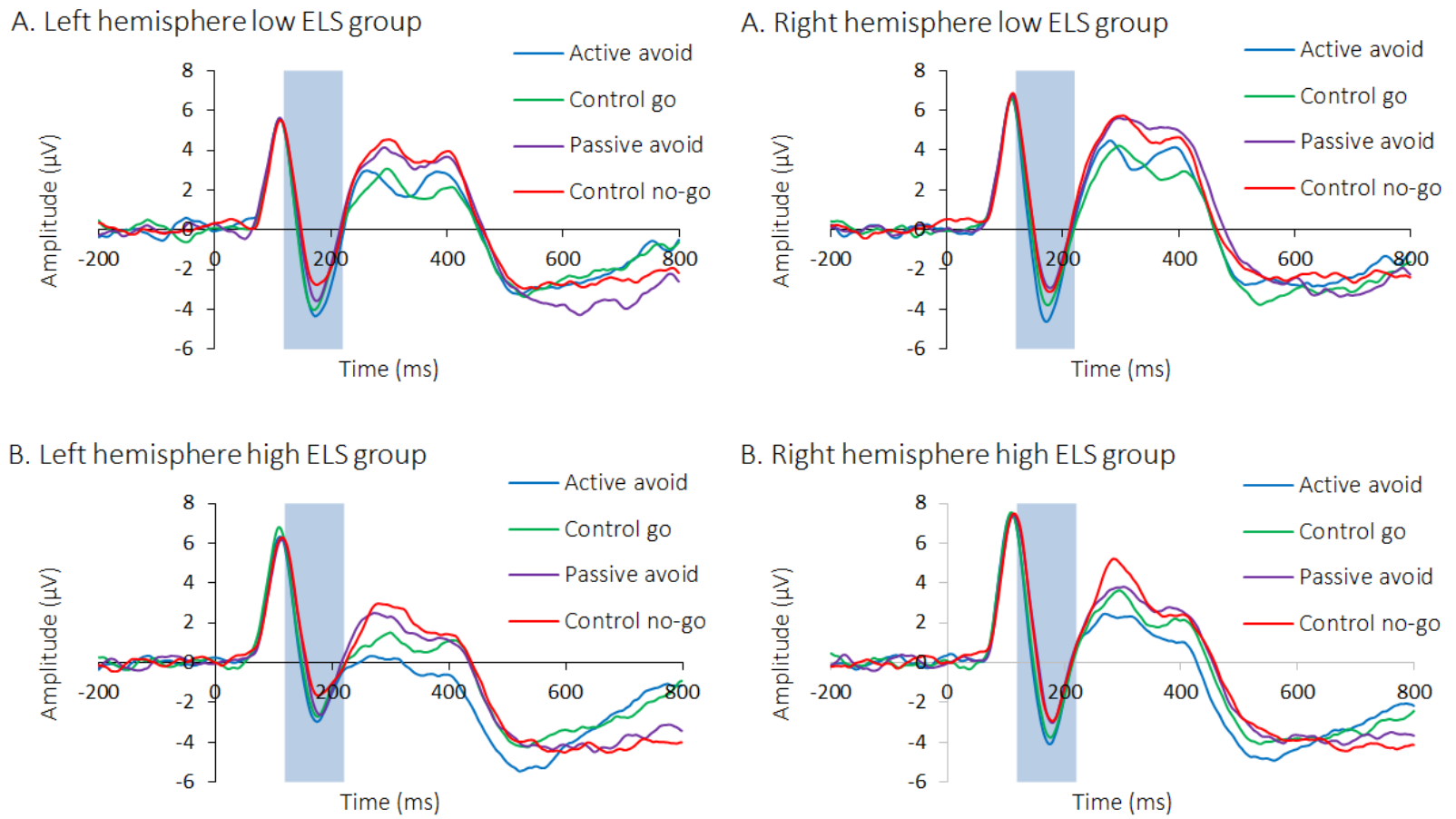

Figure 5.5. Grand average waveforms showing the N170 responses to each task condition in the left hemisphere (P7 and P9) and right hemisphere (P8 and P10) for the low (A) and high (B) ELS groups. The light blue column shows the N170 time window. Active avoid = blue line, passive avoid = purple line, control go = green line, control no-go = red line.

Table 5.3

Means and standard deviations of the N170 peak amplitude to in each task condition, by hemisphere and ELS group

Mean N170 amplitude (μV)	**Low ELS group**	**High ELS group**
Left hemisphere		
Active avoid	-5.93 (3.14)	-4.70 (4.99)
Passive avoid	-4.85 (4.09)	-4.29 (4.20)
Control go	-5.41 (3.50)	-4.39 (4.50)
Control no-go	-4.54 (3.51)	-3.34 (4.76)
Right hemisphere		
Active avoid	-6.17 (3.69)	-5.17 (5.97)
Passive avoid	-4.74 (4.85)	-4.36 (4.22)
Control go	-6.03 (4.34)	-5.04 (5.07)
Control no-go	-4.86 (4.17)	-4.09 (5.14)

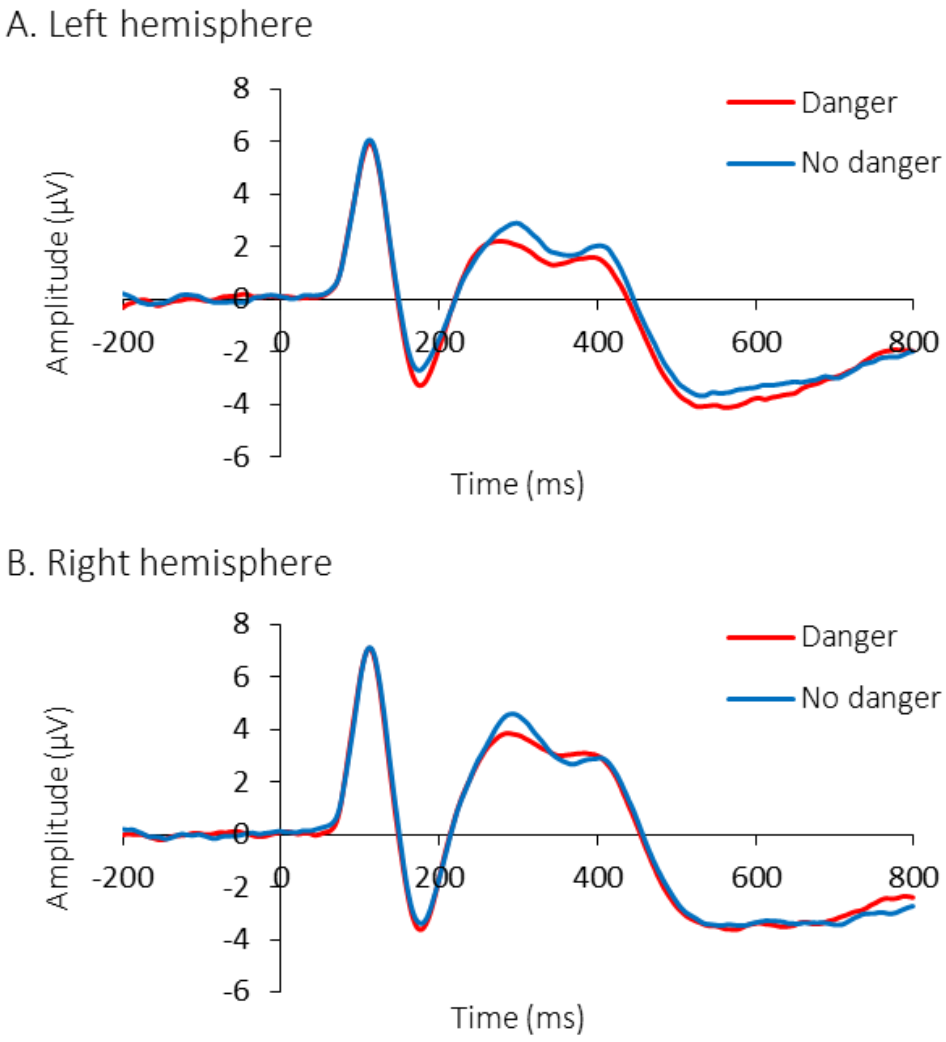

Figure 5.6. Grand average waveforms depicting N170 peak amplitude to warning stimuli which preceded danger (active avoid and passive avoid conditions) and control stimuli which did not precede danger (control go and control no-go conditions) in (A) the left hemisphere and (B) the right hemisphere. Waveforms are collapsed across both ELS groups. A mixed model ANOVA found an interaction between Danger and Laterality, such that in the left hemisphere only N170 peak amplitudes were larger to the warning stimuli than to the control stimuli.

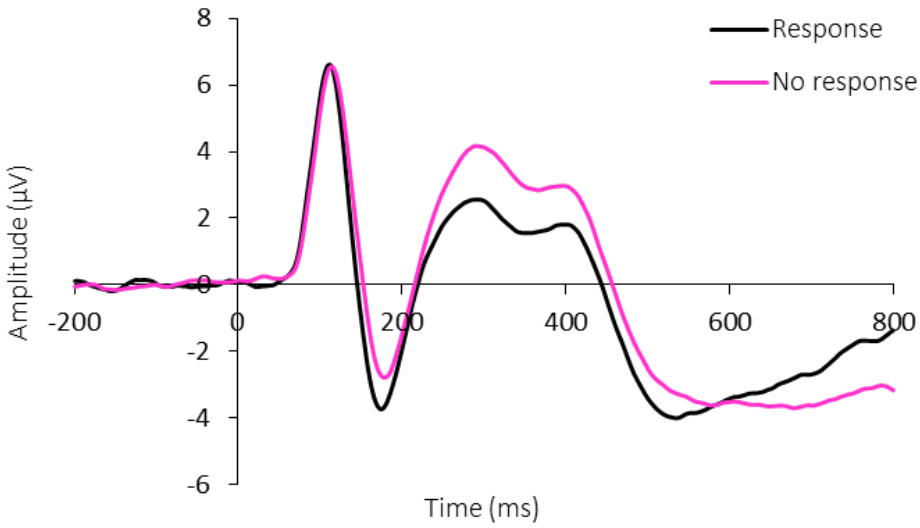

Figure 5.7. Grand average waveforms of the response in active conditions in which a response was required (active avoid and control go) and passive conditions in which a response was not required (passive avoid and control no-go), collapsed across both hemispheres and both ELS groups. The N170 peak amplitude was significantly greater in conditions which required a response from the participant than in conditions which did not require a response.

5.3.3.2. Hierarchical regression analyses

The primary aim of this study was to establish whether experiences of ELS influenced potentiation of the N170 peak amplitude to learned danger signals. This was examined in the previous section using an ANOVA. However, although the ANOVA was necessary in order to allow for comparison with previous work, it did not account for the potential confounding effects of levels of anxiety and depression. Furthermore, as shown in Table 5.1, the two ELS groups in the present study also differed significantly in their age and on a measure of impression management, yet neither of these variables could be easily incorporated into the ANOVA.

Therefore, multiple hierarchical regression analyses were used to examine the effect of ELS on the potentiation of the N170 peak amplitude whilst accounting for the potential confounding effects of age, impression management, depression and anxiety. Measures of active and passive avoidance were created by subtracting N170 responses to the warning stimuli from their respective control stimuli (i.e. active avoid minus control go; passive avoid minus control no-go). This allowed for an investigation of the effect of ELS on N170 responses during active and passive avoidance once the effects of other factors such as preparation for motor responses had been accounted for. As described in § 5.2.8.3, a two-step regression model was used to predict each dependent variable in each hemisphere. Four variables were entered in Step 1: age, PDS: Impression Management, BDI-II (depression) and STAI-T (anxiety). The categorical variable of ELS group was entered in Step 2. Details regarding the selection of the independent variables which were included in the model can be found in § 5.2.8.3.1.

5.3.3.2.1. Higher depression scores are associated with greater learning-dependent potentiation of the N170 peak amplitude to warning stimuli during active avoidance

Four hierarchical regression analyses were used to examine the effect of ELS on learning-dependent potentiation of the N170 response to the two warning stimuli (active and passive) in the left and right hemispheres (Table 5.4). The Benjamini-Hochberg procedure was used to correct for multiple comparisons (Benjamini & Hochberg, 1995). Given the

exploratory nature of the analyses, an FDR threshold of 0.1 was used. Correction for multiple comparisons was performed separately for each hemisphere. Further details regarding the control of multiple comparisons are provided in § 2.3.1.1.

The regression model accounted for a significant amount of the variance in right hemisphere learning-dependent potentiation of the N170 to the warning stimulus during active avoidance. Examination of the beta weights revealed that higher depression scores were significantly associated with greater learning-dependent potentiation to the warning stimulus during active avoidance. None of the other independent variables in the regression model (age, impression management, anxiety and ELS group) were significantly related to potentiation of the N170 peak amplitude to the warning stimulus during active avoidance.

The regression model did not explain a significant amount of variance in right hemisphere potentiation to the warning stimulus during passive avoidance. Similarly, the regression model was unable to explain a significant amount of the variance in left hemisphere learning-dependent potentiation to the warning stimuli, either during active avoidance or passive avoidance.

Therefore, consistent with the ANOVA analysis reported in § 5.3.3.1, learning-dependent potentiation of the N170 to the warning stimuli during either active or passive avoidance did not differ between the low and high ELS groups.

Table 5.4

Means and standard deviations of the N170 peak amplitude to in each task condition, by hemisphere and ELS group

Difference in N170 peak amplitude (μV)		**Coefficients**					ΔR^2	R^2
		Age	**Impression management**	**Depression**	**Anxiety**	**ELS group**		
Left hemisphere								
Active Avoid minus Control Go								
Model 1	*β*	.09	-.21	-.18	.02			
	p	.61	.20	.35	.92			
Model 2	*β*	.09	-.22	-.18	.02	-.01	.00	.05
	p	.62	.22	.39	.92	.94	.94	.77
Passive Avoid minus Control No-Go								
Model 1	*β*	-.09	.05	-.15	.12			
	p	.59	.78	.45	.60			
Model 2	*β*	-.05	.02	-.12	.10	-.09	.01	.02
	p	.77	.92	.55	.64	.62	.62	.96
Right hemisphere								
Active Avoid minus Control Go								
Model 1	*β*	-.09	-.23	-.37	-.12			
	p	.54	.13	.04*	.54			
Model 2	*β*	-.18	-.17	-.43	-.10	.19	.03	.22
	p	.29	.29	.02*	.62	.23	.23	.04[a]
Passive Avoid minus Control No-Go								
Model 1	*β*	.23	-.00	.11	-.18			
	p	.17	.99	.56	.42			
Model 2	*β*	.31	-.06	.17	-.20	-.18	.02	.07
	p	.09	.73	.40	.36	.30	.30	.66

Note. * $p < .05$. [a]Model accounts for a significant amount of the variance in the dependent variable after correction for multiple comparisons.

5.3.4. Assessing assumptions of the regression analyses

As detailed in § 2.3.2, regression analysis makes a number of assumptions about the data. The following section discusses whether the assumptions were met for the regression analyses reported above.

5.3.4.1. Outliers and influential points

Two of the four regression analyses contained one outlier, defined as a case in which the residual was greater than +/- 3 *SD*. These were participant 54 in the analysis of left hemisphere active avoidance (AA – CG) and participant 33 in the analysis of right hemisphere passive avoidance (PA – CNG). It should be noted that the latter of these cases showed a value of 3.00, and was therefore on the boundary of being considered an outlier. After confirming that the outliers were not a consequence of errors in data entry, Cook's Distances were computed to examine the extent to which the cases were influencing their respective analyses. The Cook's Distances were 0.16 in the analysis of left hemisphere active avoidance and 0.29 in the analysis of right hemisphere passive avoidance. In both cases this value was below 1, suggesting that the outliers were not exerting an undue influence on the regression models (Field, 2005).

5.3.4.2. Independence of residuals

The Durbin-Watson statistic was used to test the assumption of independence of residuals. Using the tables provided by Savin and White (1977), it was established that the upper bound for the Durbin-Watson value in the present regression analyses was 1.59, and the lower bound was 1.16. As discussed in § 2.3.2.2, values above the upper bound indicate that the assumption has been met, values below the lower bound indicate violation of the assumption, and values in between the two bounds indicate that the test is inconclusive. The Durbin-Watson statistic fell above the upper bound for all four regression analyses, indicating that the assumption of independence of residuals had been met.

5.3.4.3. Presence of linearity

Multiple regression assumes a linear relationship between the dependent variable and each of the independent variables. This assumption was investigated by visual examination of the partial regression plots between the dependent variable and each independent variable. In all cases the pattern of data points suggested that the assumption of linearity had been met. In addition, the assumption of a linear relationship between the dependent variable and the independent variables collectively was tested via examination of scatterplots in which the studentised residuals were plotted against the unstandardised predicted values. These plots also showed that the assumption of linearity had been met.

5.3.4.4. Homoscedasticity of residuals

The assumption of homoscedasticity was tested by visual examination of the residual plot described in the previous section. In all analyses these plots showed a broadly random pattern of data points, indicating that the assumption of homoscedasticity had been met.

5.3.4.5. Absence of multicollinearity

The assumption of no multicollinearity was tested via examination of the correlations between the predictors and examination of the Tolerance values for each predictor. In all cases the correlations between predictors were below 0.8, with the largest correlation being that observed between BDI scores and STAI-T scores ($r(50) = 0.62$, $p < .001$). All Tolerance values fell well above the suggested cut-off value of 0.2 (Field, 2005), with the smallest Tolerance value (0.44) corresponding to the STAI-T predictor. These tests showed that although there was some correlation between the predictors, none of the correlations was large enough to violate the assumption of no multicollinearity.

5.3.4.6. Normal distribution of residuals

The assumption of normal distribution of residuals was tested via visual examination of histograms of the standardised residuals and probability plots in which the observed cumulative probability was plotted

against the expected cumulative probability. These plots indicated that the assumption had been met for all analyses.

5.4. Discussion

The aim of this study was to examine whether higher levels of ELS are associated with altered learning-dependent potentiation of the N170 to learned danger signals in an active and passive avoidance task. It was found that N170 peak amplitudes showed learning-dependent potentiation to warning stimuli relative to control stimuli. However, this learning-dependent potentiation was not related to ELS during either active or passive avoidance. It was also found that N170 amplitudes were larger in conditions that required the emission of a motor response (active avoid and control go). Critically, the N170 learning-dependent potentiation found in this study is consistent with previous work that also showed learning-dependent potentiation of the N170 to warning stimuli during active and passive avoidance (Levita et al., 2015). However, whilst the present study found learning-dependent potentiation in the left hemisphere, previous work with the same experimental task found this effect in the right hemisphere. Using hierarchical regression, the present study also found that higher scores on a measure of depression were associated with greater right hemisphere potentiation of the N170 response to learned danger signals during active, but not passive, avoidance.

5.4.1. The low and high early life stress groups did not differ on measures of active or passive avoidance

In contrast to predictions, ELS had no effect on behavioural or neural indices of active or passive avoidance. Taken together with the finding of a significant effect of ELS on the N170 peak amplitude response to emotional facial expressions in Chapter 4, as well as the significant relationship between levels of ELS and decreased self-reported avoidance of female angry facial expressions in Chapter 3, these results could represent initial evidence that the impact of ELS on early visual responses is specific to social cues (such as facial expressions), and does not extend to non-social cues (such as those presented in the present study). The results could also be interpreted as evidence that ELS is related to altered responsivity to cues which were encountered and afforded salience in early life (e.g. emotional facial expressions), but is not related to new learning about novel cues

which are presented later in life after the stress has ended (e.g. the 'Greeble' stimuli in the present study). Alternatively, it is possible that the relatively low levels of ELS experienced by the participants in the present research contributed to the different outcomes in the two EEG studies. Specifically, individuals who were included in the high ELS group for the two EEG studies did not generally experience extreme levels of ELS. Indeed, the highest score on the CATS amongst those who took part in the EEG studies was 70, out of a possible maximum score of 152 (Sanders & Becker-Lausen, 1995). It is possible that these levels of ELS were high enough to produce measurable changes in the N170 response to emotional facial expressions (Chapter 4), but were not high enough to produce measurable changes in learning-dependent potentiation of the N170 to non-social cues of threat. All of these interpretations are tentative and require further investigation.

Avoidance learning is thought to involve both Pavlovian fear conditioning and instrumental conditioning (Krypotos et al., 2015). Given that, to the author's knowledge, no previous studies with human participants have examined the effect of ELS on avoidance learning as a whole, it is useful to examine the present findings in the context of previous studies which have focussed on fear conditioning alone. The present results are not consistent with previous studies by Bremner et al. (2005) and Cacciaglia et al. (2017) which found altered neural and physiological responsivity during fear conditioning in people who had experienced trauma. However, there are several differences between the present study and these previous studies, including differences in the participant samples, the tasks used and the measures taken. Whilst the present study recruited a sample of mentally healthy participants who had experienced low or moderately high levels of ELS, Bremner et al. (2005) tested a sample of participants with post-traumatic stress disorder (PTSD) who had experienced extreme ELS in the form of childhood sexual abuse. Though the participants recruited by Cacciaglia et al. (2017) did not have PTSD or depression, they had been exposed to extreme trauma, such as the traumatic loss of a loved one. Furthermore, in contrast to the present study, Cacciaglia et al. (2017)

recruited participants who had experienced trauma at any time, not just during early life.

Though there has been more investigation of the effects of ELS on fear conditioning in animals than in humans, the animal literature remains inconclusive, with evidence for both enhanced (Oomen et al., 2010; Quinn et al., 2014) and impaired (Kosten et al., 2006; Meerlo et al., 1999) fear conditioning in rats which experienced ELS. The lack of research examining the effect of ELS on fear conditioning in humans, along with the inconsistent findings in rat studies, highlights the need for further investigation of the effect of ELS on this important component of avoidance learning.

Regarding the instrumental component of avoidance learning, the present study found no evidence for an effect of ELS on either active or passive avoidance responding. This study is, to the author's knowledge, the first to examine the effect of ELS on responses to learned danger signals during active and passive avoidance in human participants. Previous research with rats has generally found that ELS is associated with enhanced active avoidance learning and impaired passive avoidance learning (Kosten et al., 2012). In active avoidance studies with rats, performance is typically measured as the number of correct avoidance responses made (e.g. Catalani et al., 2002; Pryce et al., 2003; Rio-Alamos et al., 2017). In the present study, accuracy rates were very high (98.2 % across the whole sample). The fact that both ELS groups in the current study were performing almost at ceiling level may have precluded the emergence of group differences in active avoidance performance. Regarding passive avoidance, the vast majority of experiments with rats have found that ELS is associated with impaired passive avoidance (Benetti et al., 2012; Benetti et al., 2015; Kosten, Karanian, et al., 2007; Kosten et al., 2012; Kosten, Lee, et al., 2007; Mello et al., 2009; Neves et al., 2015; Vivinetto et al., 2013; Zugno et al., 2013). However, in all but one of these studies (Zugno et al., 2013) there was a gap of at least an hour between the training session, in which the animal was introduced to the warning stimulus, and the testing session, in which the animal's passive avoidance of the warning stimulus was measured. Therefore, rat models of passive avoidance typically rely at least

in part on recall of information about the warning stimulus. In contrast, participants in the present study did not necessarily have to rely on memory for the aversive outcome, as their failure to respond successfully would lead to the presentation of the aversive US, allowing for the renewal of the association between the CS and the US. Therefore, methodological differences could explain the discrepancy between the findings of the current study and the findings from studies of passive avoidance in rats.

The absence of altered avoidance learning following ELS in the present study, and indeed the contradictory findings in the literature, may be explained by cross- and within- study differences in the timing of the early stress. Growing evidence in both human and animal literature suggests that the brain regions and networks which are most affected by ELS are those which are developing at the time that the stress occurs (Andersen et al., 2008; Heim & Binder, 2012). Furthermore, work by Lehmann et al. (1999) has shown that, in rats, the same early life manipulation (maternal separation) carried out at different time points can have opposing effects on active avoidance behavioural in adulthood. Specifically, Lehmann et al. (1999) found that maternal separation on PND 4 was associated with impaired active avoidance, whilst separation on PND 9 was associated with enhanced active avoidance. In the present study ELS was measured using the CATS (Sanders & Becker-Lausen, 1995), which includes questions covering the whole of childhood and adolescence. It is possible that grouping together individuals who experienced stress at different points in time may have reduced the potential for detection of temporally sensitive ELS-related changes in avoidance learning. Future work which accounts for the timing of the stress could shed more light on the potential effect of ELS on avoidance learning, though this represents a challenging area of research given that, in humans, ELS is rarely confined to one stage of development (Callaghan et al., 2014). This issue is discussed further in § 6.4.2.2.

5.4.2. Potentiation of the N170 to warning stimuli

In line with previous work (Levita et al., 2015), the present study found potentiation of the N170 to warning stimuli relative to control stimuli. However, there were some differences between the findings reported by

Levita et al. (2015) and the findings reported in the present study. Specifically, Levita et al. (2015) found that learning-dependent potentiation of the N170 to learned danger signals was greater in the right hemisphere than the left hemisphere, whereas the present study found that this learning-dependent potentiation was specific to the left hemisphere. In addition, Levita et al. (2015) found no effect of response condition (active or passive) on the N170 response, whereas the present study found that the N170 response was significantly potentiated to stimuli which required the emission of a response relative to stimuli which required the omission of a response.

At present the reasons for these differences are unclear, though they could be related to differences between the two task paradigms. Although the task used in the present study was very similar to that used by Levita et al. (2015), there were some differences between the two studies in terms of the specific parameters that were used. In the version of the paradigm used by Levita et al. (2015), participants were required to make a response whilst the stimulus was on the screen. If the response to a warning stimulus was inaccurate, the offset of the stimulus was immediately followed by the aversive tone. However, in the present study, participants were presented with the stimulus, then required to wait until they saw the yellow cross (1000 ms after the offset of the stimulus) to make or withhold their response. This temporal delay was introduced into the present paradigm in order to allow for the dissociation of the neural activity elicited by the presentation of the stimulus from the neural activity associated with making (or withholding) a response.

It is possible that the introduction of the temporal delay resulted in a separation of the two stages of avoidance responding, such that the conditioned fear response could have occurred when the warning stimuli were presented, and the instrumental avoidance response could have occurred 2000 ms later, when the yellow fixation cross was presented. In contrast, in Levita et al.'s (2015) study, participants were required to make an instrumental avoidance response as soon as the stimulus was presented, and as such the neural processes involved in the instrumental avoidance response were not artificially separated from the neural processes involved

in the conditioned fear response. Therefore, the signal recorded at the scalp following stimulus presentation in the present study likely reflected a different combination of neural sources than the signal recorded following stimulus presentation in the study by Levita et al. (2015). Differences in the neural mechanisms recruited at the time of stimulus presentation may also explain why the learning-dependent potentiation of the N170 recorded in the present study was specific to the left hemisphere, whilst the learning-dependent potentiation of the N170 recorded in Levita et al.'s (2015) study was greater over the right hemisphere.

This possibility is supported by the findings of a recent study by Camfield et al. (2016), which examined the N170 peak amplitude response during a classical fear conditioning study which did not involve instrumental avoidance. In this study, three male neutral faces were used as conditioned stimuli (CS). The experiment was divided into three blocks. The first block was a baseline block, in which the three neutral faces (CS) were presented on a black background. The second two blocks were classical conditioning blocks in which each of the three neutral faces was presented in front of a background image. These background images were either negative (CS+ negative), positive (CS+ positive) or neutral (CS-). Although the background images changed, the same face was always paired with the same category of background image (i.e. face A with negative images; face B with positive images and face C with neutral images). They found that, in the left hemisphere, the N170 amplitude increased to a greater degree from the baseline to the conditioning blocks in the negative background imagery condition than in the neutral background imagery condition. This study therefore found left hemisphere learning-dependent potentiation of the N170 to a CS paired with aversive imagery relative to a CS paired with neutral imagery. These findings accord with the present study's finding that learning-dependent potentiation to the warning stimuli was specific to the left hemisphere. This lends support to the suggestion that the left hemisphere learning-dependent potentiation of the N170 in the present study was related to the first stage of avoidance, conditioned fear responding, rather than the second, instrumental stage of avoidance responding.

The recruitment of different neural mechanisms at the point of stimulus onset may also explain why the present study found potentiation of the N170 to the active stimuli (active avoid and control go conditions), where the study by Levita et al. (2015) did not. In addition to introducing a possible change in the time at which specific avoidance mechanisms were recruited, the use of a delay in the present study meant that, in the active conditions, participants had to ensure that they did not make a response until they saw the yellow cross, 2000 ms after the onset of the active stimulus. This could have necessitated the recruitment of additional neural mechanisms which were not required in the paradigm used by Levita et al. (2015), which required an immediate avoidance response.

5.4.3. Learning-dependent potentiation of the N170 to learned danger signals – relationship with depression scores

Though there was no effect of ELS on learning-dependent potentiation of the N170 to danger signals, the present study did find that higher depression scores were associated with larger right hemisphere N170 amplitudes to the warning stimulus relative to the control stimulus during active, but not passive, avoidance. The fact that depression scores were associated with active avoidance but not passive avoidance raises the possibility that depression scores may be related to the second, instrumental phase of avoidance learning, and not to the initial Pavlovian fear conditioning phase. This is because, given that active and passive avoidance are thought to share an initial fear conditioning component, but deviate from one another in the second instrumental component (with the response being either active or passive), an effect of depression on the initial fear conditioning component might be expected to result in changes in both active and passive avoidance. Alternatively, if depression were related only to the second, instrumental stage of active or passive avoidance, distinct effects of depression on the two mechanisms could occur. Although highly speculative, this explanation is supported by work which found that, during a classical fear conditioning task, learning-dependent potentiation of the N170 peak amplitude to stimuli associated with threat did not differ between people with depression and those without depression (Camfield et al., 2016).

Taken together, the present findings and those reported by Camfield et al. (2016) suggest that depression may be associated with potentiation of the N170 during active avoidance, but not during passive avoidance or classical fear conditioning alone.

5.4.4. Study limitations and future directions

As with the previous study (Chapter 4), the present study may have been limited by its sample size. Visual examination of the N170 waveforms (Figure 5.5), and the topographical difference maps in the active and passive conditions (Figure 5.4) suggests that there could be differences between the ELS groups which did not reach significance in the statistical analyses.

It is possible that the absence of an effect of ELS group on the N170 response in the present study could be an artefact of the analytical methods employed. The N170 was quantified as the most negative peak in the averaged waveform within the given time window (§ 2.2.4). The peak amplitude method is vulnerable to noise (Luck, 2014), and whilst care was taken to remove noise generated by ocular sources, it is likely that some noise remained present in each participant's average waveform. One way to minimise this problem would be to use ICA to extract individual neural components from the data. As discussed in § 4.4.3., the way in which the present data were processed meant that such extraction was not possible. However, it is possible that use of this different analytical method could have allowed for more precise measurements of the N170 component, which in turn may have allowed for the quantification of potential group differences in the present study.

An additional factor which could explain the null effect of ELS group in the present study concerns the sample size. G*Power software (Version 3.0.10; Faul, Erdfelder, Lang, & Buchner, 2007) was used to calculate the power of the ANOVA analysis to detect a between-groups effect. The partial eta squared was 0.01, resulting in an effect size (*f*) of 0.12. Given that the ANOVA had two groups and three within-subjects factors, the sample size of 52 resulted in 0.18 power. This means that the probability of detecting a genuine between-groups effect with a sample size of 52 was low, at 18 %.

Having said this, the sample size used in the present study (n = 52) was larger than the study on which it was based (Levita et al., 2015), which had a sample size of 44. In this study, the repeated measures factors were the same, but participants were divided into groups based on age (adolescence or adulthood), rather than on ELS experience. In this study, a significant between-groups effect of age was reported. This is perhaps unsurprising, as ERP responses can change dramatically across development (Nelson & McCleery, 2008). As such it might be expected that between-group differences in Levita et al.'s study would produce larger effect sizes which could be detected with smaller samples.

Camfield et al. (2016), discussed above in § 5.4.2, carried out a related study with an all-adult sample. This study differs from the present work in that it examines depression rather than ELS, and concerns classical conditioning rather than avoidance learning. However, it is useful for a comparison of sample size as it is one of the very few studies which has examined N170 responses to non-social threat in an adult sample. This study (n = 34) used a smaller sample than the present work, but the pattern of results was similar. Specifically, they found some within-subjects effects of task condition on the N170 amplitude, but no group differences in N170 amplitude between people with and without depression.

Sample size can also influence regression analyses. Including too many predictors for a given sample size can limit the ability of the regression analysis to detect significant effects (Wilson van Voorhis & Morgan, 2007). Furthermore, in situations where the number of predictors is large relative to the number of cases, the regression model can be 'overfit', which means that its ability to predict outcomes in the population (as opposed to the specific sample it is based on) becomes limited (Schmidt, 1971). There is extensive debate across the literature as to the appropriate case-to-predictor ratio required for linear regression analysis (Austin & Steyerberg, 2015). However it is generally agreed that the more predictors are included, the larger the sample size that is required. Green (1991) found moderate support for the rule of $n \geq 50 + (8m)$, where m is the number of predictors. Following this rule, the present study would require 90 participants, notably more than the 52 that were included. Therefore, it is

possible that the null effects of ELS on the N170 in the regression analyses may have been a function of the relatively large predictor-to-case ratio that was used. As a result of the sample size and analysis strategy used in the present study, it is not possible to reach a firm conclusion as to whether ELS is associated with alterations in neural responses to danger signals in this task of active and passive avoidance. Future work should recruit a larger sample of participants in order to determine whether the absence of ELS effects on potentiation of the N170 to danger signals in the current study should be attributed to the relatively small sample size that was tested, or alternatively, whether potentiation of the N170 to danger signals is indeed unrelated to experiences of ELS.

The present study used a modified version of a previously validated active and passive avoidance task (Levita et al., 2015). Specifically, whereas the original version of the paradigm required participants to emit or omit a response as soon as the stimulus was presented, the current paradigm used a delay, such that participants were required to respond during the presentation of a yellow fixation cross 1000 ms after stimulus offset. This delay was introduced in order to ensure that the neural response to the presentation of the stimuli could be delineated from the motor response to the stimuli. However, the difference in task parameters limits comparisons between the present study and previous research. In addition, there was an unexpected level of between-participant variability in the present study, which did not occur in previous research with the original paradigm. Specifically, examination of the check-sheet responses (§ 5.2.4.2.4) suggested that some participants had difficulty acquiring the outcome contingencies of the stimulus (i.e., which stimuli predicted the aversive outcome). However, the present research found learning-dependent potentiation of the N170 to danger signals, as well as faster reaction times to the active warning stimulus than to the active control stimulus. This shows that the sample as a whole were aware of the outcome contingencies, as neither effect could be expected to occur if participants were unable to differentiate between the warning and control stimuli.

Nevertheless, future work would benefit from the introduction of additional measures to ensure that all participants are explicitly aware of the

outcome contingencies. For example, the task could be divided into a classical conditioning phase, in which the warning stimuli are repeatedly paired with the aversive outcome (without the opportunity to avoid the aversive outcome), and an instrumental phase, during which the participants learn to avoid the aversive outcome by emitting or omitting a response to the warning stimuli. In addition to reducing between-participant variability in acquisition of the outcome contingencies, this paradigm could also provide an opportunity to examine whether learning-dependent potentiation of the N170 to warning stimuli is specific to trials in which the aversive outcome can be avoided, or whether it also occurs when the aversive outcome cannot be avoided.

5.4.5. Conclusions

The present study found that ELS was not related to the degree of learning-dependent potentiation of the N170 to learned danger cues in a sample of young adults who had not been diagnosed with any mental health problems. These findings, when examined alongside the finding that ELS is associated with alterations in the N170 to emotional facial expressions (Chapter 4) could suggest that the relationship between ELS and changes in early perceptual processing may be specific to social stimuli such as facial expressions. However, confirmation of this possibility requires further work with a larger sample of participants.

Chapter 6. General discussion

Abstract

This general discussion draws conclusions from the findings of the present body of work as a whole. It first examines the present research in the context of previous literature, with a particular focus on understanding the discrepancies between the present findings and those of previous studies. The discussion then moves on to an examination of the potential implications of the present research, highlighting the present finding that, in young adults, ELS is associated with neurocognitive alterations that occur even in the absence of extreme experiences of ELS and clinically diagnosed mental health conditions. The discussion then moves on to address limitations of the present research, and to consider the methodological challenges for ELS research more broadly. After this, future directions for the present work are discussed, with a focus on replication and extension of the present findings. This leads into an examination of the future directions open to investigators in the field of ELS more broadly, especially with respect to the delineation of markers of vulnerability and resilience. This is followed by a discussion of the need for researchers to capitalise on longitudinal paradigms in order to identify neurocognitive alterations which act as mediators between experiences of ELS and the development of mental illness in adulthood.

6.1. Introduction

The following general discussion will take an overarching approach to the interpretation of the findings produced by the present body of work. In the first section (6.2), the main findings from the present research will be discussed in the context of the wider literature on the effects of ELS on neurocognitive processing, with a particular focus on the apparent discrepancy between previous findings with children and the current findings with young adults. In the second section (6.3), the results will be examined in light of their possible implications for the field, with a focus on the present finding of a pervasive impact of moderate levels of ELS on neurocognitive processing, which occurs even in those without diagnosed mental health conditions. The third section (6.4) will address the limitations of the present research, before examining some of the methodological challenges for ELS research more broadly. In the fourth section (6.5), future directions for the present body of work, and for research in the field of ELS in general will be discussed. The possibility that the alterations observed in the present work may represent markers of resilience, rather than markers of vulnerability, will be examined, and the importance of longitudinal studies will be addressed. The general discussion will end (6.6) with concluding remarks that summarise the present research and highlight its contribution to our understanding of the neurocognitive correlates of ELS in the young adult brain.

6.2. Discussion of findings

Each of the previous chapters discussed the specific findings from one individual study. The following section of the general discussion will draw a number of conclusions from the body of work as a whole, and discuss each of these conclusions in the context of the wider literature.

6.2.1. The effects of early life stress are specific to angry facial expressions at the behavioural level but extend to happy and neutral facial expressions at the neural level

The present body of work found that ELS was associated with reduced identification of anger at the behavioural level (Chapter 3) and blunted N170 responses to angry facial expressions at the neural level (Chapter 4). At first glance, this might lead one conclude that alterations in early processing of angry facial expressions (as indexed by changes in the N170 ERP component) explain the alterations in behavioural responding to these facial expressions. Indeed, it is plausible that blunted N170 responses to angry facial expressions in people who experienced high levels of ELS do contribute to the ELS-related alterations in responses to angry facial expressions at the behavioural level. However, the observed changes in early neural processing cannot fully explain the changes at the behavioural level. This is because ELS-related changes in the N170 response occurred irrespective of the emotional expression that was presented (Chapter 4), whereas the ELS-related changes in the self-reported responses were specific to angry expressions only (Chapter 3). It is possible that later, high-order mechanisms compensate for the effects of ELS on early perceptual processing, preventing the changes in early responsivity to happy and neutral facial expressions from influencing responding at the behavioural level. Suggestions for how this possibility could be investigated are presented in § 6.5.1.2. Alternatively, it is possible that the behavioural paradigm used in Chapter 3 was not sensitive enough to identify the changes in emotional face processing which were identified with the use of EEG in Chapter 4.

The disconnect between emotion-specific effects at the behavioural level and effects which are not emotion-specific at the neural level can also

be found in the wider literature on emotional face processing in people who experienced ELS. Multiple behavioural studies have found evidence for altered processing of anger in those who experienced ELS (Pollak & Kistler, 2002; Pollak et al., 2009; Pollak & Sinha, 2002), whilst evidence for altered behavioural responding to other emotional expressions is absent or inconsistent (§ 1.3.1). In contrast, at the neural level, it is not uncommon to find studies which report associations between ELS and altered responses to emotional facial expressions in general (McCrory et al., 2013; van Harmelen et al., 2013), though neural alterations specific to negative facial expressions have also been reported (Dannlowski et al., 2013).

Many of the studies which have examined the association between ELS and neural responses to emotional facial expressions have focussed on the amygdala (Hein & Monk, 2017). McCrory et al. (2013) suggest that ELS is associated with altered amygdala activity to emotional facial expressions in general, and with altered activity in higher-order brain regions to angry facial expressions specifically. This explanation is in partial accordance with the present findings, as it is thought that the amygdala can act to modulate the N170 response (Dolan et al., 2006; Levita et al., 2015). Therefore, a non-specific alteration in amygdala responding to emotional facial expressions following ELS could result in a non-specific alteration in N170 responding to emotional facial expressions following ELS. However, it should be noted that McCrory et al. (2013) found that higher levels of ELS were associated with an increase in amygdala activity to emotional facial expressions, whilst the present research found that higher levels of ELS were associated with a decrease in N170 amplitude to emotional facial expressions. This apparent discrepancy is discussed further in the following section.

6.2.2. The present findings appear at odds with much of the broader literature on neurocognitive processing following early life stress

The present body of research found that, in mentally healthy young adults, high levels of ELS were associated with reduced identification of anger in angry female faces, increased self-reported approach of angry facial expressions, reduced self-reported avoidance of angry female faces, and

blunted N170 amplitudes to angry, happy and neutral facial expressions. These findings broadly accord with a small number of studies which found neural hypo-responsivity to emotional facial expressions in participants who experienced ELS. These studies found blunted N170 amplitudes to angry, happy and neutral facial expressions in children who were maltreated (Curtis & Cicchetti, 2011), and blunted N170 amplitudes to angry, happy, sad and fearful facial expressions in children who were raised in institutions (Moulson et al., 2009). Similarly, two fMRI studies found that adult participants with high levels of ELS showed reduced amygdala activation to angry and fearful facial expressions relative to adults with low levels of ELS (Clark et al., 2017; Taylor et al., 2006).

However, despite some support in the previous literature, the present findings of reduced responsivity to emotional facial expressions, and to angry facial expressions in particular, differ from the majority of previous research which has generally shown a pattern of hyper-responsivity to emotional facial expressions, and to angry facial expressions in particular (McCrory et al., 2011; Pollak & Kistler, 2002; Pollak & Sinha, 2002). The following section discusses a number of possible explanations for this discrepancy between the current results and the wider body of literature.

6.2.2.1. Sample differences

As previously discussed, the majority of research which has examined the effects of ELS on neurocognitive processing has been carried out with children. To the author's knowledge, there is only one behavioural study which has examined the effect of ELS on mentally healthy adults' identification of basic emotional facial expressions such as anger and happiness (Gibb et al., 2009). Though Germine, Dunn, McLaughlin, and Smoller (2015) also examined emotional face processing, the paradigms they used were focussed on memory for facial expressions, discrimination between different facial expressions and interpretation of complex facial expressions such as suspicion. As such they did not examine the relationship between ELS and interpretation of basic emotional expressions. In terms of ERP research, to the author's knowledge, only one study has examined the relationship between ELS and N170 peak amplitude to emotional facial

expressions in mentally healthy adults (Chu et al., 2016).

Given therefore that the majority of the literature in this field has focussed on child populations, it is perhaps unsurprising that the present findings do not initially appear to fit with the existing consensus. The brain undergoes extensive maturation from childhood to adulthood (Koolschijn & Crone, 2013; Lebel & Beaulieu, 2011; Lebel et al., 2008), and as such it cannot be assumed that the effects of ELS will be the same in the child brain as in the adult brain. This is reflected in studies examining the effect of ELS on the structure of the hippocampus (Teicher & Samson, 2016). Studies with adult participants have typically reported an association between higher levels of ELS and reduced hippocampal volume, a relationship that is discussed in detail in § 1.2.2.1. However, in their review article, Teicher and Samson (2016) report that, despite the relative strength of evidence for a relationship between ELS and reduced hippocampal volumes in adult participants, many studies with child participants have not found evidence for such an association (e.g. Carrion et al., 2001; De Bellis et al., 1999). In light of this evidence for effects of ELS on the adult brain which are not present, or have not yet expressed themselves, in the child brain, one potential explanation for the difference in findings between the present studies and previous work is that the present research used adult participants, whilst the majority of previous studies used child participants.

6.2.2.2. Stimulus differences

The previous section discussed the potential role of participant age in explaining the discrepancy between the present findings and much of the broader literature on emotional face processing following ELS. Another potential reason for the discrepancy concerns the stimuli that were used in the present research. These facial stimuli were taken from a database of facial expressions (the 'FACES' database; Ebner et al., 2010). In creating this database, the researchers used two methods to generate angry expressions from the actors (Ebner et al., 2010). Firstly, actors were asked to imagine a situation in which they felt angry and to express the emotion on their face. Secondly, participants were given 'face training' in which they were informed about the position of the facial muscles during the

presentation of anger and asked to use this information to generate their own expression of anger. The angry expressions produced via these methods may not reflect the high level of intensity and threat displayed by a person who is abusing children in their care. Indeed, the mean anger rating (on a scale ranging from 0 'Not at all' to 100 'Very much so') for angry facial expressions in the present research was 72.06, whilst the mean happiness rating for happy facial expressions was 85.88 (Chapter 3). This suggests that the angry facial expressions used as stimuli in the present research were not as extreme as they could have been.

In light of this, it is possible that people with high levels of ELS, who are likely to be more familiar with expressions of anger, rated the angry expressions used in the study as less angry because they could tell that these specific stimuli did not represent full-blown, genuine anger. This may also explain why people with high levels of ELS were less likely to avoid and more likely to approach the angry facial expressions than people with low levels of ELS; this pattern of reduced self-reported avoidance would be expected if the stimuli were not considered to be genuinely threatening. However, it should be acknowledged that most of the studies which found hyper-sensitivity to anger also used posed photographs as emotional face stimuli (e.g. Gibb et al., 2009; Pollak & Kistler, 2002), and the facial stimuli used in the present study were taken from a validated database (Ebner et al., 2010). Therefore, stimulus characteristics are unlikely to fully explain the discrepancy between the present findings and previous research. In light of this, the following section discusses possible additional explanations for this discrepancy.

6.2.2.3. The present findings in the context of rat models of early life stress

The previous sections discussed methodological differences which could explain some of the discrepancies between the present research and the broader literature. However, differences in the age of the sample and in the stimuli used cannot fully account for the present findings, as a study by Gibb et al. (2009), which also used photographs of posed emotional facial expressions (Tottenham et al., 2009), found increased identification of anger

in adult participants with high levels of ELS. Therefore, given that differences in methodological factors cannot fully explain the difference between the present findings and those of previous studies, the following section will address additional work from the rat literature which could account for the present results.

6.2.2.3.1 Early life stress is associated with alterations in fear conditioning, active avoidance and approach of threat in adult rats

As discussed in § 1.4.5, there is some evidence for both reduced fear conditioning and reduced active avoidance of threat in rats which experienced ELS (Madruga et al., 2006; Meerlo et al., 1999; Toth et al., 2008). In addition, increased approach of threat has been reported in rats that experienced ELS. These rats show more active defensive behaviours, such as approaching a predator odour, and fewer passive defensive behaviours, such as freezing (Perry & Sullivan, 2014). Similarly, humans who encountered abuse as children are more likely to show active responses to threat, such as aggression (Malinosky-Rummell & Hansen, 1993; Nicholas & Bieber, 1996). These findings with rats could explain why the participants in the present research showed reduced self-reported avoidance and increased self-reported approach of angry (threatening) facial expressions. However, if this were the case, then one might expect to find a similar pattern of responding to the warning stimuli presented in the avoidance EEG study (Chapter 5), yet responses to these threatening stimuli were not associated with ELS. Therefore, the following section will describe additional findings from rat work which could provide a more parsimonious explanation for the pattern of results found in the present research.

6.2.2.3.2. The sensitive period and attachment to an abusive caregiver

Rats, like humans and other species which depend on a caregiver for survival, show strong attachments to their caregivers regardless of the quality of care that is provided (Perry & Sullivan, 2014; Raineki et al., 2015; Rincon-Cortes & Sullivan, 2014). Indeed, attachment to an abusive caregiver is physiologically adaptive, as without any care the infant will not survive. Attachment to a dam is particularly important during the first days

of a rat's life. Rat pups are born blind and deaf, and have to use odour to locate the dam and receive care. This is supported by a sensitive period lasting from PND1 to PND9 during which rat pups readily learn attachments to odour and aversion learning is minimised (Rincon-Cortes & Sullivan, 2014). This is necessary as the dam may be harsh in her care, carrying the pups around roughly and stepping over them in the nest. If aversion learning were not suppressed, the rat pup could learn to avoid the dam, which would result in the pup's death. Work by Raineki and colleagues (2015) has found that pairing a neutral odour (CS) with a shock (US) during a pup's sensitive period will actually result in a preference for that odour. In addition to this, the cues appear to have a paradoxical 'rescue' effect in adulthood (Raineki et al., 2015; Rincon-Cortes et al., 2015). When adult rats that were abused as pups were presented with odours associated with their abuse, their behaviour was normalised: depressive and social behaviour were improved such that the abused animals no longer differed from rats that were raised in a control condition with no ELS (Raineki et al., 2015).

The rat work described above could explain the pattern of findings reported in the present research with human participants. If a human infant's caregiver is frequently angry, the infant will not reject the caregiver. Rather, they will attach to the caregiver to secure their survival. In this way, the angry face of the caregiver may function in a similar way to the odour associated with shock in the rat model. In rats, preference for the CS (odour) that was paired with the US (shock) continues into adulthood (Raineki et al., 2015). If this finding is applied to human infants, it might be expected that attachment to angry facial expressions (equivalent to an odour CS in rats) would also continue into adulthood in maltreated individuals. This in turn could result in increased approach and reduced avoidance of angry facial expressions. Though this explanation is highly speculative, it is bolstered by the finding that the relationship between higher levels of ELS and reduced self-reported avoidance of angry expressions was specific to angry female faces (Chapter 3). Though infants attach to more than one caregiver, the primary caregiver in early life is often the mother, as she is typically the person who feeds the infant.

The rat work described above could provide an explanation for the

present unexpected finding of a relationship between higher levels of ELS and increased approach of angry facial expressions. In addition, it may also explain why the present findings appear to contradict the general consensus in the wider human literature that higher levels of ELS should be associated with increased avoidance of threat (e.g. Kelly et al., 2015; Pollak et al., 2009). Rat pups only learn to approach odours associated with pain during their sensitive period (Rincon-Cortes et al., 2015). Once they grow older they quickly learn to avoid cues that predict negative outcomes (Rincon-Cortes & Sullivan, 2014). Therefore, it is possible that maltreatment of a human infant during their sensitive period could lead to an attachment to angry faces, whilst maltreatment after this period could lead to avoidance of angry faces.

A definitive account of a sensitive period has not yet been elucidated in human research (Rincon-Cortes & Sullivan, 2014). However, there is evidence to suggest that an analogous period does exist (Gunnar & Fisher, 2006). In rat pups, hypo-sensitivity to threat is mediated by low levels of the stress hormone corticosterone (CORT). When CORT levels are low, amygdala function, and amygdala-dependent aversive learning, are suppressed (Rincon-Cortes & Sullivan, 2014). A comparable period of hypo-sensitivity to threat, involving reduced reactivity of cortisol (the human analogue of CORT), also appears to occur in human infants. This period emerges towards the end of the first year and continues into childhood (Gunnar & Fisher, 2006; Rincon-Cortes & Sullivan, 2014). In light of this, it is possible that a caregiver's frequent anger could have different neurological impacts on the child depending on when in the child's life it occurred. The impact of the timing of ELS on subsequent neurocognitive outcomes is discussed further in § 6.4.2.2.

6.2.3. Early life stress has different effects on early neural processing of emotional facial expressions and early neural processing of non-social learned danger signals

Taken together, the findings from this body of work suggest that ELS is associated with alterations in behavioural and neural processing of social stimuli (emotional facial expressions; Chapter 3; Chapter 4), but is

not associated with behavioural or neural processing of non-social stimuli (warning stimuli; Chapter 5). These findings could be interpreted as a specific effect of ELS on the processing of social stimuli. That is, whilst both angry facial expressions and the warning stimuli discussed in Chapter 5 represent sources of threat, only angry facial expressions represent a source of social threat.

Alternatively, this pattern of findings (atypical processing of emotional facial expressions alongside typical processing of warning stimuli) could reflect differences in the time at which the stimulus category was first encountered. It is unlikely that the participants in the present study were familiar with the 'Greeble' images that were used as warning stimuli (Chapter 5), and even if they had encountered them before, the learned association with the aversive outcome would have been new. In contrast, whilst the participants are unlikely to have seen the individuals posing the emotional facial expressions before, they will have encountered the stimulus categories of angry, happy and neutral facial expressions in early life, during the time at which the stress occurred. Therefore, participants' learned responses to these stimulus categories would have been created many years prior to the present research, whilst their novel learned responses to the 'Greeble' stimuli would have been created during the course of the active and passive avoidance task described in Chapter 5. In summary, ELS may be associated with altered processing of social stimuli but not non-social stimuli, or alternatively it may be associated with alterations in processing of stimuli which were encountered in early life but not with stimuli which were absent during early life.

These interpretations are not necessarily mutually exclusive. In fact, examination of the data in the context of the theory latent vulnerability can encompass both of these interpretations. Given that the theory of latent vulnerability posits that neurocognitive alterations are an adaptive response to a maltreating environment (McCrory & Viding, 2015), this theory should not predict alterations in the processing of every form of threat, but rather it should predict alterations in the processing of specific stimuli that represent threat within the child's environment. Therefore, it would be expected that a child in a maltreating environment would show neurocognitive adaptations

in emotional face processing, as in this context emotional facial expressions could be used to predict the likelihood of abuse. The theory of latent vulnerability would predict that this neurocognitive adaptation (latent vulnerability) would remain as the child grew older, resulting in an adult profile of atypical processing of emotional facial expressions alongside typical processing of threatening stimuli which were not predictive of danger in the early environment.

6.3. Implications of the present findings

As discussed in the previous section, the present body of work found that, in mentally healthy young adults, ELS was associated with reduced identification of anger in angry facial expressions, increased approach of angry facial expressions, reduced avoidance of angry facial expressions, and blunted N170 peak amplitudes to angry, happy and neutral facial expressions. This pattern of findings is in the opposite direction to much of the previous literature on the effects of ELS, which has typically reported hyper-responsivity to threat in children with high levels of ELS. The previous section discussed possible reasons for the discrepancy between the current research and previous findings. The following section will discuss the implications of the current findings.

6.3.1. Early life stress does not have to be extreme to affect psychological, behavioural and neurological outcomes

6.3.1.1. Early life stress scores in previous studies

The following section will compare the CATS scores obtained by the participants in the current research with those obtained by participants in previous studies. Throughout this thesis, the CATS total scores are presented as raw scores (with a possible range of 0 to 152). However, previous research has typically presented mean scores (with a possible range of 0 to 4), which are calculated by dividing the total score by the number of items in the scale (38). Therefore, for ease of comparison with previous research, this section will discuss the present scores in their mean form (raw total divided by 38). The present research involved the recruitment of two samples, the first of which took part in Study 1 (Chapter 3), and the second of which took part in the EEG studies presented in Chapters 4 and 5. The mean CATS total scores for these samples were 0.65 and 0.74 respectively. These scores are broadly in alignment with previous studies with nonclinical population samples. Kent and Waller (1998) reported a mean score of 0.77 amongst a sample of female psychology and nursing students, whilst Sanders and Becker-Lausen (1995) reported mean scores of 0.75 and 0.73 in two large samples of university students. More recently, Lang and Lenard

(2015) found mean scores of 0.53 for men and 0.67 for women in an opportunity sample of research assistants.

Interestingly, the mean score of 1.11 for the high ELS group in the EEG sample was more comparable to mean CATS scores previously reported in patient samples than to CATS scores reported in population samples. Toda et al. (2016) found a mean CATS total score of 0.87 in a sample of participants with major depressive disorder, whilst Hartt and Waller (2002) reported a mean CATS total score of 1.19 in a sample of participants with bulimia. The mean of 1.11 in the high ELS group used in Chapters 4 and 5 occurred even though none of the participants reported any current or past diagnosis of a mental health problem. This finding could suggest that these participants were living with undiagnosed mental health problems, or alternatively that they were resilient individuals who had remained mentally well even though their experiences of ELS were similar to those experienced by patient samples. These possibilities are discussed further in § 6.5.3.

Many studies which examine the effects of ELS recruit individuals who have experienced extreme forms of neglect and abuse, such as being raised in an institution or experiencing abuse which has been documented in clinical or legal records (e.g. Moulson et al., 2009; Pollak & Kistler, 2002). However, very few of the participants who contributed to the current research had experienced such extreme levels of ELS. Even in the high ELS group in the EEG studies, the mean score on the CATS was approximately 42 (mean taken from the sample included in the analyses in Chapter 4), out of a maximum possible score of 152. The highest recorded score across all participants who took part in the present research was 91, though values above 50 were the exception rather than the rule, occurring in only 6.8 % of the full sample used in Chapter 3, and 15.5 % of the full sample included in Chapter 4. However, despite these relatively low levels of ELS overall, higher relative rates of ELS were nevertheless associated with higher scores on measures of depression and anxiety, and with significant alterations in behavioural and neural processing of emotional facial expressions. This finding has important implications for research in this field, as it shows that the effects of ELS are not restricted to those who experienced the most

extreme maltreatment. Indeed, the present findings support the need for a broader societal understanding of what constitutes a potentially harmful early environment.

6.3.2. Early life stress affects behavioural and neural processing in young adults with no diagnosed mental health conditions

One of the crucial findings from the present body of work is that ELS is associated with alterations in behavioural and neural processing of emotional facial expressions even in those with no present or past diagnosis of mental illness. This suggests that the neurocognitive changes associated with ELS may not be exclusive to those with clinically significant mental health problems (though see § 6.4.1.3). Accurate processing of emotional facial expressions is essential for successful social interactions and the maintenance of positive inter-personal relationships (Frith, 2009). In light of this, it is possible that people who experienced high levels of ELS may encounter more difficulties in their social relationships, due to changes in the way they process social cues of emotion. For example, the present research shows that higher levels of ELS are associated with more self-reported approach of individuals displaying angry facial expressions. If this self-reported effect translates into 'real-life' behaviour, it could result in inappropriate approach of angry individuals, which could lead to higher rates of interpersonal conflict (McCrory et al., 2017). This in turn could put the individual at greater risk of mental health problems. Indeed, in the present research, higher levels of ELS were associated with higher scores on questionnaire measures of anxiety and depression. This suggests that though adults who experienced high levels of ELS may be mentally healthy in clinical terms, their quality of life may nevertheless be lower than that of people who experienced low levels of ELS.

6.3.3. Early life stress, depression and anxiety have distinct effects on emotional processing

The present research replicated the well-established relationship between higher levels of ELS and higher scores on measures of depression and anxiety (Heim & Nemeroff, 2001; Kessler et al., 2010). However,

despite this relationship, the effects of anxiety and depression on neural processing were distinct from the effects of ELS. In fact, ELS and depression had opposite effects on the peak amplitude of the N170 to emotional facial expressions, such that ELS was associated with reduced N170 peak amplitudes and depression was associated with increased N170 peak amplitudes (Chapter 4). An additional dissociation between ELS and depression was found in the self-report responses to emotional facial expressions in Chapter 3, such that the effects of ELS were specific to angry facial expressions, whilst the effects of depression were specific to happy facial expressions.

These distinct effects highlight the critical importance of accounting for differences in levels of depression and anxiety when studying the effects of ELS on behavioural and neural processing. As discussed in § 1.2.1.1, many studies in the field of ELS research have not accounted for the possible effects of co-morbid psychological variables. In fact, it is not uncommon to find studies which compare a group of people with high levels of ELS and a diagnosis of a mental health condition with a group of people with low levels of ELS and no diagnosis of a mental health condition (e.g. Bremner et al., 2005; Carrion et al., 2001). This leads to substantial difficulties in delineating the neural effects of ELS from the neural effects of clinical symptomology.

Whilst it is clear that research examining the effects of ELS needs to do more to control for the effects of mental illness, the conflation of these variables is perhaps even more common in clinical research. Despite the well-established correlation between higher rates of ELS and increased risk of mental illness (Heim & Nermeroff, 2001; Kessler et al., 2010), ELS is rarely considered in clinical studies which examine the effect of mental illness on the brain. For example, as discussed in § 4.4.2, the majority of studies to date which examined the impact of depression on N170 amplitudes to emotional facial expressions did not control for ELS (Camfield et al., 2016; He et al., 2012; Jaworska et al., 2012; Maurage et al., 2008; Riwkes et al., 2015). In fact, Teicher and Samson (2016, p.245) go so far as to suggest that ‘maltreatment has likely been an insidious confound in nearly all psychiatric neuroimaging studies’. In light of this, a key

implication of the present research is that studies of ELS must control for mental illness, and studies of mental illness must control for ELS.

6.3.4. Implications for the broader literature on the neurocognitive correlates of early life stress

The present findings provide evidence that the relationship between ELS and processing of emotional facial expressions is not a straightforward case of ELS giving rise to behavioural and neural hyper-responsivity to anger. Rather, the participants in the present research showed behavioural hypo-responsivity to anger in angry facial expressions, and neural hypo-responsivity to angry, happy and neutral facial expressions. This suggests that the relationship between ELS and processing of threat (such as angry facial expressions), and between ELS and processing of social stimuli more broadly, may be more complex than has been previously assumed by researchers in this field.

Additional implications of the current research arise from the present finding that young adults who were exposed to ELS did not show the hyper-responsivity to anger that has previously been observed in children who were exposed to ELS (McCrory et al., 2011; Pollak et al., 2009; Pollak & Sinha, 2002). This suggests that conclusions which are based on findings from child populations cannot be directly extrapolated to adult populations, highlighting the significant need for more research which examines the behavioural and neural effects of ELS in adult participants. However, it is important to note that the present work was cross-sectional, and it is therefore not possible to say whether this particular group of participants would have shown hyper-responsivity to anger if tested as children. In addition, as discussed in § 6.3.5.1, the adult participants in the present research did not experience the extreme levels of ELS (such as abuse documented by governmental authorities) that were encountered by the child participants in many of the previous studies (e.g. McCrory et al., 2011; Pollak et al., 2009). A thorough understanding of the possible manner in which neurocognitive alterations associated with ELS vary across development requires prospective longitudinal studies which follow the

same group of individuals over time (McCrory et al., 2017). The importance of such longitudinal studies is discussed further in § 6.5.4.

6.3.5. Implications for the theory of latent vulnerability

Taken as a whole, the findings of the present research are broadly in accordance with a core tenet of the theory of latent vulnerability (McCrory & Viding, 2015), that ELS is associated with neurocognitive changes which are specific to the early environment that was experienced. For example, the present work found a relationship between ELS and alterations in behavioural responses to angry facial expressions but no relationship between ELS and behavioural responses to happy or neutral facial expressions. This pattern is in line with what would be expected if those with high ELS had experienced an early environment characterised by increased frequency or saliency of angry expressions. In addition, it was found that differences in the N170 response between high and low ELS groups were specific to social stimuli (emotional facial expressions), with no between-group differences in N170 responses to threatening non-social stimuli. As discussed in § 6.2.3, this pattern supports the proposition that neurocognitive changes arise as a response to the early environment; of the two forms of stimuli, only facial expressions would have been present in participants' early lives.

However, it should be noted that the direction of the findings themselves were not generally in favour of other work which has been carried out within the framework of latent vulnerability. For example, work by McCrory, Viding and colleagues has generally found increased threat responsivity in those who experienced ELS (McCrory et al., 2017), yet the present findings could be interpreted as reduced threat responsivity. These discrepancies raise the possibility, discussed in detail in § 6.5.3, that the present findings highlight a pattern of responding that reflects resilience to ELS, rather than vulnerability that has arisen from it. An alternative explanation is that the present sample was better suited to an examination of the behavioural and neural correlates of normative early experiences, rather than an examination of the theory of latent vulnerability itself. This is discussed in detail in the following section.

6.3.5.1. Limitations of conceptualising the present findings within the theory of latent vulnerability

Work on the neurocognitive effects of ELS, especially in terms of face processing, has primarily focussed on either children, or on adults with mental health problems (§ 1.2.3). Therefore, the focus of the present research project was the impact of ELS on mentally healthy adults. However, there are limitations to this approach, especially in the broader context of the ELS literature. Given the close positive association between high levels of ELS and subsequent mental illness, those with very high levels of ELS are likely to be over-represented amongst samples of individuals with mental illnesses (Alvarez et al., 2011; Negele et al., 2015; Teicher & Samson, 2016). In light of this, excluding individuals who report a diagnosis of a mental illness could result in the exclusion of a group of participants with very high levels of ELS whose data could be especially informative. Furthermore, excluding these individuals risks artificially limiting the measure of ELS used in the research, both by increasing the likelihood of removing those with the highest levels of ELS, and reducing the numbers of people with relatively high levels of ELS in the sample as a whole.

The authors of the theory of latent vulnerability caution against the conflation of adversity in the normal range with severe maltreatment (McCrory et al., 2017). They position the theory of latent vulnerability as a framework which is designed to accommodate the effects of severe maltreatment, not the effects of variations in lower level adversity. In light of this, it is acknowledged that the present research is necessarily limited in its ability to contribute fully to an analysis of the theory of latent vulnerability itself.

The theory of latent vulnerability states that high levels of ELS are associated with changes in neurocognitive processes (which can be observed in children and adolescents), and that these changes in turn increase the risk of mental illness later in life. The emergence of mental health problems typically occurs relatively early in the lifespan, with approximately half of lifetime conditions starting by the mid-teens (Kessler et al., 2007). Therefore, it is acknowledged that by excluding young adults with

diagnoses of mental illness, the present research could be excluding the very people who exemplify the trajectory specified by the theory of latent vulnerability. Without these people in the sample, latent vulnerabilities will be more difficult to detect. This represents a potential limitation of the present research. Additional limitations of the research are discussed in the following section.

6.4. Limitations and methodological challenges associated with early life stress research in human participants

The present research was limited by its use of a retrospective self-report measure of ELS, and by sample characteristics such as the mental health of the participants and the level of ELS that they experienced. The present section discusses these limitations of the present research, before addressing the role played by the type and timing of ELS in affecting potential long term outcomes.

6.4.1. Limitations of the present research

6.4.1.1. The use of a self-report measure to quantify experiences of early life stress

One of the major challenges for work examining the effects of ELS in human participants is the difficulty in quantifying and defining individuals' experiences. The present research measured ELS with a retrospective self-report measure of the participants' home environment during their childhood and adolescence (the CATS; Sanders & Becker-Lausen, 1995). The use of such self-report measures has some disadvantages; individuals may deliberately or inadvertently provide inaccurate answers, may not remember past abuse, and may differ in their interpretations of the questions. For example, one question in the CATS (Sanders & Becker-Lausen, 1995) is 'How often were you left alone as a child?' Some participants may interpret the concept of 'often' as referring to a daily occurrence, whilst others may consider 'often' to represent a monthly occurrence. In addition, the CATS provides a measure of home environment across the whole of childhood and adolescence, and does not include a way to determine when the early stress occurred. As discussed in § 3.4.3, this represents a potential limitation of the measure, as the time at which ELS is experienced could have extensive implications for future psychological and behavioural outcomes. As a result of these limitations, the conclusions which can be derived from this research are tentative and require further validation.

However, despite these disadvantages, questionnaires can be a very useful tool for measuring experiences of ELS; although under-reporting of

traumatic experiences does occur, over-reporting is rare (Hardt & Rutter, 2004), and adults' retrospective reports of childhood trauma are relatively stable over time (Yancura & Aldwin, 2009). In addition, questionnaire measures of ELS are able to capture experiences of maltreatment which do not typically come to the attention of authorities, such as emotional neglect or abuse. In this way, questionnaire measures of ELS provide a more nuanced picture of early experiences than studies which use governmental records to recruit individuals with documented cases of severe abuse or neglect (e.g. McCrory et al., 2011; Pollak & Kistler, 2002). Having said this, recruitment of individuals without experiences of extreme early adversity may preclude the identification of some ELS-related neurocognitive alterations which might be apparent in adults who experienced extreme levels of ELS. This potential limitation will be discussed in the following section.

6.4.1.2. Participants in the present research did not have extreme experiences of early life stress

A limitation of the present research is that very few of the individuals who took part experienced extreme levels of ELS. The maximum CATS score for the high ELS group in the EEG studies (Chapters 4 and 5) was 70, out of a possible maximum of 152, and many of the participants in the high ELS group scored below 50. Therefore, on the whole, the high ELS group did not experience extreme levels of ELS. It is possible that the relatively moderate levels of ELS experienced by the high ELS groups in the present research precluded the emergence of experimental effects which might have been present if a group of participants with higher levels of ELS had been recruited. In addition, the absence of extreme levels of ELS in the present research gives rise to difficulties in comparing the present findings with the findings of previous studies, which have typically recruited individuals with extreme experiences of ELS. This is particularly evident in the literature on emotional face processing, where the majority of behavioural and ERP studies to date have been carried out with children who experienced extreme deprivation in the form of institutionalisation (e.g. Moulson et al., 2009; Young et al., 2017),

or extreme abuse in the form of physical abuse which has come to the attention of governmental social services (e.g. McCrory et al., 2011; Pollak et al., 2009). However, whilst the absence of experiences of extreme ELS amongst the participants in the present research represents a limitation in terms of comparability with previous literature, the fact that the present research nevertheless found significant differences between the low and high ELS groups is in itself a testament to the pervasive effects of ELS on the human brain.

6.4.1.3. The mental health of the participants in the present research

The present body of work demonstrates that even relatively moderate levels of ELS are associated with changes in psychological, behavioural and neural alterations in young adults who have not been clinically diagnosed with any mental health conditions. However, it is important to acknowledge that, based on their questionnaire scores, some of the individuals who took part in this research might be diagnosed with a mental health condition if they were assessed by a clinician. For example, examination of the HADS scores obtained by the final sample of participants described in Chapter 4 reveals that one person received a score indicating the probable presence of depression, and 16 people received scores indicating the probable presence of an anxiety disorder (Snaith, 2003).

Therefore, it is essential that future studies which examine the effects of ELS in mentally healthy participants utilise a more rigorous measure of mental wellbeing, such as a structured clinical interview, to ensure that individuals who are recruited to the study do not present with mental health conditions which could go undetected by self-report measures. Having said this, it is important to acknowledge that, though it was possible that some of the participants who took part in the present research could have been experiencing clinical levels of depression or anxiety, the research was nevertheless able to avoid many of the confounds commonly associated with research with clinical populations. For example, none of the participants were taking psychoactive medications, and none of

the participants reported having received any therapeutic intervention for their mental health (Feuerriegel et al., 2015). Having addressed some of the limitations of the present research, the following section will discuss some of the methodological challenges for ELS research as a whole.

6.4.2. Methodological challenges for research on the effects of early life stress in human participants

6.4.2.1. The effect of type of early life stress on subsequent outcomes

Many studies in the field of ELS research, including the studies presented in this thesis, examine ELS as a single construct which encompasses a variety of experiences such as physical abuse, neglect, sexual abuse and emotional abuse. However, this does not account for the growing body of evidence which suggests that different types of ELS may have different effects on neurocognitive development (McLaughlin et al., 2014). McLaughlin et al. (2014) posit that two dimensions of ELS, deprivation and threat, have different effects on the developing brain. They suggest that deprivation is associated with grey matter reductions in association cortices involved in cognitive and social processing, whilst threat is associated with alterations in regions involved in fear learning and extinction, including the amygdala and hippocampus. This theory is supported by work showing that neglect (deprivation) and abuse (threat) have different effects on children's cognitive abilities (Hildyard & Wolfe, 2002), foster children's morning cortisol levels (Bruce, Fisher, Pears, & Levine, 2009), children's behavioural responses to emotional facial expressions (Pollak, Cicchetti, Hornung, & Reed, 2000) and adults' risk for major depression (Infurna et al., 2016). Indeed, a central tenet of the theory of latent vulnerability is that neurocognitive alterations following ELS represent survival adaptations to maltreating environments (McCrory & Viding, 2015). As such, it would be expected that the pattern of adaptation to an environment characterised by high levels of deprivation would be different to the pattern of adaptation to an environment characterised by high levels of threat.

However, whilst examination of the differential impact of deprivation and threat is likely to yield important findings regarding the neurocognitive profile of adults who experienced ELS, in practice the recruitment of participants who only experienced one specific form of ELS is particularly challenging. This is because experience of one type of ELS in isolation is rare (Dong et al., 2004; Kim, Mennen & Tickett, 2017). A study with adult participants found that 87 % of the people who reported one adverse childhood experience (ACE) also reported one or more additional ACEs (Dong et al., 2004), whilst a study with maltreated adolescents found that, over a four year period, neglect co-occurring with emotional and physical abuse was reported more frequently than neglect, emotional abuse or physical abuse alone (Kim et al., 2017).

Having outlined the potential issues with examination of ELS as one construct, it is nevertheless important to acknowledge that subdividing ELS into separate dimensions may not be the best approach for exploratory studies, such as the current research. The present research examined the effect of ELS on mentally healthy adults' emotional face processing and their avoidance of threat, two areas which have previously received very little investigation in mentally healthy adult populations. As such, an initial examination of the effects of ELS as a wider construct was warranted, in order to determine whether or not ELS as a whole is related to alterations in neurocognitive processing in this previously neglected population. Now that this initial work has begun to investigate the relationship between ELS and mentally healthy adults' early perceptual processing of emotional facial expressions, future work can examine whether or not this relationship is differentially related to specific types of ELS.

6.4.2.2. The effect of timing of early life stress on subsequent outcomes

In addition to work showing differential effects of deprivation and threat on neurocognitive outcomes, a growing body of evidence suggests that the effects of ELS also vary as a function of the time at which the stress occurred (Kosten et al., 2012). Lehmann et al. (1999) used a paradigm in which rat pups were separated from the dam for 24 hours on either PND4,

PND9 or PND18. They found that, as adults, rats which had been separated from the dam on PND4 showed reduced fear conditioning to a tone that had been paired with an aversive outcome, and male rats separated from the dam on PND4 showed very poor performance on an active avoidance task. In contrast, rats which were separated on PND9 or PND18 did not differ from control rats on the measures of fear conditioning or active avoidance. In fact, male rats separated from the dam on PN9 even showed a tendency towards enhanced active avoidance, suggesting that the same manipulation (24 hour separation from the dam) introduced during different developmental periods could have opposite effects on behavioural outcomes. Indeed, work with humans has begun to investigate the concept of sensitive periods in development during which individuals are most vulnerable to the effects of environmental stress.

Central to the theory of sensitive periods of development is the theory that the brain regions which are undergoing maturational processes at the time of the stress will be the most sensitive to the effects of that stress (Andersen & Teicher, 2008). Andersen et al. (2008) carried out a seminal study in which they used MRI to examine the neuroanatomy of women who had experienced childhood sexual abuse, but no other forms of abuse, at specific times in their development. The authors examined the relationship between regional brain volumes and sexual abuse during four time periods: three to five years, six to eight years, nine to ten years, 11 to 13 years and 14 to 16 years. It was found that hippocampal volume was significantly related to abuse occurring during the first developmental stage (three to five years), volume of the corpus callosum was associated with abuse which occurred between the ages of nine and ten, and volume of the frontal cortex was associated with abuse between the ages of 14 and 16 years. These findings broadly accord with the developmental time-course of each of these brain regions; whilst the hippocampus undergoes rapid early development, the prefrontal cortex matures later in development, and is less labile than the hippocampus during the first few years of life (Andersen et al., 2008).

Evidence for temporally specific effects of ELS on different brain regions may explain some of the discrepancies in findings across studies. However, it also presents a methodological problem for the study of ELS in

human participants. Whilst animal studies allow researchers to exercise precise control over the timing and duration of ELS, this is clearly not possible with human participants. Even naturalistic experiments which examine the effects of ELS following documented cases of abuse are rarely able to examine temporally specific effects, as children who experience abuse at one stage of life are also likely to experience abuse at other developmental stages as well. Researchers working with a cohort of children from the Bucharest Early Intervention Project have addressed this problem by studying children who were taken into high quality foster care after first being cared for in an institution (Zeanah et al., 2003). The assumption in this case is that the time at which a given child was taken into foster care represents the time at which their ELS ended. As such, the developmental stage(s) at which the ELS occurred can be well defined. However, in most ELS research, it is not possible to demarcate the time at which ELS began and ended. The following section will discuss some of the ways in which future studies could address the methodological issues raised in the present section.

6.5. Future directions

The relationship between ELS and adult mental illness is very well established (Heim & Nemeroff, 2001; Kessler et al., 2010), yet the mechanisms which explain this relationship remain unclear. In light of this, much more research with cross-sectional and longitudinal paradigms is needed, not only to extend our knowledge of such mechanisms, but also to inform interventions which seek to support those who experienced high levels of ELS. Therefore, the following section will discuss some of the potential future directions for the body of work presented in this thesis, and for the field of ELS research as a whole.

6.5.1. Future directions for the present body of work

6.5.1.1. Replication of the current findings

As discussed in § 6.2.2, the findings of the present research were surprising, as they were in the opposite direction to much of the broader literature on the effects of ELS. Therefore, it is particularly important to replicate these studies in order to validate the present findings. In addition to replicating the experiments with larger samples of participants, it would also be informative to examine whether the same experimental paradigms produce similar results in different groups of participants, such as male participants (in the case of the EEG studies) and older adults.

Given that all the participants in the present EEG studies were female, future studies should utilise the same paradigms with a sample of male participants, or a sample which includes both male and female participants. This is because there is some evidence that the effects of ELS on the brain may be sexually dimorphic. For example, the effects of ELS on human hippocampal volume appear to be more pronounced in male adults than in female adults (Everaerd et al., 2012; Frodl, Reinhold, Koutsouleris, Reiser, & Meisenzahl, 2010; Samplin, Ikuta, Malhotra, Szeszko, & DeRosse, 2013; Teicher & Samson, 2016). Therefore, repeating the present EEG experiments with a male or mixed gender sample of participants would make it possible to determine whether or not the present finding of ELS-related alterations in early perceptual processing of emotional facial

expressions is specific to female participants, or whether it extends to male participants as well.

A second direction for replication of the current research concerns the age of the participants. All the participants who took part in the research reported in this thesis were aged between 18 and 25 years old. Work investigating the maturation of the human brain has found that the brain continues to develop throughout adolescence and early adulthood. In fact, the cingulum and uncinate fasciculus, fronto-temporal white matter tracts involved in emotion processing, do not finish maturation until after the age of 25 years (Lebel et al., 2008). Importantly, ELS has been associated with alterations in both of these tracts (McCarthy-Jones et al., 2017; Ugwu, Amico, Carballedo, Fagan, & Frodl, 2015). Therefore, future studies should examine the effects of ELS on neural processing in adults aged 30 and above, in order to determine whether the effects of ELS observed in the current study were specific to the still developing brain, or whether they represent alterations which persist after the brain has reached maturity.

6.5.1.2. Extension of the current findings

A key aim of the present research was to examine the relationship between ELS and alterations in early neural processing (see § 2.1.2). It was found that ELS was associated with processing of angry, happy and neutral facial expressions at the neural level, yet was only associated with processing of angry facial expressions at the behavioural level. This suggests that people who experienced ELS may show compensatory alterations in later neural processes which ensure that atypical early processing of happy and neutral facial expressions does not result in atypical behavioural responding to these expressions (see § 2.1.2 for discussion of the terms ‘early’ and ‘late’ in reference to neural processing). This possibility should be investigated in future research.

For example, future EEG studies could examine the relationship between ELS and the P3 ERP response during processing of emotional facial expressions. The P3 is an ERP response which occurs relatively late (usually well after 300 ms; Luck, 2014), and is comprised of two subcomponents, the P3a and the P3b. Evidence suggests that the P3 is

related to attentional processing, and indexes activity in frontal, parietal and temporal regions of the brain (Polich, 2007). Its association with frontal brain regions along with its relatively late occurrence in the processing stream suggests that the P3 reflects more complex, higher-order processes than the N170, which primarily indexes early perceptual processes (Eimer, 2011a). Previous work has found ELS-related increases in children's P3 responses to angry facial expressions (§ 1.2.2.4), and reduced P3 amplitudes to happy facial expressions in adults with depression (Cavanagh & Geisler, 2006). These findings suggest that the P3 may represent a fruitful avenue for further investigation of the effects of ELS on adults' processing of emotional facial expressions. In addition to EEG studies, fMRI paradigms could be used to examine activation associated with responses to emotional facial expressions in the anterior cingulate and the orbitofrontal cortex, as these regions are involved in higher-order emotion processing (Jehna et al., 2011; Troiani, Dougherty, Michael, & Olson, 2016) and show neuroanatomical changes in people who experienced ELS (Cohen et al., 2006; Dannlowski et al., 2012; De Brito et al., 2013).

Whilst the present findings raise the possibility that ELS could be associated with alterations in early neural processing, it is nevertheless important to acknowledge that the dissociation between the behavioural and early neural correlates of ELS in the present research is based on data from two different groups of participants. One of these groups included male and female participants aged 18 to 19 years, whilst the other included only female participants aged 18 to 25 years. As such, it is possible that the observed dissociation could be attributed to differences between the samples. Therefore, future work should aim to examine the behavioural and neural effects of ELS on emotional face processing in the same study. For example, participants could self-report their behavioural tendencies to approach or avoid specific facial expressions whilst the EEG is being recorded. The EEG data could then be examined to determine whether participants with high and low levels of ELS show differences in early and late neural responses to the emotional facial expressions, and whether the relationship between a participant's neural responses to a given facial

expression and their self-reported ratings of that facial expression differs according to their experiences of ELS.

Finally, as the present research used a cross-sectional approach, it is not possible to determine whether the neurocognitive alterations associated with high levels of ELS act as latent vulnerabilities which increase the risk of mental illness later in life (McCrory & Viding, 2015). This possibility should be investigated in future work using longitudinal paradigms which follow participants for an extended period of time across development. The need for longitudinal paradigms in ELS research is discussed further in § 6.5.4. Having addressed some of the potential future directions for the present research, the following section will examine the future of ELS research more broadly.

6.5.2. Overcoming methodological challenges in the field of early life stress research

Some of the methodological limitations associated with ELS research are difficult to overcome, as ELS in human participants cannot be experimentally controlled. However, there are steps that researchers could take to deal with some of the methodological issues. Firstly, researchers could aim to identify a general time period during which the early stress occurred. The questionnaire used in the present research, the CATS (Sanders & Becker-Lausen, 1995), provides a measure of home environment across childhood and adolescence, which does not differentiate between different stages of development. Future work would benefit from asking participants to provide information on their home environment during distinct stages of development. For example, Andersen et al. (2008) examined the neurological effect of sexual abuse during the following development stages: preschool (3 to 5 years), latency (6 to 8 years), pre-pubertal (9 to 10 years), pubertal (11 to 13 years) and adolescence (14 to 16 years).

Given the co-occurrence of different types of ELS, attempts to recruit participants who experienced only one type of ELS are likely to prove difficult. Indeed, McLaughlin et al. (2014), who argue against measuring ELS as a single construct, do not recommend recruitment of

individuals who experienced only one type of ELS. This is because, given the frequency with which different forms of ELS co-occur, individuals who experience only one type of ELS are not representative of the majority of people who experience ELS. Instead, McLaughlin et al. (2014) suggest that future work should aim to measure the underlying dimensions of ELS, such as deprivation and threat, and examine the relationships between these dimensions and subsequent neurocognitive development. Using this approach, it is possible that researchers will be able to partial out the neurocognitive effects of early experiences of deprivation from the effects of early experiences of threat without having to recruit individuals who experienced only one or the other. Use of this approach is likely to have extensive benefits for a wide range of studies which seek to examine the long-term consequences of ELS.

6.5.3. Neurocognitive alterations as markers of vulnerability or markers of resilience?

6.5.3.1. Neurocognitive adaptations as markers of resilience

Throughout this thesis, the neurocognitive alterations associated with ELS have been interpreted in the context of the theory of latent vulnerability (McCrory & Viding, 2015) as adaptations to a maltreating environment which increase the risk of mental illness later in life. However, it is possible that the same neurocognitive alterations associated with vulnerability in some adults could be associated with resilience[2] in other adults, especially if the individual lives in an unsafe environment for which neurocognitive adaptations to early maltreating environments help protect them from further harm (Ellis, Bianchi, Griskevicius, & Frankenhuis, 2017).

It is also possible that specific neurocognitive processes may be protective for some people who experienced ELS (markers of resilience), and other, different neurocognitive processes may be harmful for some

[2] It is important to specify that in this discussion, the term 'resilience' is not used to represent a general psychological 'toughness' or positive approach to life. Rather, markers of resilience are conceptualised as specific neurocognitive processes which could moderate the relationship between high levels of ELS and subsequent mental illness, such that the likelihood of developing a mental illness following high levels of ELS would be reduced.

people who experienced ELS (markers of vulnerability). These neurocognitive processes may be adaptations associated with experiences of ELS (Yamamoto et al., 2017), or alternatively, they may be processes which did not occur as adaptations to ELS, but which nevertheless act as protective factors for those who did experience ELS (Dennison et al., 2016). Yamamoto et al. (2017) provide some evidence for an ELS-related neurocognitive alteration acting as a resilience marker against subsequent mental illness. Specifically, the researchers examined amygdala activation during a sad mood induction. They found that ELS was associated with increased amygdala activation during the sad relative to the neutral mood condition, and that this increased reactivity was associated with reduced scores on a measure of depression symptomology. Though these findings need to be replicated, they suggest that ELS-related alterations may not always represent vulnerability, and could instead represent resilience. Other work, by Dennison et al. (2016), used a longitudinal design to examine the relationship between reward processing and vulnerability to depression. They found that high levels of reactivity to reward, as indicated by faster reaction times to rewarding stimuli and greater basal ganglia activation to positive relative to neutral images, appeared to be a marker of resilience to depression amongst adolescents with high levels of ELS. Specifically, amongst individuals with low reward reactivity, high levels of ELS at baseline were associated with increased symptoms of depression two years later. However, this relationship was not present in individuals with high levels of reward reactivity. This work suggests that individual differences in neurocognitive mechanisms can represent markers of resilience in people who experienced ELS.

6.5.3.2. Conceptualising the present findings within the framework of resilience

The altered behavioural and neural processing of emotional facial expressions in the present research could represent a marker of vulnerability, or alternatively a marker of resilience. Participants who took part in the present research were screened to ensure that they did not report any current or past diagnosis of a mental health condition. In light of this, it

is possible that the individuals who took part in the present studies were resilient to the negative effects of ELS. If this were indeed the case, it is possible that the pattern of blunted N170 responses to emotional facial expressions could represent a mechanism which has helped the participants to remain mentally well in spite of their experiences of ELS. In this interpretation, the blunted N170 response does necessarily occur as an adaptation to ELS; it could also be explained by other factors such as genetic differences. Alternatively, the pattern of blunted N170 responding to emotional facial expressions could be conceptualised as an adaptation to ELS which acts as a marker of resilience, reducing the individual's risk of developing a mental illness later in life. Both of these interpretations are highly speculative, and require investigation with longitudinal paradigms. The importance of longitudinal research in the field of ELS is discussed further in § 6.5.4.

On the other hand, although none of the participants in this research had been diagnosed with a mental health condition, participants with high levels of ELS did show significantly higher scores on questionnaire measures of depression and anxiety than those with low levels of ELS (Chapter 3; Chapter 4; Chapter 5). It is important to acknowledge that around 25 % of mental health conditions do not appear until after the mid-20s (Kessler et al., 2007). Given that all the participants in the present research were aged 25 or below, it is possible that some of these individuals may go on to develop a mental illness in the future. Therefore, the individuals who took part in this research cannot be reliably classified as resilient to mental illness unless they are tracked longitudinally beyond early adulthood. The utility of using a longitudinal approach when examining the potential neurocognitive consequences of ELS will be discussed further in the following section.

6.5.4. The importance of longitudinal studies

The present research, and most of the wider literature, used a cross-sectional approach to investigate neurocognitive alterations associated with ELS. As a result, it is not possible to determine whether the observed alterations represent markers of vulnerability or markers of resilience, as

this would require research that tracks individuals with high levels of ELS over time. This highlights the need for longitudinal studies which can examine the way in which ELS-related alterations in neurocognitive mechanisms could mediate the relationship between ELS and later mental illness. Longitudinal studies should first record levels of ELS and any ELS-related neurocognitive alterations, then return to the sample a number of years later to measure their levels of anxiety and depression, and to ascertain whether the same neurocognitive alterations can be observed. The resultant data can then be analysed to determine whether specific ELS-related neurocognitive alterations are persistent or change over time, and whether they are associated with increased or decreased rates of mental illness later in life.

To date, only four studies to the author's knowledge have used a longitudinal approach to examine how neurocognitive alterations mediate the relationship between ELS and subsequent mental illness (Danese et al., 2017; Hanson, Hariri, & Williamson, 2015; Kim-Spoon, Cicchetti, & Rogosch, 2013; Kim & Cicchetti, 2010). Of these four studies, only one tracked its participants for long enough to provide information on ELS-related neurocognitive alterations across development, from childhood to adulthood (Danese et al., 2017). Two studies (Kim-Spoon et al., 2013; Kim & Cicchetti, 2010) examined measures of emotional processing (emotion negativity-liability and emotion regulation) as potential mediators between ELS and symptoms of mental health difficulties in children aged 6 to 12 years. Emotion liability-negativity concerns the speed with which an individual reacts to an emotional stimulus and the length of time it takes them to recover from a negative emotional reaction, whilst emotion regulation refers to an individual's ability to modulate their emotional arousal (Kim-Spoon et al., 2013). Kim and Cicchetti (2010) found that, at baseline when the children had a mean age of 8.1 years (Time 1), ELS was associated with lower emotional regulation abilities, which in turn were associated with more externalising symptoms, such as aggressive behaviour, a year later at Time 2. The second study found that at Time 1 (M = 7.5 years), ELS was associated with higher emotion liability-negativity, and that this was associated with poorer emotion regulation a year later (Time 2;

Kim-Spoon et al., 2013). In addition, poorer emotion regulation at Time 2 was associated with higher externalising symptoms at Time 2 (Kim-Spoon et al., 2013). However, whether these alterations in emotion processing could act as a latent vulnerability that increases the children's risk of developing a mental illness later in life is not known (McCrory & Viding, 2015). In order to test this possibility, it would be necessary to track the children for longer, into adulthood.

In another study, Hanson et al. (2015) examined the longitudinal relationships between fMRI measures of reward-related ventral striatum activity, mood, and emotional neglect in a large sample of adolescent participants (n = 106). Participants were first scanned between the ages of 11 and 15 and then again 2 years later. The researchers found that higher levels of emotional neglect were associated with smaller changes in reward-related ventral striatal activity between the two time periods. The extent to which reward-related activity changed over time partially mediated the relationship between emotional neglect (recorded at Time 1) and depression scores recorded at Time 2, two years later. These findings suggest that blunted development of reward-related activity during adolescence is associated with higher levels of depression in people who experienced high levels of emotional neglect. However, given that participants were only assessed at two time points during mid-adolescence, it is not possible to determine whether blunted development of reward-related activity represents a latent vulnerability which would be associated with higher rates of depression in adulthood.

The only piece of work which, to the author's knowledge, has followed participants over decades from childhood to adulthood showed some surprising findings which have important implications for research examining neurocognitive alterations in individuals who experienced ELS. Danese et al. (2017) followed two cohorts of participants, one of which consisted of individuals from the UK who were followed from birth in 1994 to age 18 in 2012, and another of which consisted of individuals from New Zealand who were followed from birth in 1972 to 38 years in 2010. The researchers recorded the occurrence of childhood victimisation (as a measure of ELS) which occurred between the ages of 3 and 12 years old. In

the UK study, forms of victimisation assessed were: domestic violence, frequent bullying by peers, physical maltreatment, physical neglect and emotional or sexual abuse. In the New Zealand study, forms of victimisation recorded were: maternal rejection, harsh parental discipline, two or more changes in the child's primary caregiver, physical abuse and sexual abuse. In addition to the prospective records of these indices of victimisation, both studies collected retrospective self-report measures of victimisation using the Child Trauma Questionnaire (Bernstein & Fink, 1998). Danese et al. (2017) also measured the children's IQ scores at age 5 (UK study) and age 3 (New Zealand study), as well as their socioeconomic status.

The authors took various measures of cognitive functioning in young adulthood (UK study, age 18) and adulthood (New Zealand study, age 38). These measures assessed IQ, executive function, processing speed, memory, perceptual reasoning and verbal comprehension. It was found that higher rates of childhood victimisation (i.e., ELS) were significantly associated with poorer cognitive functioning in adulthood. However, in most cases, this relationship lost significance after accounting for childhood IQ and socioeconomic status. This finding calls into question the results of numerous cross-sectional studies which have assumed a causal relationship between childhood victimisation and the presence of neurocognitive alterations in adulthood.

However, Danese et al.'s (2017) findings should be considered in the context of two key factors. Firstly, low socioeconomic status is itself a form of ELS (Lazzarino, Yiengprugsawan, Seubsman, Steptoe, & Sleigh, 2014; Packard et al., 2011). Consequently, although Danese et al. (2017) showed that childhood victimisation may not be directly related to poor cognitive functioning in adulthood, it cannot be concluded that ELS as a whole is unrelated to poorer cognitive functioning. Rather, the findings suggest that the impact of childhood victimisation on adult cognitive functions may be mediated by the level of daily stress within an individual's environmental context. Specifically, lower socioeconomic status is associated with higher levels of chronic financial and environmental stress and reduced access to resources which could mitigate the impact of victimisation (e.g. high quality schooling, more access to books), whilst higher socioeconomic status is

associated with lower levels of chronic financial stress and more opportunities to access resources which could reduce the impact of childhood victimisation on the brain. The second important factor which should be considered when interpreting Danese et al.'s (2017) findings is that the researchers only assessed cognitive functions; they did not assess social or emotional functions such as threat responsivity. The theory of latent vulnerability (McCrory & Viding, 2015), emphasises the adaptive value of ELS-related alterations in neurocognitive functioning, with ELS-related changes expected to occur in selective functional domains which are relevant to survival in maltreating environments. In light of this, changes in domains which are not directly related to survival in these environments, such as IQ, might not necessarily show ELS-related alterations. In fact, as discussed below, Danese et al.'s (2017) findings could be considered to support the findings of the present research.

Although the present research did not take measures of executive function or IQ, it might be assumed that the participants would have scored highly on these measures, given that the majority were university students who would have had to demonstrate effective cognitive processing in order to achieve the grades required for entry to their university courses. Therefore, it might be predicted that the participants who showed ELS-related alterations in processing of emotional facial expressions in the present study would not have shown ELS-related alterations in measures of IQ and cognitive processing, had these functions been assessed. However, this is a speculative assumption that requires further investigation. Nevertheless, it could be argued that the work by Danese et al. (2017) does not directly challenge the conclusions presented in this research, as its conclusions are specific to executive functions, and not to emotional or social functioning.

6.6. Summary and concluding remarks

The doctoral research presented in this thesis aimed to examine behavioural and neural correlates of ELS in mentally healthy young adults. The first study, presented in Chapter 3, examined the relationship between ELS and self-reported identification of anger and happiness in images of male and female individuals displaying angry, happy and neutral facial expressions, and the relationship between ELS and self-reported approach and avoidance of these stimuli. It was found that ELS was associated with reduced identification of anger in angry female faces, reduced avoidance of angry female faces, and increased approach of angry male and female faces. The second study, presented in Chapter 4, examined the relationship between ELS and early neural processing of male and female angry, happy and neutral facial expressions. Relative to female participants with low levels of ELS, female participants with high levels of ELS showed reduced N170 amplitudes to all emotional facial expressions. The third study, presented in Chapter 5, examined the relationship between ELS and learning-dependent potentiation of the N170 component to warning stimuli during a task of active and passive avoidance learning. In this study, female participants with high levels of ELS did not differ from those with low levels of ELS in the degree of learning-dependent potentiation of the N170 response to the warning stimuli.

This work represents the first investigation of the relationship between ELS and self-reported behavioural tendencies to approach or avoid stimuli displaying angry, happy and neutral facial expressions, and the first to show a relationship between high levels of ELS and reduced identification of anger in angry facial expressions. In addition, this thesis presents the findings of one of the first studies to examine the relationship between ELS and early neural responses to emotional facial expressions in mentally healthy adults. The present results reveal that in mentally healthy young adults, ELS is associated with a pattern of blunted responding to emotional facial expressions at the neural level, and reduced responsivity to angry facial expressions at the behavioural level. This pattern is surprising in the context of previous literature, which has generally shown hyper-responsivity to angry facial expressions, and increased neural activity to

emotional facial expressions more widely (§ 6.2.2). The present pattern of results may reflect a phenomenon reported in the rat literature, whereby the critical importance of forming an attachment to an abusive caregiver paradoxically supports a preference for stimuli which represent the abuse. Alternatively, the discrepancy between the present findings and previous literature may be explained by methodological differences. For example, research has shown that the type and timing of ELS can play an important role in subsequent neurocognitive outcomes. This could also explain why the present research did not find effects of ELS on N170 responses to warning stimuli in the task of active and passive avoidance learning (Chapter 5).

The present body of work comprises some of the first studies to examine the relationship between ELS and changes in behavioural and ERP responses to emotional stimuli in mentally healthy adults. The findings show that neurocognitive alterations associated with ELS can occur even in people who experienced relatively moderate levels of ELS. Furthermore, the findings show that ELS-related neurocognitive alterations are not restricted to adults with mental health conditions; rather they can be observed in adults with no past or present diagnoses of mental illness. An interesting question raised by these findings is whether the neurocognitive alterations observed in this population represent markers of latent vulnerability to future mental illness, or alternatively whether they represent markers of resilience to future mental illness. This question should be answered in future work with longitudinal paradigms which follow individuals across development, from the time of the early stress through to adulthood.

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Appendices

Appendix A. Screening form for participation in the EEG studies

SCREENING FORM

This is the screening form for Elizabeth Kirkham's EEG study. The study is being supervised by Dr Liat Levita. If you have any questions, please contact Elizabeth Kirkham (ekirkham1@sheffield.ac.uk).

This form contains personal questions relating to your medical history and your family history.

Please complete this form yourself and be as accurate as possible.

It is important that you complete every question since your responses will determine whether you can take part in this study.

All information collected using this form will be treated as highly confidential.

Personal details	
First name	
Last name	
Contact number	
Email address	
Date of birth	
Gender	
Handedness (Left, right, ambidextrous)	

What do you consider your country of origin to be?	
Have you taken part in an EEG study before? If so, how many times?	
Can we make your name and information available to colleagues who are seeking research participants?	
Are you happy to be contacted about taking part in future studies run by our lab?	
Additional comments	

Please answer all of the following questions.

If you answer YES to any of the questions, please provide details in the spaces provided.

Your answers to these questions will determine whether it is safe for you to participate in this study. Please answer the questions carefully.

Medical History		
Do you suffer from epilepsy, fits, blackouts, fainting turns or unexplained loss of consciousness, recurrent headaches or migraines?	Yes	No
Details:		
Have you suffered a head injury leading to loss of consciousness requiring a hospital admission?	Yes	No
Details:		

Medical History		
Do you suffer from any other medical condition, including heart problems?	Yes	No
Details:		
Do you have a heart or neural pacemaker?	Yes	No
Details:		
Are you currently taking any prescribed drugs?	Yes	No
Details:		
Do you currently use any recreational drugs, or have you had problems with alcohol or drug addictions in the past?	Yes	No
Details:		
What is your visual correction? *(please tick/highlight)* • Uncorrected vision (no glasses or contacts) • Glasses and contacts • Contacts only • Glasses only & can see at arm's length without them • Glasses only & cannot see at arm's length without them		
Do you have any other problems with your sight (e.g. scotoma, colour blindness, blindness in one eye, night blindness, reduced visual field, blurred vision, or detached retina)?	Yes	No
Details:		
Do you have any problems with your hearing (e.g. loss of hearing, tinnitus)?	Yes	No
Details:		

Medical History		
Do you wear a hearing aid?	Yes	No
Details:		
Have you ever been diagnosed with a mental health condition or developmental disorder (e.g. depression, anxiety, panic attacks, schizophrenia, autism, ADHD)?	Yes	No
Details:		
Are you receiving treatment for any mental health problems (medication or psychological therapy)?	Yes	No
Details:		
Do you have any other medical conditions which the experimenter needs to be aware of?	Yes	No
Details:		

Family History

Have ANY OF YOUR CLOSE RELATIVES ever been diagnosed with a mental health condition or developmental disorder (e.g. depression, anxiety/panic attacks, autism, schizophrenia, ADHD)?

If <u>YES</u>, please give details of the condition and the relationship of the person to yourself.

Relationship	Condition	Details

Family History		

Is there anything else you'd like us to know before you come for the EEG study?	

Appendix B. Example of the check-sheet used in the active and passive avoidance study

Participant ID: _____ Date: _____
Study Version: _____ Questionnaire Version: ____

Thank you for taking part in this study! Please answer the following questions:

1. Please put a mark on the scale below to indicate how aversive you found the loud sound:

Not at all — **Very aversive**

2.

A. Was this a character ever followed by a loud sound?

☐ Yes
☐ No

B. Could you avoid it?

☐ Yes
☐ No

C. If you could avoid it what action did you take?

☐ Made an action – pressed the space bar
☐ Inhibited an action – did not press the space bar

3.

A. Was this a character ever followed by a loud sound?

☐ Yes
☐ No

B. Could you avoid it?

☐ Yes
☐ No

C. If you could avoid it what action did you take?

☐ Made an action – pressed the space bar
☐ Inhibited an action – did not press the space bar