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A matter of habit?

Early life stress and cognitive flexibility in infants

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Abstract

The long-term associations between chronic early life stress such as maltreatment, and cognitive functioning are well documented. However, less is known about the relation between early life stress exposure through experiences of more common potentially stressful life events such as parental separation or moving to a new house, and specific aspects of cognitive functioning in the short term. Cognitive flexibility refers to the ability to shift between response strategies and employ alternative strategies. It is an important ability for successful adaption to changing or novel situations. Previous research has shown that under acute stress, 15-month-old infants display elevated levels of rigid behaviour, being less likely to disengage from performing a habitual action that is no longer effective than their non-stressed counterparts. The present study explores the relation between experiences of potentially stressful early life events and infants' tendency to display this pattern of behaviour that is, cognitive flexibility. Thirty-one 14- to 16-month-old infants participated in an instrumental learning task in their own homes. The task involved the infants initially learning to push two buttons. Each button lit up and produced its own distinct sound when pushed. Next, to establish a habit of button pushing (habit-acquisition), infants were allowed to push one of the buttons until they did not push the button for a period of time (10-s). Finally, at test, infants were given access to both buttons. Pushing the buttons did not result in any light or sound effects. Infants' behaviour during test was assessed. Increased engagement with the habituated button relative to engagement with both buttons was taken as a measure of reduced cognitive flexibility. Participants' caregivers indicated the number and severity of any potentially stressful life events that had occurred for the family during the prenatal and postnatal period. Analyses revealed no significant associations between frequency or severity of stressful life events – experienced during the prenatal or postnatal period – and rigid habitual behaviour in infants. This suggests that potentially stressful early life events do not necessarily lead to higher levels of rigid behaviour in infants. Possible explanations of the present findings are discussed.

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Introduction

Stress is common in modern society and its effects extend beyond physical health and well-being: stress also influences the way we feel and think. Often, these effects are negative. For this reason, stress is generally considered harmful. A general and widely accepted definition of stress in the literature states that stress is the result of experiences that are emotionally and physiologically taxing to such an extent that it surpasses an individual's resources for coping (Avishai-Eliner, Brunson, Sandman, & Baram, 2002; Gunnar & Quevado, 2007; McEwen, 2007; Pechtal & Pizzagalli, 2014). Infants and young children are often considered to be particularly vulnerable to stress exposure. A historic and extreme demonstration of the long-term consequences of exposure to stress in early life, is the fate of the Romanian orphans. After the fall of the dictator, Nicolai Ceausescu in 1989, the international community was horrified by revelations of the grim conditions of state-run orphanages in Romania. This prompted one of history's most comprehensive studies on the effects of institutionalisation, specifically the effects of deprivation and neglect, on the development of young children. Using a methodologically rigorous experimental design where orphans were randomly assigned to be adopted or to remain institutionalised, 'The Bucharest Early Intervention Project' (BEIP), found significant cognitive and language delays, behavioural problems and attention and emotional regulation problems as well as interpersonal relationship issues in young children raised in Romanian orphanages (Chisholm, 1998; Nelson, Furtado, Fox, & Zeanah, 2009; Nelson, Zeanah, Fox, Marshall, Smyke, & Guthrie, 2007; Rutter, 1998; Smyke, Koga, Johnson, Fox, Marshall, Nelson, & Zeanah, 2007). Follow-up studies revealed that, while intervention in the form of foster care placements of some of the orphans, resulted in many of these problems being ameliorated - with some children even catching up to non-institutionalised counterparts - some continued to exhibit cognitive deficits, clinically significant behavioural problems and insecure or atypical attachment patterns (Chisholm, 1998; Gunnar, Morison, Chrisholm, & Schudar, 2001; Nelson et al., 2009). Importantly, developmental outcomes observed in the follow-up assessments were predicted by the length of duration the children spent in the profoundly deprived conditions of the orphanages. In general, the earlier adoption occurred, the more positive the results (Gunnar et al., 2001; Morison & Ellwood, 2000; Nelson et al., 2007; Rutter, 1998). This highlights the crucial role that experiences during the first few months of life can have on development. Although these studies did not look at stress specifically, the results nevertheless highlight the negative effects of early life experiences such as deprivation and neglect, and the undoubted stress associated with such adverse conditions.

While extreme cases such as the fate of the Romanian orphans are rare, many infants or young children will be exposed to stress via more common life events that are experienced by their caregivers such as separating from a partner or spouse, the death of someone close or moving to a new house. At the moment, surprisingly little is known about how the occurrence of such events might be associated with cognitive functioning early in life. The present thesis explores the relations between potentially stressful early life events - in which we include the prenatal period – and an aspect of cognitive functioning in infants: cognitive flexibility.

Early life stress (ELS)

Pechtal and Pizzagalli (2011) define ELS as, “the exposure to single, or multiple events during childhood that exceeds the child’s coping resources and leads to prolonged phases of stress” (p.55). Exposure to stress can start in the womb. Prenatal exposure to stress hormones such as cortisol, is necessary for normal brain development in the developing foetus as well as for maturation of tissues and organs – particularly, the lungs – during late gestation (Bergman, Sarkar, Glover, & O’Connor, 2010; Dean & Matthews, 1999; Kapoor, Dunn, Kostaki, Andrews, & Matthews, 2006; de Vries, Holmes, Heijnis, Seier, Heerden, Louw, Wolfe-Coote, Meaney, Levitt, & Seckl, 2007). However, elevated levels of maternal stress hormones in humans can cross the blood-barrier and may impact on a range of developmental domains (Bergman et al., 2010; Davis & Sandman, 2010; Romens, McDonald, Svaren, & Pollak, 2015). For example, associations have been found between prenatal exposure to elevated cortisol levels and delayed motor development in infancy (Buitelaar, Huizink, Mulder, de Medina, & Visser, 2003); poorer general outcomes in language (Weinstock, 2008); and difficult infant temperament as well as cognitive, behavioural and emotional problems (de Weerth, van Hees, & Buitelaar, 2003; Essex, Shirtcliff, Burk, & Ruttle, Klein, Slattery, Kalin, & Armstrong, 2011; Van den Bergh, Mulder, Mennes, & Glover, 2005). These studies highlight how maternal stress exposure can <u>in</u>directly impact on the development of the child during the prenatal period. Indirect stress exposure can also occur postnatally.

Postnatal exposure to stress. In the postnatal period – that is, shortly after birth and during early development, stress can be experienced either directly, such as in cases of child maltreatment and neglect or, indirectly through a phenomenon termed affect contagion. Affect contagion occurs when an individual, ‘catches’ the affective state - including stress - of another person by simply being around that person, engendering similar internal states themselves (Buchanan, Bagley, Stansfield, & Preston, 2012). Studies have found the occurrence of physiological synchronisation between mother and child dyads in measures of cortisol levels, particularly in highly stressful environments such as those characterised by violence and/or restrictive or punitive parenting styles (Hibel, Granger, Blair, & Fox, 2009), and high anxiety (Williams, Cash, Daup, Geronimi, Sephton, & Woodruff-Borden, 2013). Waters, West and Mendes (2014) found experimental evidence for physiological synchronisation in measures of cardiovascular activity between mothers and infants between 12-14 months of age, following a highly stressful task performed by the mothers. In this study, baseline measures of cardiovascular activity (heart rate) were taken of mother and infant separately. The dyads were then separated, and the mother was assigned to one of three conditions: *positive-evaluation*, *negative-evaluation* or *control*. In each condition, mothers were asked to engage in a stressful task, namely to deliver a five-minute speech about their strengths and weaknesses. After this task, they participated in a five-minute ‘question and answer’ (Q & A) session before reuniting with their infant. In the positive-evaluation condition, evaluators provided positive feedback such as smiling, nodding and leaning forward, during participant delivery of their speech. In the negative-evaluation condition, evaluators provided negative feedback such as frowning, crossing arms, shaking head and leaning back. In the control condition, mothers delivered the speech and verbally answered questions written on a card while alone in a room. When the dyads were reunited, infant cardiovascular activity was again measured (in mothers, cardiovascular responses were measured from baseline throughout the duration of the task, up until the debriefing period). As hypothesised, the study found that the negative-evaluation condition elicited greater cardiovascular activity in mothers than the positive-evaluation and control condition. Crucially, the infants of mothers in the negative-evaluation also showed significantly higher heart rate reactivity when reunited with the mother than infants of mothers in the other two conditions. Further, it was found that the higher the cardiovascular reactivity in mothers, the greater the infants' heart rate responses. This pattern was found to increase over time for dyads in which the mother received negative-evaluation but not for dyads in the other two conditions. This study, once again highlights that, while infants may not fully comprehend the nature of stressful experiences of their caregivers, nor be directly exposed to stressors, they can in a sense, 'pick up on it' and indirectly experience the physiological effects of stress themselves.

Stress and the hypothalamic-pituitary-adrenal axis (HPA)

In order to understand how stress experiences can lead to certain developmental outcomes, it is important to understand the physiological changes that stress experiences produce. One of these physiological changes is alterations in the hypothalamic-pituitary-adrenal (HPA) axis. Alterations in the HPA axis can in turn, affect the stress response. The HPA axis is a neuroendocrine system and is the primary stress system - the other being the sympathetic nervous system (SNS) - that becomes activated when we experience stress. The central components involved in the HPA axis system are located in the hypothalamus, pituitary and brainstem. As well as being involved in responding to stress, the HPA system also maintains a diurnal rhythm of hormone production (cortisol in humans and corticosterone (CORT) in animals) (Dozier, Manni, Gordon, Peloso, Gunnar, Stovell-McClough, Eldrith, & Levine, 2006; Frodl & O'Keane, 2013). The typical diurnal cortisol profile in humans follows a gradual descent from morning to evening. That is, levels are at a peak shortly after waking and thereafter gradually decline throughout the day reaching its lowest levels in the evening.

During experiences of acute stress, the HPA axis is activated and a cascade of biological events ensues. Corticotropin-releasing-hormone (CRH) is released from the hypothalamus, which then acts on the pituitary gland causing the release of adrenocorticotropic hormone (ACTH). ACTH acts on the adrenal gland to secrete glucocorticoids (GC) for example, cortisol (Romens et al., 2015). Glucocorticoids bind with corticosteroid receptors and regulate further release of ACTH and CRH once the perceived stressor subsides causing a negative feedback, resulting in the shutdown of the HPA axis system and restoring homeostasis (Cottrell & Seckl, 2009; Lupien, McEwen, Gunnar, & Heim, 2009; O'Regan, Welberg, Holmes, & Seckl, 2001; Tsigos & Chrousos, 2002). Exposure to repeated uncontrollable chronic stress, can disrupt the normal stress response. In rodents for example, it has been observed that chronic stress decreases the number of corticosteroid receptors, resulting in an increase in circulating levels of glucocorticoids (Weinstock, 1997). Decreased GC receptor cells inhibit the negative feedback action required to restore normal basal levels of cortisol, resulting in elevated circulating levels of ACTH (Barbazanges, Piazza, Le Moal, & Maccari, 1996). Despite the constraints inherent in human research in this area, a growing body of literature suggests associations between early life stress exposure and altered HPA axis functioning (Mello, Mello, Carpenter, & Price, 2003; Lupien et al., 2009). In both animals and humans, alterations in levels of stress hormones and corticosteroid receptors can impair the efficiency of the HPA axis, and can manifest in poor or sluggish regulation, blunted, heightened and/or prolonged stress response (Barbazanges et al., 1996: Kapoor et al., 2006: Weinstock, 1997).

Effects of early stress on HPA functioning

In animals and humans, the specific prenatal psychobiological mechanisms of altered HPA axis functioning in offspring following prenatal stress exposure are currently not fully understood. However, it is hypothesised that prenatal exposure to elevated levels of stress hormones can impact on the stress response via a process termed epigenetic programming. In this view, foetal exposure to elevated stress hormones can have long-lasting or permanent negative effects on the developing brain and result in epigenetic changes that alter gene expression, in this case, in genes that regulate the HPA axis (Essex et al., 2011; Fisher, Van Ryzin, & Gunnar, 2011; Kapoor, Kostaki, Janus, & Matthews, 2009; Kertes, Kamin, Hughes, Rodney, Bhatt, & Mulligan, 2016; O'Donnell, O'Connor, & Glover, 2009; Seckl & Meaney, 2004; Weaver, Cervoni, Champagne, Alessio, Sharma, Seckl, Dymov, Szyf, & Meaney, 2004; Welberg & Seckl, 2001).

Animal studies. Studies on the effects of prenatal stress exposure on HPA axis functioning in animals have found mixed results in that, depending on the type and sex of the animals studied, significant effects or no effects were observed. The types of maternal stress employed include: restraint stress, restriction of nutrient intake, high frequency strobe light and unpredictable noise. The inconsistencies in results of the studies may stem from variations in methodology employed (Kapoor & Matthews, 2005; Kapoor et al., 2006; Weinstock, 2005, 2008). These include the nature (type of stress and chronicity), age and time of day at which the offspring was tested postnatally, whether basal or post-stress levels of ACTH and CORT were measured, the strain of the animal used, and timing of the maternal stress exposure. For example, in guinea pigs, Kapoor and Matthews (2005) found elevated basal ACTH levels in the offspring of mothers exposed to stress during gestation days 50-52. Maternal stress exposure during days 60-62 however, resulted in normal basal ACTH levels in the offspring but elevated stress response. This is suggestive of critical periods during development that are more susceptible to the effects of stress exposure on HPA functioning. Despite the variability in the studies, overall, prenatal stress exposure has been observed to result in increased basal CORT and ACTH levels as well as increased HPA axis responsiveness to stress (Darnaudéry & Maccari, 2008; Egliston, McMahon, & Austin, 2007; Jarvis, Moinard, Robson, Baxter, Ormandy, Douglas, Seckl, Russell, & Lawrence, 2006; Koehl, Darnaudéry, Dulluc, Van Reeth, Le Moal, & Maccari, 1999; Lingas & Matthews, 2001; Maccari, Piazza, Kabbaj, Barbazanges, Simon, & Le Moal, 1995; Morley-Fletcher, Rea, Maccari, & Laviola, 2003; Vallée, Mayo, Dellu, Le Moal, Simon, & Maccari, 1997).

Postnatal stress studies of animals have largely been conducted with rodents and non-human primates. The types of stress observed include: early postnatal disruptions in mother and offspring interactions, in the form of daily separation of infants from their mother for either short term, or longer-term periods; low quality maternal care – in rodents this is characterised by low licking and grooming of their pups; and adverse care such as maltreatment – not uncommon in some non-human primates such as the macaques (Sanchez, 2006). Overall, the studies have found that these stressful early life experiences result in both elevated basal CORT levels as well as stress-induced elevated ACTH levels (Meaney & Szyf, 2005; Sanchez, 2006; Welberg & Seckl, 2001). Moreover, in rodents, HPA hyperactivity – particularly in response to chronic stress – has been shown to persist into later life (Francis & Meaney, 1999; Sanchez, Ladd, & Plotsky, 2001). In contrast, in non-human primates, while chronic ELS - including mother-infant separation paradigms mimicking those used in rodents, as well as child maltreatment observed in much more naturalistic environments - produce initial increased basal CORT levels in infancy and during early stages of development, by the time the primates are juveniles, blunted, lower than normal CORT secretions are observed (Levine & Mody, 2003; Sanchez, Noble, Lyon, Plotsky, Davis, Nemeroff, & Winslow, 2005; Sanchez, 2006). Thus, these studies suggest that chronic stress in early life may induce differential trajectories of HPA axis functioning in later life depending on the animal. At birth, the primate brain for example, is developmentally at a much more advanced state than the rodent brain (Glover, O'Connor & O'Donell, 2010; Sanchez et al., 2005). In rodents, glucocorticoid receptor (GR) expression is low at birth and expression rate does not reach its peak until adulthood, whereas in non-human primates, GR expression is relatively stable from birth through to adulthood (Sanchez et al., 2005). These developmental variations may, in part, account for the differences observed in the long-term effects of ELS on HPA axis functioning – at least in rodents and non-human primates.

Human studies. In contrast to the animal literature, there are no experimental data available on the effects of prenatal stress exposure in human samples. Retrospective and prospective studies of prenatal stress exposure on HPA axis functioning in offspring have generally focused on assessing diurnal cortisol profiles and measures of cortisol and ACTH in response to stress. These are observed alongside measures of maternal self-reported and/or researcher assessed stress and/or cortisol levels during various periods of pregnancy. The types of stressors studied include maternal stressful life events (Entringer, Kumsta, Dellhammer, Wadhwa, & Wüst, 2009), general psychosocial stress and/or pregnancy-specific stress/anxiety (Davis, Glynn, Waffarn, & Sandman, 2011; Gutteling, de Weerth, & Buitelaar, 2004; Tollenaar, Beijers, Jansen, Riksen-Walraven, & de Weerth, 2011), general anxiety (Grant, McMahon, Austin, Reilly, Leader, & Ali, 2009; O'Connor, Ben-Shlomo, Heron, Golding, Adams, & Glover, 2005; Van den Bergh, Van Calster, Smits, Van Huffel, & Lagae, 2008), and exposure to extreme natural disaster (Huizink, Bartels, Rose, Pulkkinen, Eriksson, & Kaprio, 2008). The age range of the offspring evaluated in the studies spans from infancy through to young adult age. Overall, the studies found associations between prenatal stress exposure and measures of basal and stress-induced cortisol and ACTH in the offspring. Generally, the higher the maternal stress exposure, the higher the basal cortisol and stress response. However, as in the animal studies, certain periods of pregnancy showed greater associations than others. For example, in their samples of adolescents, Huizink et al. (2008) and Van den Bergh et al. (2008) found associations between maternal stress exposure and diurnal cortisol profiles of the adolescents *only* if the stress exposure was during the second trimester (14-27 weeks) but not in the first or third. In contrast, in another study, elevated maternal cortisol concentrations in late second and third trimester were found to have the greatest association with cortisol reactivity of newborn infants to a heel-stick blood draw (Davis et al., 2011). Moreover, stress-induced HPA hyper-reactivity may persist into adulthood. Entringer et al.'s (2009a) study consisted of one group of young adults from mothers who were exposed to psychosocial stress during pregnancy (such as the death or severe illness of someone close and relationship conflicts), and a control group of young adults whose mothers were not exposed to psychosocial stress during pregnancy. In the study, both groups participated in the Trier Social Stress Test (TSST), a paradigm that reliably induces significant cortisol, ACTH and cardiovascular responses. In this procedure, participants deliver a free speech and perform a mental arithmetic in front of an audience. Prior to the task, participants in the prenatal stress group had significantly lower cortisol levels compared to the control group - suggestive of an adaptive counter-regulatory effect in response to severe prenatal exposure (Entringer et al., 2009a). However, following the stressful task, the authors found significantly higher levels of ACTH concentrations and a higher increase of cortisol levels in participants whose mothers experienced prenatal stress compared to the control group. Potential postnatal confounding factors contributing to the effects of prenatal stress such as poor maternal care and the presence of other stressors were controlled for. Taken together, these studies suggest that while links are observed between prenatal stress exposure and HPA functioning of offspring at various ages, including in adulthood, there is a need for consistent replications of the studies. This has proven a challenging task given that the results of the existing studies demonstrate that the effects of prenatal stress exposure on the HPA axis are not limited to one specific type of stress.

In studies on how postnatal stress exposure impacts on HPA axis functioning in humans, the findings portray great variability as well. Commonly studied postnatal forms of stress include: child maltreatment (physical, sexual and neglect), institutionalisation, foster care placement, parenting stress, as well as early parental loss and/or loss of other prominent figure(s) through, death, separation or divorce. Ages of samples studied, vary from infancy through to adulthood. A study with 12-20-month-old infants found a relation between parenting stress and higher diurnal cortisol levels (Saridjan, Huizink, Koetsier, Jaddoe, Mackenbach, Hofman, Kirschbaum, Verhulst, & Tiemeier, 2010). Young children (under the age of six) who spend some time in foster care placements (between two and up to 45 months) showed atypical cortisol presentations (Fisher et al., 2011). Bruce, Fisher, Pears and Levine (2009) found both high and low levels of cortisol upon awakening. Dozier et al. (2006) and Fisher et al. found atypical cortisol profiles throughout the day - slightly lower in the morning and elevated in the evening. These findings are not dissimilar to those of non-human primate studies of intermittent mother-infant separations where atypical cortisol responses are also observed (for example, Sanchez, 2005). Gunnar et al. (2001) assessed salivary cortisol profiles in children adopted from Romanian orphanages six and half years after adoption. Higher cortisol levels during the day were found in the orphans adopted after the age of eight months, compared to children adopted before four months and the control group of children who were not adopted. Children adopted before four months exhibited cortisol profiles similar to the control group. This study did not assess stress response nor account for concurrent behaviour of children and family stress. It is possible that raised cortisol profiles may have been due to indirect effects of institutionalisation on children’s behaviour, or family stress stemming from problem behaviours of children (Gunnar et al., 2001). In adults, early parental loss (through death) was associated with higher diurnal cortisol profile (Nicolson, 2004) – even when trait anxiety and current depression were controlled for – and particularly if parental loss was experienced in the context of an abusive home environment (Luecken & Appelhans, 2006). In contrast, Meinlschmidt and Heim (2005) reported *low awakening* cortisol levels in young adults with early loss experiences (through, death, separation or divorce) particularly if multiple losses were experienced. Atypical daily cortisol profiles have been observed in children with exposure to childhood maltreatment. For example, Cicchetti, Rogosch, Gunnar and Toth (2010) observed lower morning and slightly elevated evening cortisol levels in children aged between 7-13 years with a history of childhood physical and sexual abuse. In another study by Cicchetti and Rogosch (2001) of 9-year-old children, maltreatment history resulted in atypical daily cortisol profiles also that were dependent on maltreatment subtype. In adults with early childhood maltreatment histories, higher cortisol awakening levels have been observed (Gonzalez, Jenkins, Steiner, & Fleming, 2008) and that was sustained throughout the morning. Lower baseline cortisol as well as suppressed cortisol and blunted ACTH response to psychosocial stress compared to those without reported early maltreatment, have also been observed (Carpenter, Carvalho, Tyrka, Wier, Mello, Mello, Anderson, Wilkinson, & Price, 2007; Carpenter, Shattuck, Tyrka, Geracioti, & Price, 2011).

Overall, in general, these studies suggest a link between *dysregulation* of HPA axis functioning and postnatal stress exposure rather than a specific direction of outcome. The variabilities of the findings are likely due to the diversity of methodology employed – which specific measures are assessed and when, the age of samples, and whether other possible confounding variables are controlled for - the diverse range of stressors as well as the nature of the stress. For example, chronicity, duration and the differences in timing of stress exposure during development.

Stress hyporesponsive period. Another possible factor that needs to be considered when looking at studies of HPA axis reactivity in response to stress in young children is the possibility of a stress hyporesponsive period (SHRP). In rodents, there is a marked decrease in stress response of the HPA axis between postnatal days 4-14 (Levine, 2001; Schmidt, 2010). During this period, CORT levels in rats are low and it is difficult to induce an elevation. The function of the hyporesponsive period is believed to protect the developing infant from exposure to excess glucocorticoids (Levine, 2001). It has been suggested that there is an equivalent period in humans estimated to begin nearing the end of the first year of life (Gunnar & Donzella, 2002; Tarullo & Gunnar, 2006; Wilkinson & Goodyer, 2011). Shortly after birth, healthy infants exhibit a strong stress response to stressors such as physical examinations, heel-pricks and inoculations. However, towards the end of the first year, significant elevations in cortisol are more difficult to induce at a group level. This may be, at least in parts, due to ethical constraints surrounding the nature of stress induction in infants in an experimental context. For example, the need to terminate the task if intense negative reactivity is induced in the child, the need for the presence of the parent, and severity of the stressor. That is, older infants' tolerance to stress inductions might be higher than that of younger infants and thus require stronger stressors that would be ethically undesirable (Gunnar, Talge, & Herrera, 2009). In humans, the end of the hypothesised SHRP has yet to be pinpointed. Studies of fear-eliciting circumstances that have been conducted with young children up to school age (five-years-old) have found mixed results in that some were either unsuccessful in inducing or finding a significant rise in cortisol in the samples, while some, (for example, Goldberg, Levitan, Leung, Masellis, Nemeroff, & Atkinson, 2003; Lewis & Ramsey, 1995; van Bakel & Riksen-Walraven, 2004), were successful. Thus, while the SHRP is evidenced in rodents and some evidence suggests it *may* exist in humans, the evidence remains inconclusive. Studies have shown conflicting results in stress induction in infants and young children and ethical issues limit our understanding of the extent of the SHRP in humans. For these reasons, and simply because it is difficult in the laboratory to mimic stress responses that may occur in stressful life circumstances, we should not assume if a SHRP exists in humans, that it provides some sort of 'barrier' to the effects of stress exposure during early life on development. As we have seen, exposure to more enduring or chronic stress in early life has the potential to exert alterations in HPA axis functioning. Beyond the HPA axis, stress exposure in early life can also affect brain development. This in turn, can affect cognitive functioning.

Early life stress and later cognitive functioning.

It is well known that during the early years, brain development is characterised by rapid growth and development. Given this, it is rational to posit that the developing brain may be particularly vulnerable to stressful early life experiences during this period. Human and rodent animal studies of postnatal stress exposure, especially recurrent or prolonged chronic stress, have found negative effects on brain development in areas particularly susceptible to the effects of stress hormones. Specifically, chronic stress can impact on the structural and functional development of the prefrontal cortex (PFC) (Arnsten, 2009; Baudin, Blot, Verney, Estevez, Santamaria, Gressens, Giros, Otani, Daugé, & Naudon, 2012; Liston, Miller, Goldwater, Radley, Rocher, Hof, Morrisson, & McEwen, 2006), and the hippocampus (Fenoglio, Brunson, & Baram, 2006; Gould & Tanapat, 1999; McClelland, Korosi, Cope, Ivy, & Baram, 2011; Oomen, Soeters, Audureau, Vermunt, van Hasselt, Manders, Joëls, Lucassen, & Krugers, 2010; Teicher, Andersen, Polcari, Anderson, Navalta, & Kim, 2003; Yang, Han, Cao, Li, & Xu, 2006). The prefrontal cortex and the hippocampus are important areas involved in cognitive functioning. The PFC is involved particularly in the regulation of thoughts, emotions and behaviour to allow us to successfully respond to a changing environment (Arnsten, 2009). The hippocampus is reported to contain the largest region of corticosteroid receptors in the brain and is crucial in terminating the stress response (Barbazanges et al., 1996; Lupien & Lepage, 2001; Son, Geum, Chung, Kim, Jo, Kim, Lee, Kim, Choi, Kim, Lee, & Kim, 2006). In addition, the hippocampus is involved particularly in learning and memory processes (Fenoglio et al., 2006; Oomen et al., 2010; Yang et al., 2006).

Prenatal stress. Animal studies have shown consistently that prenatal stress exposure can have negative effects on cognitive functioning. The animals typically studied are rodents – particularly rats. The age range of animals studied start from as young as five-weeks-old (peri-adolescent in the rat) to older adult. Measures of cognitive functioning in the animals are derived from observation of performance on apparatus such as the Morris water maze (MWM). The MWM (or its variant, the Barnes maze that does not require use of water) is the most widely used apparatus for rodents in measuring spatial learning and memory (Vorhees & Williams, 2006). The apparatus is a circular pool that contains a hidden submerged platform in the centre of a quadrant of the pool. Distal 2-D and 3-D cues in the room are made available for orientation purposes. Animals are placed at one of four different starting points (NESW) along the perimeter facing the wall. Animals are required to find the submerged platform, usually within 60 seconds. Failing that, experimenters either pick up, or guide, the animal to the platform (learning phase). During test phases, measures of latency to find the platform, swim speed, path length and directionality in relation to platform are recorded. Increases in latency to find the platform, path length and more indirect swim paths indicate impairment in these cognitive functions (Vorhees & Williams, 2006). Another measure of cognitive functioning often assayed in animals is novel object recognition memory. The degree of exploration of a novel object, relative to a familiar object, is considered an index of recognition memory (Bevins & Besheer, 2006).

The types of prenatal stress employed in the animals include: restraint stress (mild or chronic, lasting for less than one hour, once a day or several hours multiple times a day) high frequency strobe light exposure, unpredictable foot shocks, prolonged proximal exposure to a large cat, social stress or a combination of these. Duration of prenatal stress exposure is usually 1-2 weeks and typically employed towards the latter stages of gestation. Independent of type of stress employed, and even mild in nature, prenatal stress exposure, impairs spatial learning and working memory (Aleksandrov, Polyakova, & Batuev, 2001; Gué, Bravard, Munier, Veyrier, Gaillet, Recasens, & Maurice, 2004; Lemaire, Koehl, Le Moal, & Abrous, 2000; Markham, Taylor, Taylor, Bell, & Koenig, 2010; Son, Geum, Chung, Kim, Jo, Kim, Lee, Kim, Choi, Kim, Lee, & Kim, 2006; Szuran, Pliška, Pokorny, & Welzl, 2000; Vallée, Maccari, Dellu, Simon, Le Moal, & Mayo, 1999; Yaka, Salomon, Matzner, & Weinstock, 2007; Yang et al., 2006; Zagron & Weinstock, 2006), long-term memory (Gue et al., 2004; Lordi, Patin, Protais, Mellier, & Caston, 2000; Markham et al., 2010), reference memory as well as object recognition memory (Markham et al., 2010). The ages of the animals in these studies varied. However, significant prenatal stress effects on the above measures of cognitive functioning was evident across the ages – whether it was the young, adolescent, adult or older adult being studied. In addition, the effect of prenatal stress was found to be dependent on timing of prenatal stress exposure. For example, Kapoor et al. (2009) found that prenatal stress exposure during gestation days (GD) 50-52 (a period of rapid brain growth) resulted in impaired spatial learning on the MWM, while prenatal stress exposure during GD 60-62 resulted in enhanced spatial learning ability in adult male guinea pigs. Lordi et al. (2000) also found that stress exposure during GD 10 (a time of neural tube development) impaired spatial memory in adult rats. In contrast, stress exposure during GD 19 did not impact spatial memory. Presumably, this lack of effect is due to the foetus' more mature development stage – again highlighting critical periods of development in utero that are more vulnerable to the effects of early stress. The results of these studies demonstrate the potentially negative effects prenatal stress exposure can have on cognitive functioning.

It is important to acknowledge the vast physiological differences between animals and humans and therefore the need to exercise caution when generalising animal findings to humans. At the same time, it is worth pointing out the advantages of a controlled experimental environment employed in animal studies – that are otherwise impractical and/or unethical in human studies. Experimental environments for example, allow for the control of other confounding variables such as genetics, type of stress, duration and chronicity of stress (Davis & Sandman, 2010; Romens et al., 2015).

Despite the limitations surrounding prenatal stress studies in human samples, studies have revealed associations between prenatal stress exposure and cognitive functioning. The types of prenatal stress studied include: maternal anxiety (Brouwers, van Baar, & Pop, 2001; Loomans, van der Stelt, van Eijsden, Gemke, Vrijkotte, & Van den Bergh, 2012; Van den Bergh, Mennes, Oosterlaan, Stevens, Stiers, Marcoen, & Lagae, 2005), cortisol levels (Bergman et al., 2010; Davis and Sandman, 2010), psychosocial stress (Entringer, Buss, Kumsta, Hellhammer, Wadhwa, & Wüst, 2009; Gutteling, de Weerth, Zandbelt, Mulder, Visser, & Buitelaar, 2006; Zhu, Sun, Hao, Chen, Jiang, Tao, Huang, & Tao, 2014), daily hassles (everyday stress) (Buitelaar et al., 2003), and natural disaster (Laplante, Barr, Brunet, Du Fort, Meaney, Saucier, Zelazo, & King, 2004). The ages of the offspring samples include infants, primary school age, adolescents, and young adults. The measures/tests of cognitive functioning include the Bayley

Mental Development Index (MDI) (from the Bayley Scale of Infant Development). The MDI is one of the most widely used test for infants and younger children and evaluates sensory-perception, memory, problem solving and early language (Lowe, Erikson, Schrader, & Duncan, 2012). Other tests include the Test of Memory and Learning (TOMAL) targeted at children and adolescents aged five to 20-years-old. The TOMAL is a comprehensive memory battery of five verbal and five non-verbal memory subtests, plus supplementary subtests measuring, recall, learning and attention (Reynolds & Bigler, 1996).

Overall, prenatal stress exposure is found to be associated with measures of cognitive functioning in infants, young children, adolescents and young adults. In general, in infants and young children (two-years-old and under), high maternal cortisol exposure, high negative impact scores on life events questionnaires, high daily hassles stress, moderate-high maternal anxiety and high stress brought about by natural disaster, were associated with lower scores on the MDI. The associations tended to only be significant if prenatal stress exposure was during the first trimester (Bergman et al., 2010; Buitelaar et al., 2003; Davis & Sandman, 2010; Laplante et al., 2004; Zhu et al., 2014). During normal gestation, maternal cortisol levels increases as pregnancy progresses (Davis & Sandman, 2010). A placental barrier enzyme – 11β-hydroxysteriod dehydrogenase type 2 (11β-HSD2) – regulates foetal cortisol exposure by rendering cortisol to its inactive form, cortisone (Berman et al., 2010). However, this enzyme provides only a partial barrier and as mentioned, excess cortisol can cross the blood-brain barrier impacting on brain development. The time-dependent effects of prenatal stress exposure on cognitive functioning is suggestive of critical or 'sensitive' periods in development during which the brain, undergoing growth spurts at the time of stress, is particularly vulnerable to the effects of early stress exposure (Fox, Levitt, & Nelson, 2010; Lupien et al., 2009).

In five and six-year-old children, maternal anxiety (Loomans et al., 2012) and stressful life events (Gutteling et al., 2006) on the one hand, and measures of cognitive functioning on the other hand show moderate associations. Loomans et al. (2012) assessed processing speed and found greater intra-individual variability in performance on a simple reaction task. Gutteling et al. (2006) administered the TOMAL to five and six-year-old children and found that high negative impact scores on the life events questionnaire predicted lower scores only on the attention index. Authors of both studies note that the degree of stress/anxiety in the samples were relatively low, however. However, van den Bergh et al. (2005) found high maternal anxiety during early stages of pregnancy was associated with lower scores on performance in a cognitive task measuring attention and working memory in a sample of 14-15-year-old adolescents compared to age-matched adolescents of mothers experiencing low anxiety during the same gestation period. Studies of prenatal stress exposure and cognitive functioning in adulthood are scarce. In one of the few existing studies, Entringer et al. (2009b) found that young adult women who were exposed to maternal psychosocial stress demonstrated impaired working memory performance compared to controls who were not exposed to prenatal psychosocial stress. However, the association was found only after the administration of exogenous hydrocortisone in the groups. Under basal conditions the two groups did not differ in performance, indicating a modulating effect of cortisol on prefrontal cortex-dependent cognitive tasks – such as the one used in this study – in young women exposed to prenatal stress. This is believed to be a result of the effect of excess cortisol on reduced expression rates of glucocorticoid and mineralocorticoid receptors in the prefrontal cortex (Entringer et al., 2009b). The lack of difference in performance between the two groups under basal conditions is not to say that differences will not emerge later in life. In animal studies, associations between prenatal stress exposure and reduced cognitive functioning ability have been observed throughout the lifespan. Although the studies vary in methodology – age groups studied, measure(s) of cognitive functioning assayed, type and nature of prenatal stress exposure, whether other confounding variables were controlled for – taken together, as observed in animal models, studies with human samples are suggestive of potentially detrimental effects of prenatal stress exposure on cognitive functioning outcomes in humans.

Postnatal stress. Studies of postnatal stress effects on cognitive functioning in animals have found negative associations. The studies have largely been conducted with rodents. The types of postnatal stress employed include: restraint stress (six hours a day for 28 days) (Luine, 2002), maternal separation (three hours a day for two or three weeks) (Aisa, Tordera, Lasheras, Del Rio, & Ramirez, 2007; Bohacek, Farinelli, Mirante, Steiner, Gapp, Coiret, Ebiling, Durán-Pacheco, Iniguez, Manuella, Moreau, & Mansuy, 2015; Hulshof, Novati, Sgoifo, Luiten, den Boer, & Meerlo, 2011), psychosocial (presence of a large female cat for five days a week for five weeks, or cohabitation with a new older male rat every day for 21 days) (Touyarot & Sandi, 2004), limited bedding/nesting materials (Naninck, Hoeijmakers, Kakava-Georgiadou, Meesters, Lazic, Lucassen, & Korosi, 2015), and a combination of physical and social stress, lasting anywhere from 30 seconds to four hours a day either once or twice a day for 28 days (Isgor, Kabbaj, Akil, & Watson, 2004). The measures of cognitive functioning assayed include spatial learning and memory on the MWM or the radial arm maze, object recognition memory and object location memory. Overall, the studies found impairing effects of postnatal stress on these measures of cognitive functioning in the rodents. In general, postnatally stressed animals demonstrated poorer performance in spatial learning and memory (Aisa et al., 2007; Isgor et al., 2004; Naninck et al., 2015; Park et al., 2001; Touyarot & Sandi, 2004) and in object recognition and object location memory (Hulshof et al., 2011; Luine, 2002; Naninck et al., 2015) than non-stress controls.

Associations between postnatal stress exposure and measures of cognitive functioning have also been observed in human samples. The age range of participants studied include children as young as three-years-old through to adulthood. However, the most common age range studied are preadolescents, adolescents and young adults. The most common type of early stress studied is early maltreatment/abuse and neglect (De Bellis, Hooper, Spratt, & Woolley, 2009; Eisen, Goodman, Qin, Davis, & Crayton, 2007; Gould, Clarke, Heim, Harvey, Majer, & Nemeroff, 2012; Hanson, Adluru, Chung, Alexander, Davidson, & Pollak, 2013; Majer, Nater, Lin, Capuron, & Reeves, 2010; Mezzacappa, Kindlon, & Earls, 2001; Navalta, Polcari, Webster, Boghossian, & Teicher, 2006; Spann, Mayes, Kalmar, Guiney, Womer, Pittman, Mazur, Sinha, & Blumberg, 2012). The Childhood Trauma Questionnaire (CTQ) is a self-report questionnaire often used as a measure for traumatic events/experiences in childhood and includes five categories: physical, emotional and sexual abuse and emotional and physical neglect (Gould et al., 2012). Each category contains five items that participants rate on a five-point Likert scale ranging from “never true” to “very often true”. Examples of questions include: “people in my family hit me so hard that it left bruises and marks” (physical-abuse item) or “I knew there was someone to take care of me and protect me (emotional neglect-inverse item) (Majer et al., 2010). Other early stress studied include: parental separation in the form of foster care placement(s) (Lewis, Dozier, Ackerman, & Sepulveda-Kozakowski, 2007; Lewis-Morrarty, Dozier, Bernard, Terracciano, & Moore, 2012; Mueller, Maheu, Dozier, Peloso, Mandell, Leibenluft, Pine, & Ernst, 2010), and circumstances surrounding war (Pesonen, Räikkönen, Kajantie, Heinonen, Henriksson, Leskinen, Osmond, Forsén, Barker, & Eriksson, 2011; Pesonen, Eriksson, Heinonen, Kajantie, Touvinen, Alastalo, Henriksson, Leskinen, Osmond, & Barker, 2013), institutionalisation in orphanages (Bauer, Hanson, Pierson, Davidson, & Pollak, 2006; Bos, Fox, Zeanah, & Nelson, 2009, Colvert, Rutter, Kreppner, Beckett, Castle, Groothues, Hawkins, Stevens, Sonuga-Barke, 2008), and psychosocial and community stressors (Fishbein, Warner, Krebs, Trevarthen, Flannery, & Hammond, 2009). Overall, relative to normative samples, associations were found between postnatal stress exposure and poorer performance in measures of cognitive functioning in areas of memory (working memory, spatial working memory, visual and verbal), visual attention, visual learning and executive functioning (Bauer et al., 2006; Bos et al., 2009; De Bellis et al., 2009; Eisen et al., 2007; Fishbein et al., 2009; Gould et al., 2012; Hanson et al., 2013; Majer et al., 2010; Pesonen et al., 2011). Furthermore, in a longitudinal study, Pesonen et al. (2013) observed persistence of the negative associations between early postnatal stress (in this case, maternal separation during early toddler years) and cognitive functioning into old age. Participants were tested at

20 years of age for general cognitive ability, then again 50 years later, and displayed comparable results in the two sessions.

Cognitive control (or response inhibition) and set-shifting are considered specific measures of executive functioning that have commonly been studied in young children, preadolescent/adolescents and young adults in relation to ELS. Cognitive control is the ability to inhibit a prepotent (dominant) response and execute an alternative. For example, a cognitive control task that is used for younger children is the 'day/night' task in where children are asked to respond with 'night' when presented with a card with a picture of a sun against a white background, or respond with 'day' if the card is a picture of stars and a moon on a black background (Lewis et al., 2007). Another example used for older children is the 'Stroop task'. In this task participants are required to say the colour of the ink that a colour word is written. For example, the word 'red' may be written in green ink. Generally, the automatic response is to read the written word on a card, or in the case of the 'day/night' task, to respond with the dominant associations with 'sun' (day) and 'stars and moon' (night). Therefore, cognitive control is essential in successfully completing both tasks (Lewis et al., 2007). Set-shifting is the ability to shift attention from one rule (set, principle, dimension, attribute or characteristic) to another (Konishi, Nakajima, Uchida, Kameyama, Nakahara, Sekihara, & Miyashita, 1998). The Dimensional Change Card Sort (DCCS) is one task used as an index of set-shifting in young children. In this task, the experimenter asks the child to sort a series of cards (such as red rabbits and blue boats) into separate piles, according to one dimension (rule), such as colour (pre-shift). After a series of trials, the child is then asked to sort the cards according to another dimension, such as shape (post-shift). Associations are observed between early postnatal stress exposure and poorer performance in cognitive control and set-shifting tasks relative to controls with no early stress exposure. These observations have not only been found in young children (four-six-years-old), with a history of early maltreatment and/or neglect and/or foster care placement(s) (Lewis et al., 2007; Lewis-Morrarty et al., 2012), but also in preadolescents, adolescents and young adults with histories of child maltreatment or institutionalisation as infants or toddlers, (Colvert et al., 2008; Mezzacappa et al., 2001; Mueller et al., 2010; Navalta et al., 2006; Spann et al., 2012) which may indicate a persistency of the impairing influence prenatal stress can have on specific executive functioning.

In sum, a lack of experimental data with humans, variability in methodology and lack of replications in studies presents difficulties in establishing the exact role of stress exposure during early life and cognitive functioning outcomes. Adding further to these issues are the role that other factors such as genes, nutrition, education, and general socioeconomic status, may play. Despite this, the findings of these studies, supplemented with studies with animals under more controlled experimental conditions, are very suggestive of negative effects ELS can have cognitive functioning. Memory is one aspect of cognitive functioning that has been widely studied in the context of stress, particularly acute stress.

Stress and memory systems

It is well known that stress can impact on learning and memory. In the general literature on memory, the most commonly used distinctions are explicit and implicit memory. Explicit memory (or sometimes referred to as declarative memory) refers to our ability to consciously recall names, places, dates and events (Sauzéon, Déjos, Lestage, Pala, & N'Kaoua, 2012; Schneider, 2000). Implicit memory (or nondeclarative or procedural memory) on the other hand, comprises of several abilities such as, the capacity to learn habits and skills (Schneider, 2000). Likewise, in the literature on the role of stress on memory, multiple memory systems are also distinguished. These systems are believed to be anatomically and functionally distinct (Schwabe & Wolf, 2013; Schwabe, Oitzl, Philippsen, Richter, Bohringer, Wippich & Schachinger, 2007). Of interest, is the hippocampus-dependent memory and the caudate nucleus-dependent memory. Caudate nucleus-dependent memory is characterised by simple but rigid and inflexible 'habit' response strategies, processes and behaviour such as stimulus-response (S-R) associations (Schwabe, Dalm, Schächinger, & Oitzl, 2008; Schwabe, Bohbot, & Wolf, 2012). S-R associations are habitual behaviour that is guided by the triggering stimulus and is independent of consequence or outcome (Gasbarri, Pompili, Packard, & Tomaz, 2014; Schwabe, Schächinger, Kloet, & Oitzl, 2010). On the other hand, hippocampus-dependent memory, although more cognitively demanding, promotes flexible 'cognitive' learning and response strategies that is goal-directed (Schwabe et al., 2008; 2012). In addition, hippocampus-dependent 'cognitive' memory is consciously accessible, allowing for transfer of acquired knowledge to novel or changing environments and for successful adaption (Schwabe & Wolf, 2009). In contrast, caudate nucleus-dependent ‘habit’ memory, although useful for performing routine procedures, is not often accessible or helpful in changing situations (Schwabe et al., 2008). The two memory systems are not considered to be independent of each other, but instead possibly working in parallel and simultaneously in a cooperative manner (Schwabe & Wolf, 2013; Schwabe et al, 2012; 2010; 2007). However, accumulating studies strongly suggests they may also be in competition at times and that stress may be a modulating factor in their engagement (Schwabe et al., 2012; 2010; 2008; 2007). Stress hormones (corticosteroids) can promote a shift from flexible ‘cognitive’ to rigid ‘habit’ learning strategies and behaviour (Schwabe & Wolf, 2009; Schwabe, Tegenthoff, Höffken, & Wolf, 2013; Schwabe et al., 2007; 2008; 2010; 2012). This has been well established in animal and human adult samples.

To examine the effect of stress on the use of both memory systems, studies have used tasks that can engage both the hippocampus-dependent and the caudate nucleus-dependent memory systems such as spatial learning tasks (Schwabe et al., 2007; 2008; 2010). For example, Schwabe et al. (2007) found that adult humans who experienced psychosocial stress (TSST) prior to a spatial learning task, favoured use of rigid S-R strategies over ‘cognitive’ spatial strategies than non-stress participants. In the spatial learning task, participants sat in front of a 3-D model of a room that contained a square table in the centre with four identical cards each lying face down in a quadrant of the table. On the underside of one of the cards read “win-card” while the rest read “no-win”. In one corner of the table was a plant (stimulus). In addition, each wall contained one cue: door, picture, window or clock. Furthermore, the walls were removable to allow rotation.

Participants were asked to point to the card they thought was the “win-card”. The participants were not made aware that the “win-card” was always in the same quadrant. The task consisted of 13 trials. For the first 12 trials, the plant was always next to the quadrant with the “win-card”. Between each trial, participants closed their eyes while the room was turned, and the open wall replaced and another removed to provide a new angle view into the room. To establish that learning was in fact occurring and correct guesses of “win-card” was not by chance, “win-card” had to be chosen on three consecutive trials without change on the following trials. On the thirteenth trial, the stimulus (plant) was moved to another corner. Pointing to the quadrant in which the “win-card” was in in the thirteenth trial was evidence of use of spatial strategy. This is because the use of more than one cue in this task is more cognitively demanding and thereby, indicative of employing a spatial learning strategy. On the other hand, choosing the card next to the plant, was taken as stimulus-response strategy. This is because use of a single cue requires less cognitive demand and thereby, indicative of simple stimulus-response learning. Only 11% of the stress group used a spatial strategy compared to 35% in the non-stress group (Schwabe et al., 2007). Thus, stress reduced ‘cognitive’ spatial learning capacity by more than 50%.

In another study by Schwabe & Wolf (2009), the authors found that healthy human adults who were exposed to stress prior to performing an instrumental learning task (tasks that allow participants to learn which behaviour(s) or action(s) elicit a specific consequence or outcome), continued to choose an action that lead to a specific outcome even when the outcome had been devalued. Specifically, in the stress group, prior to the instrumental learning task, participants were exposed to a socially evaluated cold pressor test where they immersed their hand and wrist into ice water (0-2 degrees) for three minutes (or until they could no longer tolerate it). In addition, participants were monitored and videotaped by an unfamiliar person during hand immersion. In the control group, participants immersed their hand into warm water (35 – 37 degrees) for three minutes and were not monitored or videotaped by an unfamiliar person. The instrumental learning task had three trial sets: chocolate milk, orange juice and water (neutral). For each trial set, participants choose between two actions (represented by symbols on a computer screen). One action was associated with a high probability (p = 0.70) of a reward outcome (delivery of one millilitre of either, chocolate milk, orange juice or water, via tubes to mouth of the participants). The other action was associated with low probability (p = 0.20) of the delivery of a common outcome (peppermint tea). Each trial set contained 75 trials. Following completion of the trials, participants ate either oranges or chocolate pudding until they had had enough (subjective satiety). This activity intended to decrease the value of one outcome (food) in relation to the other. Finally, in the test phase (extinction), participants repeated the instrumental learning task. However, this time in each trial and for each action, the rewards were not delivered. Instead, the common outcome (peppermint tea) or, water in the neutral trial, was delivered with a probability of p = 0.20. Across the three trial sets during extinction, the stress group selected the choice of action that was associated with a high probability of the now devalued outcome as often as the high probability action of the valued (that is, the non-devalued) outcome. In addition, the stress group chose the high probability action significantly more often than the low probability action. In contrast, the non-stress group demonstrated a tendency to avoid the now devalued outcome, selecting the high probability action associated with the devalued outcome significantly less often than the valued outcome in the first 15-trial block. Thereafter, the non-stress group randomly selected low and high probability actions across all trial types, demonstrating successful extinction learning (Schwabe & Wolf, 2009). Thus, the non-stress group was suggestive of goal-directed 'flexible' behaviour, indicated by significant reduction in choice of action associated with the devalued outcome relative to the valued outcome. On the other hand, the stress group demonstrated S-R 'habit' behaviour as indicated by persistence in choice of action associated with the devalued outcome despite its devalued effect and, despite no reinforcement.

At the moment, evidence on the modulating effect of stress on the engagement of hippocampus-dependent versus caudate nucleus-dependent memory have been conducted on current stress experiences. Little is known about ELS effects on these memory systems. However, Schwabe et al. (2012) found that stress exposure (major negative life events) in humans as early as in the prenatal period predicts learning strategies in adulthood such that affected persons favour rigid stimulus-response strategies and learning over more flexible spatial strategies. In this study, presented on a computer screen, was a virtual radial eight-arm maze. In the virtual maze, two proximal cues (tree and rock) and two distal cues (mountain and another tree) were made available. In the first part of the task four of the arms were blocked while the other four were opened and contained an object (small golden statue) at the end (not visible from the central platform). Using the forward, left and right keys on the keyboard, participants were tasked to retrieve the objects. In the second part, the participants were allowed access to all arms, however the objects were moved to the previously blocked arms, and participants were instructed to avoid the previously opened arms. Immediately following the last training trial, participants completed a probe (test) trial. The first part mimicked the first part of the training trials. However, in the second part, all the visual cues (both proximal and distal) were removed. If the removal of the visual cues impaired performance of the participants in the second part of the probe trial, this was indicative of the use of spatial strategies. Again, this is because spatial strategies that make use of multiple landmarks and assess their relation to each other, for example, are more elaborate and therefore more cognitively demanding. On the other hand, if performance was not affected by the removal of the cues, this was taken as use of a S-R strategy. This is because, use of a single stimulus, or in this case using a single start point as a stimulus for example, is simpler and less cognitively demanding. Strategy used was also established by analysis of participants' verbal report of how they solved the task. Reports of associations of the arms with numbers or letters or counting the arms from a single start point serving as the stimulus, were classed as S-R strategies. Reports of at least two visual cues and no mention of associations or counting open and closed arms were classed as using spatial strategies. As predicted, the removal of the cues significantly impaired performance of spatial learners compared to response learner (Schwabe et al., 2012). Moreover, participants with prenatal stress exposure to major negative life events reported increased use of a response strategy and decreased in their use of spatial strategy compared to participants with non-stress participants (Schwabe et al., 2012). The effect remained even after controlling for current acute and chronic stress and perinatal complications, early adversity and age and sex of the participants (Schwabe et al., 2012). This suggests that ELS exposure – in this case, prenatal – is associated with later general tendencies to employ rigid stimulus-response strategies over flexible 'cognitive' ones such as, spatial strategies. Furthermore, this study demonstrates this to be the case even in the absence of current stress.

As mentioned, studies of the modulating role of stress on cognitive flexibility have largely been conducted with human adult samples. However, a recent study has provided initial evidence that stress may have a similar effect in infants.

Stress and cognitive flexibility in infants

Flexible 'cognitive' learning and response strategies has also been observed in infants (Seehagen, Schneider, Rudolph, Ernst, & Zmyj, 2015). However, as in adults, stress can interfere with flexible 'cognitive' learning and response strategies in infants. In Seehagen and colleagues' study, 15-month-old infants were randomly assigned to a stress or no-stress condition. In the no-stress condition, infants played in a room with the parent in the absence of the experimenter for a period of 18-minutes. In the stress condition, infants underwent three potentially stress-inducing experiences: stranger episode (contact with an unfamiliar adult), robot episode (self-propelling robot), and separation episode (separation from the parent). The stress manipulation process also lasted a total of 18-minutes. Prior to the stress manipulation period, infants in the stress and no-stress condition displayed similar low levels of cortisol. However, following stress induction, infants in the stress condition exhibited a significant increase in cortisol while no-stress infants did not. In addition to increased cortisol levels, infants in the stress condition displayed longer duration of crying than infants in the no-stress condition. Infants of the stress condition also indicated wanting to be picked up by their parent for longer than did no-stress infants. Finally, parental ratings of their infant's calmness taken pre-and-post stress manipulation, revealed a significant decrease in calmness rate from pre-to-post stress induction in infants in the stress condition. On the other hand, calmness rate of infants in the no-stress condition remained high. Following a debrief period in where the parent played with the infant for 12-minutes in the room, the infants performed an instrumental learning task. In this task, the infants sat on their parent's lap across a table from the experimenter. On the table was a rectangular box with two buttons embedded on the top that, when pushed, each lit up and produced a distinct sound. The task consisted of three phases. During phases I and II, a screen blocked the view of and access to one of the buttons. In phase one (learning), the experimenter demonstrated how to push the visible button, then the infant was given access to the same button. After the infant successfully pushed the button, the procedure was repeated with the other button. In the second phase (habit-acquisition), the infant was again given access to one of the buttons and could push the button as many times as he/she liked until they did not push the button for a period of ten seconds. In the third phase (test), the screen was removed so that the infant had access to both buttons. The infant was given free play for a period of 30 seconds. However, this time the effects (light and sound) of pushing the buttons were removed. Results revealed that in the test phase, infants in the no-stress group pushed the habituated button less often during the last 10 seconds of the 30 second phase than in the first 10 seconds. That is, once the association between the action and outcome (effect) was terminated, the no-stress infants displayed steady disengagement from the habituated button (button they had learnt to push during phase II) across the test phase. In contrast, infants in the stress group *increased* the number of times they pushed the habituated button from the first 10 seconds to the last 10 seconds of the phase. That is, the stressed infants increased persistency in their engagement (stimulus-response action) with the habituated button, even when it was no longer effective. These results demonstrate that, consistent with human adult samples, infants are also vulnerable to the effects of acute stress on cognitive flexibility. However, at the moment, literature is lacking on the effects of ELS on cognitive flexibility in infants, in the absence of current acute stress.

Aims of present study

As reviewed above, there is an abundance of research on the deleterious consequences of chronic ELS on human development, including on cognitive functioning. Much of the research on cognitive functioning looks at the consequences in older children and in adulthood. The literature on the impact of acute stress on cognitive flexibility predominantly focusses on animal models and human adults. However, Seehagen et al. (2015) found similar effects of acute stress on cognitive flexibility in infants. Given that potentially stressful life events are commonplace, exposure to life events is also common in the majority of infants and young children. Therefore, investigating the association between exposure to early life events and cognitive functioning, is important. The present study explores whether there is an association between potentially stressful early life experiences and cognitive flexibility in infants that are *not* currently under acute stress.

The first main aim of the study is to determine whether there is a relation between infant cognitive flexibility and: a) the *number* of life events, and b) the *severity* of life events experienced pre- and postnatally. Specifically, I ask whether infants who have experienced a higher number of life events and/or life events with high severity will display more rigid behaviour patterns than infants who have experienced fewer life events and/or life events of low severity. A second aim is to determine whether there is a difference between exposure to stressful life events in the prenatal period and exposure to stressful life events in the postnatal period in their relationship to infant cognitive flexibility.

It is hypothesised that, given the impairing role of stress on memory systems, particularly on systems that facilitate cognitive flexibility, even when we are not currently under stress; there will be an association between a) the number of life events and b) severity of life events experienced and infants' behaviour during the instrumental learning task. Specifically, it is expected that a higher number or increasing severity of life events will be associated with rigidity in infants' behaviour – that is, that infants will display *increasing* engagement with the habituated button. It is also hypothesised that, given the capacity of stress hormones to cross the blood-brain barrier thereby impacting on a range of developmental domains including on cognitive functioning, there will be an association between <u>pre</u>natal stress exposure and infant behaviour during the instrumental learning task. It is also hypothesised that, given the power *indirect* exposure to stress can have on the physiological stress system of infants, there will also be an association between <u>post</u>natal stress exposure and infant behaviour during the instrumental learning task. Specifically, I predict that the higher the number or severity of life events experienced in either period, the more the infants' behaviour during the 30-s test phase of the instrumental learning task will be characterised by rigidity.

Method

Participants

Participants were recruited via posters distributed to early childcare centres, Plunket rooms and parent and child group (‘mums and bubs’ coffee groups) venues around the western Bay of Plenty area. In addition, participants were recruited via electronic advertisement on the social media website, Facebook and through an adverstisement in the local newspaper. The final sample consisted of N = 31 infants between 14 and 16 months of age. The mean age was 14.6 months, (SD = 0.5). There were 14 females and 17 males. Eleven additional infants were tested but not included in the final sample due to experimenter error (n = 5), infant failure to touch the stimulus (n = 2), fussiness (n = 2) and equipment malfunction (n = 2). All infants were healthy without any known history of developmental delays. All infants in the final sample were born full term (37+ weeks gestation). Most of the infants identified as New Zealand (NZ) European (n = 23), the rest of the infants identified a second ethnicity in addition to NZ European; NZ Māori, Chinese, Filipino, South African, and Samoan. All the participating caregivers in the final sample were the biological mothers of the infants. The study was approved by the School of Psychology Ethics Committee at the University of Waikato.

Materials

Questionnaires.

Life events questionnaires. Potentially adverse life events that might have affected the participating caregiver were identified from previous research and influenced the content of the early life events questionnaires for the present study (Table 1; see appendix E and F for full list). In particular, the events were sourced from The Social Readjustment Rating Scale (SRRS), developed by Holmes and Rahe (1967) and from the Psychiatric Epedimiology Research Interview (PERI) Life Events Scale (Dohrenwend, Askenasy, Krasnoff, & Dohrenwend, 1978). These authors used life events as an indication of stress exposure. The SRRS is a widely used measure in life events and stress research (Dohrenwend, 2006; Scully, Tosi, & Banning, 2000). It is a self-report measure that contains a list of 43 life events that was empirically derived from the authors' own clinical experience with patients from an urban setting in north-western United States. Each of the 43 life events is differentially weighted according to the relative degree necessary for readjustment – that is, for adaptation or accommodation. The scale was constructed to determine the probability of disease onset for an individual, based on the total sum score of the weight for all events experienced. The conclusion being that, the greater the score, the greater the probability of life events being associated with disease onset and the greater the probability of experiencing disease (Holmes & Rahe, 1967). It has since influenced the contents of several life events lists (Dohrenwend et al., 1978; Scully et al., 2000). The PERI Life Events Scale was constructed with the purpose of developing methods for psychiatric epidemiological research in community populations (Dohrenwend et al., 1978). It contains an extensive list of 102 life events covering areas of significance to individuals. These areas include: family, having children, love and marriage, school, work, residence, finances, crime and legal matters, health, and social activities. In the present study, due to time constraints and for the sake of feasibility, only items that have been repeatedly used before in previous research (Entringer et al., 2009a; 2009b) but that covered major areas in life were selected for the life events questionnaire. The areas covered in the questionnaire were: relationships, change(s) in living circumstances, health, financial and employment problems, legal problems, victimization, and involvement in an accident(s) or natural disaster.

The questionnaire consisted of two parts, one covering the prenatal period and one covering the post-natal period (from birth through to the day of assessment). The prenatal section included 27 items. The prenatal section also included a brief questionnaire about the mother's pregnancy. Items regarding the pregnancy included complications that the birth mother may have experienced during her pregnancy, perceived quality of lead maternity care received and immediate neonatal issues such as the need for an incubator or an oxygen tent (See Appendix D). The post-natal section included the same list of life events as the pre-natal with the addition of one item regarding the health of the participating infant since his/her birth, thus totalling 28 items. In each list, caregivers indicated whether or not they experienced the events listed. In the prenatal section, caregivers also indicated in which trimester(s) a particular event occurred. For both the prenatal and post-natal sections, caregivers also indicated how 'undesirable' or 'negatively' they perceived its effect on them if they responded 'yes' to an event. A '0' indicated 'not at all negative', '1' 'somewhat negative', '2' 'moderately negative' and '3' 'very much negative'. The inclusion in the construct of the questionnaire of a subjective appraisal of the events is useful in providing further information about the relations between life events and outcomes (Dohrenwend et al., 1978). For example, Lobel, Dunkel-Schetter & Scrimshaw, (1992) tested the effects of medical risk and prenatal stress on birth weight and gestational age at delivery and found that stress during pregnancy contributed significantly and independently to earlier delivery and low birth weight. Importantly, it was noted that the number of life events was not a significant component of the stress factor, only when appraised as stressful.

Table 1.

Types of Life Events During and After Pregnancy Included in Study

Type of event	
Relationship issues	Got married, divorced, or separated
Change in living situation	Moved house, someone moved in/out, someone close moved away, extra responsibilities; caring for older relative or someone's child
Health issues	Severe illness, physical injury, or hospitalisation
Financial and employment issues	Job loss, new job, excessive pressure or conflict at work, financial pressure or problem, loss of house
Legal problems	Trouble with the law, immigration, or Child, Youth and Family
Victimization	Discriminated, harassed, assaulted
Natural Disaster	E.g. hurricane or fire

Infant mental state questionnaire. To assess if infants might have felt stressed when participating in the instrumental learning task, caregivers were asked to rate how they perceived their infant's mental state during the task. The mental state questionnaire (based on Steyer, Schwenkmetzger, Notz, & Eid, 1997) has been used in previous infant research on the effect of stress on cognitive flexibility (Seehagen et al., 2015) and is comprised of a list of eight mental state descriptions such as ‘relaxed’, ‘tense’, and ‘placid’ (Table 2). Caregivers rated each mood description on a five-point likert scale based on their perception of their infant’s mental state for the duration of the learning task with ‘1’ being ‘not at all’ and ‘5’ being ‘very much so’. Caregiver ratings were summed up to obtain a total score. The maximum score that can be obtained is 40 and the lowest is eight. The mental states: ‘placid’, ‘relaxed’, ‘even-tempered’ and ‘calm’ were reversed for scoring (i.e., a rating of ‘5’ would be reversed to become ‘1’, ‘4’ as ‘2’ and so forth). A low score indicated ‘calmness/low arousal’ while a high score indicated ‘stress/high arousal’.

Table 2.

*Infant Mental State**

	Not at all				Very
	1	2	3	4	5
Restless	O	O	O	O	O
Placid	O	O	O	O	O
Agitated	O	O	O	O	O
Relaxed	O	O	O	O	O
Even-tempered	O	O	O	O	O
Tense	O	O	O	O	O
Nervous	O	O	O	O	O
Calm	O	O	O	O	O

**Note:* Caregivers rate each description based on their perception of their infant’s mental state during the learning task.

Modified Bayley behaviour observation inventory. To obtain some information about the infants’ more general behavioural tendencies, caregivers were asked to complete a questionnaire regarding their infant’s typical everyday behaviour. This questionnaire was a modified version of the Bayley Behaviour

Observation Inventory (Bayley, 2006) and consisted of seven out of the 13 items in the original version. The seven items that were selected for the present study were useful in providing information about how the infants typically approach and engage in novel tasks as well as whether behaviour such as smiling, laughing and exploratory behaviour that may have been displayed during the session are generally typical of the infants. The rest of the items that feature on the original inventory were excluded due to their irrelevance to the present study, particularly in providing further information about the infants' behaviour during the instrumental learning task. Caregivers were asked to indicate the degree to which they perceived each behaviour description applied to their infant on an everyday basis on a three-point scale. Specifically, caregivers rated whether each behaviour description was 'not at all typical' (child is rarely or is never like this), 'somewhat typical' (child is like this some of the time) or is 'very typical' (child is like this most of the time) of the infant. The items in the list were: 'smiles and laughs' (positive affect), 'show enthusiasm and excitement' (enthusiasm), 'explores objects in the environment' (exploration), 'readily takes part in activities' (ease of engagement), 'cooperates with adult requests' (cooperativeness), 'unable to focus on task' (distractibility) and 'approaches new tasks with apprehension' (fear/anxiety). The original questionnaire, in addition to the caregiver rating, includes an examiner rating for each behaviour description. The examiner would rate through observation of the infant during the experimental situation. However, in the present study, the examiner rating was excluded from this questionnaire due to time constraints and the number of tasks the experimenter was set with during the session. Given the brevity of the instrumental learning task and the visit in general, providing an informed rating by the experimenter for the items would be difficult.

Apparatus

Instrumental learning task. The stimulus used in the instrumental learning task was a rectangular box (7 x 40 x 11 cm) composed of synthetic material with a plastic round red button and a round blue button (diameter of each: 8 cm) that were embedded on the top side (Figure 1). The box was made specifically for research purposes and was not commercially available. It was modelled from Hauf and Weichert (2007). Each button lit up and produced its own distinct sound while being pushed. In addition, a screen (25 x 40 x 1 cm) made of the same material as the box was used to block the infant's view of and access to one of the buttons during the first and second phase of the task.

Figure 1: Each button lights up and produce its own distinction sound when pushed. A screen blocks access to one button during Phase I and Phase II

Procedure

General procedure. Caregivers who had expressed interest to participate with their child were contacted via phone or email to discuss the aim and procedures of the study. If the caregiver wished to continue, a suitable time and day to visit the caregiver and their infant in their own home was scheduled. This was a time that was convenient for the caregiver and when the infant was likely to be alert and playful. The visit typically lasted approximately 30 minutes. On arrival at the participant's home, the experimenter provided the caregiver with an information sheet that outlined the purpose and the procedures of the study. The experimenter also provided a verbal explanation of the study. This was followed by an opportunity to discuss any further questions the caregiver had. The caregiver then provided written informed consent. The caregiver was reminded of their right to withdraw at any time for any reason from the study with no penalty. The experimenter then engaged with the infant for a period of time – usually no more than between five to ten minutes. Once it was established that the infant appeared comfortable the experimenter conducted the instrumental learning task. Next, the caregiver was asked to complete the mental state questionnaire and the behaviour observation inventory immediately after the instrumental learning task, followed by the life events questionnaires. At the end of the session, the experimenter thanked the participants and gave the caregiver another opportunity to ask further questions. The infant received a small gift. The experimenter took a photo of the infant for a certificate that was posted out to the participant.

Instrumental learning task. The task was video recorded for offline coding. Prior to commencing the task, the experimenter instructed the caregiver to position the infant on their lap in such a way that the infant could easily access the stimulus (in that their arms were not too restrained) while firmly holding the infant by the hips to encourage him or her to stay on the caregiver's lap. The caregiver was also instructed to refrain from touching the stimulus, demonstrating or verbally describing target actions or stimulus. As in the Seehagen et al. (2015) study, general statements such as "*look*" and "*what's this*?" provided by the experimenter and/or the caregiver were permitted, however, to gain or (re)direct the infant's attention to the task if necessary. This type of 'empty narration' is often used for maintaining the infant's attention without providing any additional information about the target actions (Hayne & Herbert, 2004; Simcock & Barr, 2011) and is widely used in infant research, for example, in imitation studies (Hayne, Herbert, & Simcock, 2003; Herbert & Hayne, 2000; Seehagen & Herbert, 2010).

The instrumental learning task consists of three phases. Across all three phases the infant sits on his or her caregiver's lap across a table from the experimenter. The camera is set up and placed on one end of the table so that it is side on to the participants and the experimenter. In the first phase (the learning phase), the stimulus is placed on the table between the infant and experimenter, out of the infant's reach. The screen is placed so that it blocks the infant's view and access to one of the buttons. The experimenter then demonstrates how to push the visible button three times, with approximately a two-second pause between each demonstration. Pushing causes the button to light up and produce a distinct tone that persists until pushing is released. The experimenter performs the demonstrations with distinct, deliberate movements. The stimulus is then immediately placed within reach of the infant and the infant is given access to the same button to reproduce the effect (Figure 2). The procedure is repeated if the infant fails to reproduce the effect within 15 seconds. Once the infant produces the effect once, the exact same procedure is repeated with the other button (Figure 3). In the second phase (habit-acquisition) the infant is given access again to only one of the buttons and is allowed to push the button as many times and as long as he or she likes until he or she does not push the button for a period of 10 seconds (Figure 4). Pushing produces the same light and tone effects as in the first phase. After no pushing has occurred for at least 10 seconds, the stimulus is removed from the infant's reach. The order of the buttons demonstrated and presented in phases one and two were counterbalanced across infants. In the third and final (test) phase, the experimenter turns off the apparatus inconspicuously and removes the screen. The stimulus is then once again, placed within reach of the infant. The infant now has manual access to both buttons and is allowed to operate them at will for a period of 30 seconds from first touching the apparatus. With the apparatus turned off, pushing of buttons no longer produces the light and sound effects. This extinction procedure ensures that the infants only use information about associations between a particular action and outcome that they acquire during phases I and II, (Schwabe & Wolf, 2009; Seehagen et al., 2015).

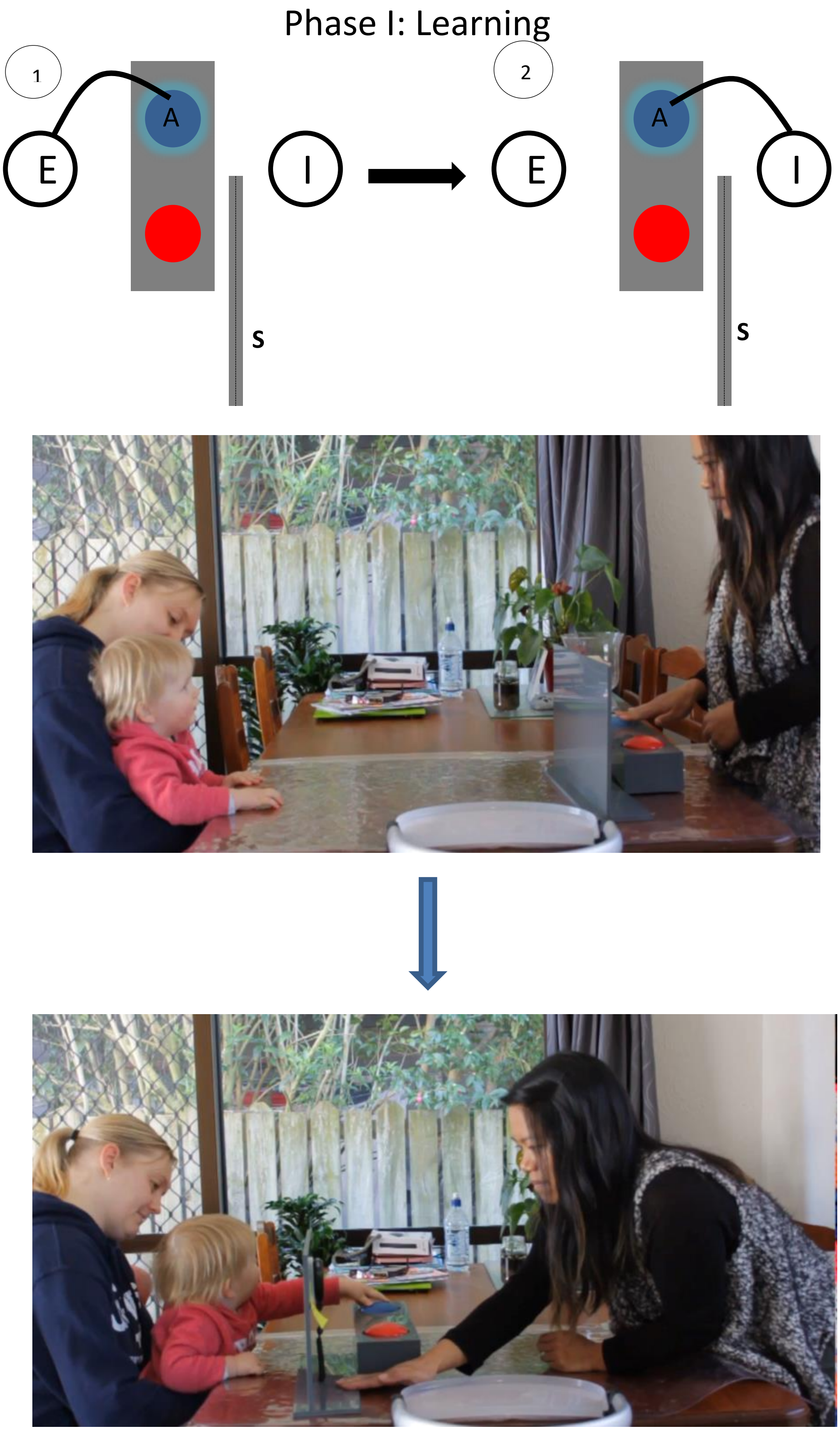

Figure 2: Experimenter demonstrates how to push first button before allowing infant to imitate action. E = experimenter; I = infant; S = screen

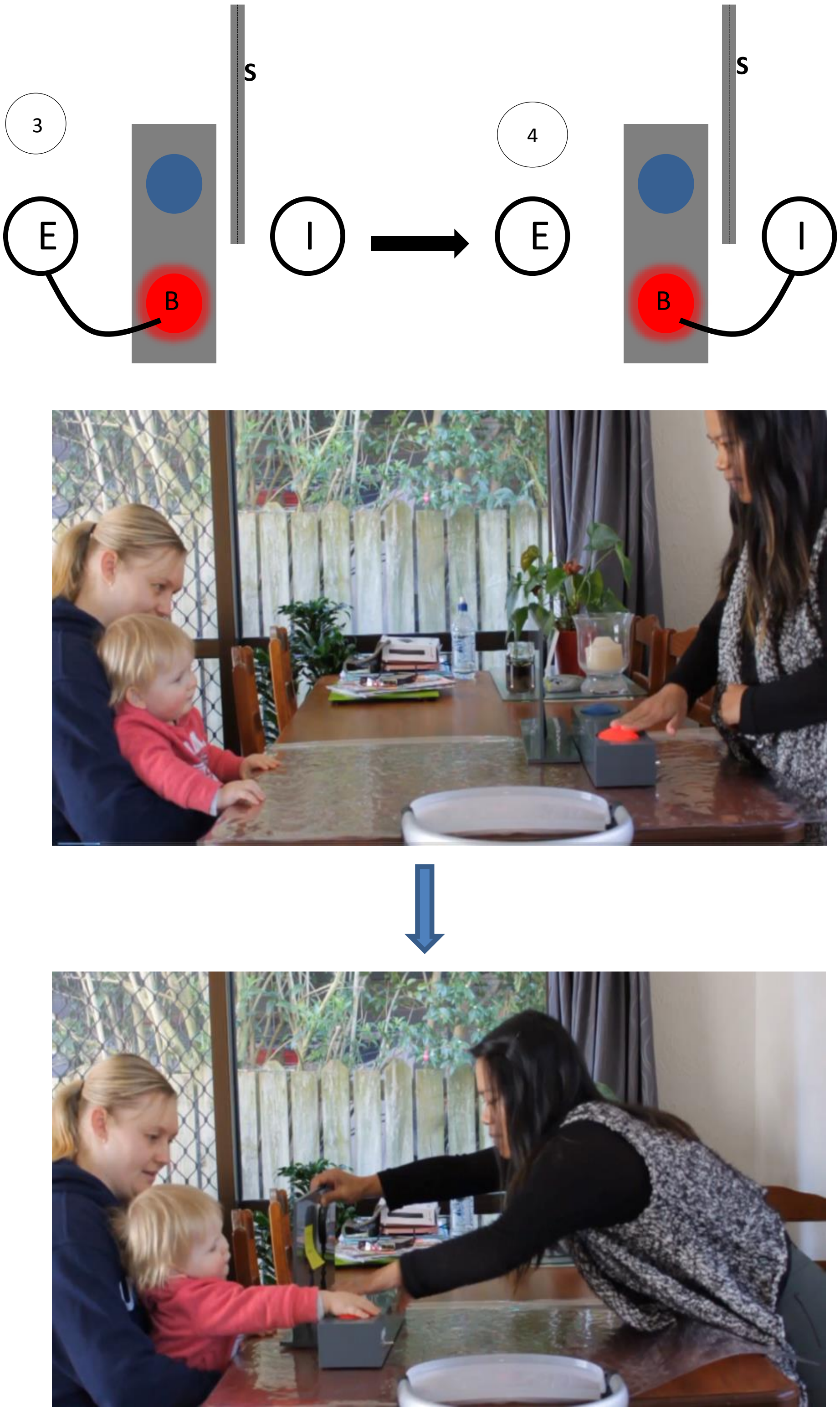

Figure 3: Experimenter demonstrates how to push second button before allowing infant to imitate. E = experimenter; I = infant; S = screen

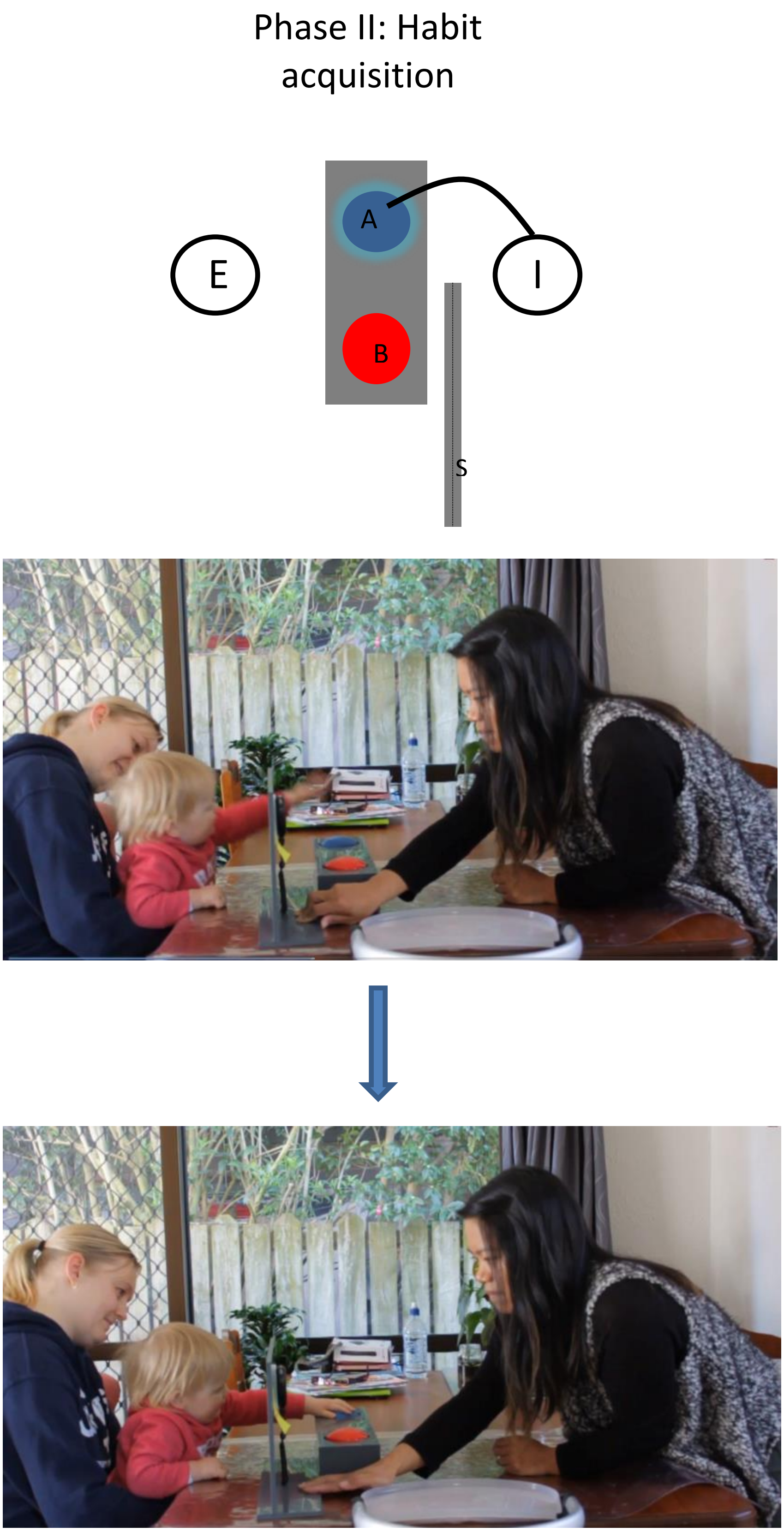

Figure 4: Infant pushes habituation button until he/she does not push for a period of 10-s. E = experimenter; I = infant; S = screen

Phase III: Test

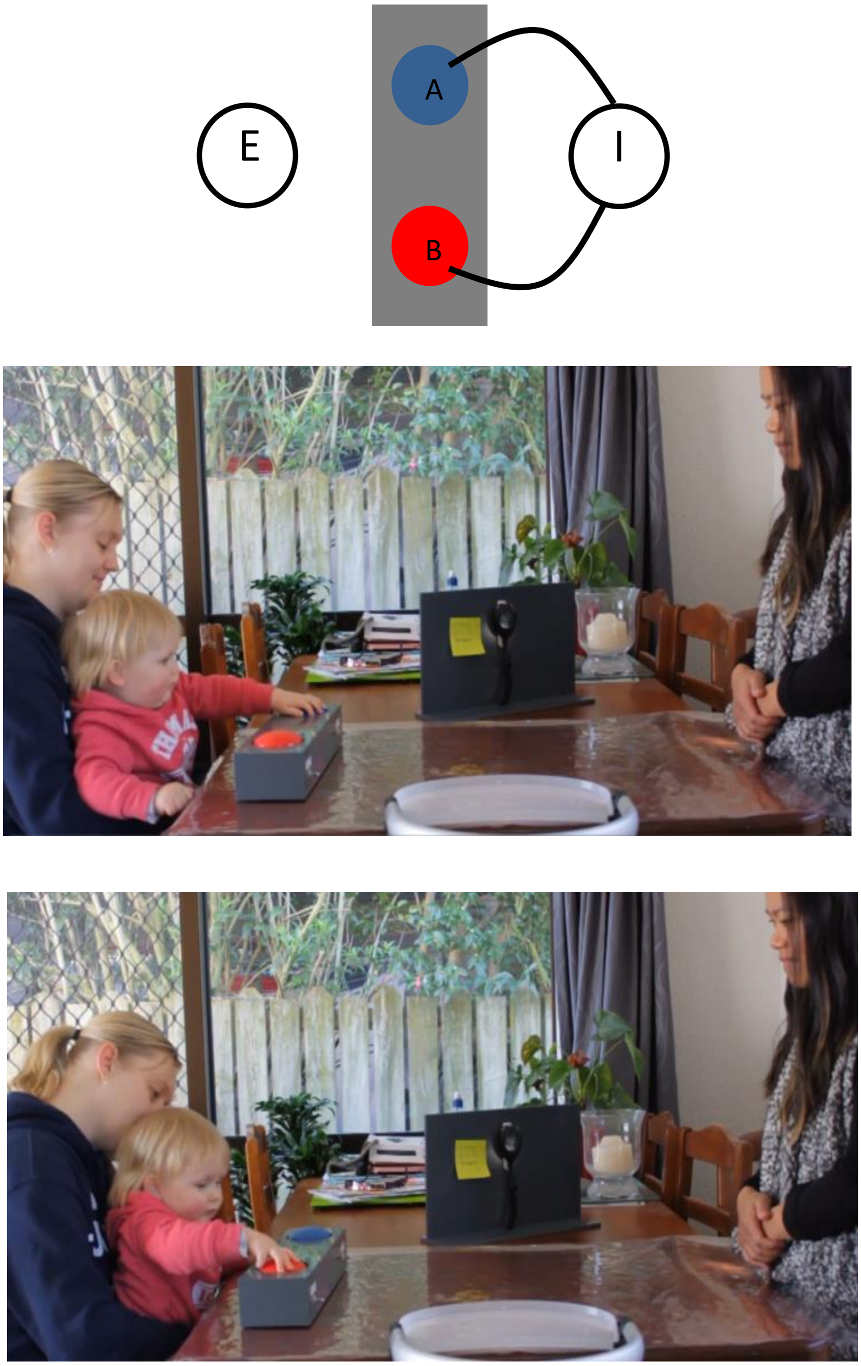

Figure 5: Apparatus is switched off and infant has access to both buttons for a period of 30-s. E = experimenter; I = infant

Coding

Each infants' video of the instrumental learning task was coded using the software 'The observer XT'. In phase I (learning), the experimenter coded the number of times the experimenter demonstrated pushing each button before the infant pushed the respective button him or herself. In phase II (habit-acquisition), the experimenter coded the number of times the infant produced the effects. In the final phase (test), because the effects were no longer producible, the experimenter coded the number of times the infant *touched* each button during the first 10-s interval of the 30-s test phase from first touch of apparatus. Next the experimenter coded the number of times the infant touched each button during the second 10-s interval. Finally, the experimenter coded the number of times the infant touched each button during for the last 10-s interval. Ten infant test videos were coded by a second independent coder (a trained research assistant) to establish inter-rater reliability (IRR). In phase I, agreement was 100% for the number of demonstrations required for each button. In phase II, agreement was 89% for the number of times the effect was produced. In the test phase, agreement was 81% for the number of times infants touched each button.

Statistical Analysis

Data analysis was conducted with IBM SPSS Statistics software Version 20. Statistical significance level was set at 0.05 (two-tailed). Correlation analyses were conducted to determine relationship between infants' behaviour during instrumental learning task and the frequency and severity of stress exposure during the prenatal and postnatal period. For additional analyses, the infants were divided into a low-stress and a high-stress group. First, the groups were divided based on the number of life events indicated during the prenatal period. Then, the infants were divided based on the severity of life events during the prenatal period. The same procedure was applied for the postnatal period. For each combination of low-stress and high-stress group, independent t-tests were conducted to compare infants' behaviour during phase I and phase II of the instrumental learning task between the two groups. To assess cognitive flexibility, and again for each combination of low-stress and high-stress group, mixed-model ANCOVAS were conducted to compare infants' engagement with the habituated button during the test phase of task between each group.

Results

Participant characteristics

Table 3.

Characteristics of Study Sample (n = 31)

	Mean (SD)/Range or Number (%)
Infant age at testing (months)	14.6 (0.5)/14-16
Maternal age (years)	32 (4)/24-39
Infant ethnicity	
NZ European	23 (74%)
NZ Maori	1 (3%)
Biracial/Multiracial	7 (22%)
Planned pregnancy	26 (84%)
No. of other children	
None	14 (45%)
1	14 (45%)
2 or more	3 (10%)
Maternal education	
No qualification	0
Secondary	4 (13%)
Tertiary	22 (71%)
Higher education	5 (16%)
Maternal occupation	
Housewife	8 (26%)
Teacher/Education	6 (19%)
Healthcare/Medical	2 (6%)
Trades and services	5 (16%)
Retail and consumer products	2 (6%)
Other	8 (26%)
LMC service rating	4.5*
Necessary requirements during or after birth	
Emergency caesarean	8 (26%)
Forceps or ventouse	2 (6%)
Incubator	1 (3%)
Oxygen tent	0
Extended stay in hospital	9 (29%)
Other	6 (19%)

* Maximum score = 5 where 1 = very poor, 5 = excellent

As can be seen from Table 3, the sample predominantly consisted of mothers who had completed tertiary education and of infants who had either none or no more than one sibling.

Caregiver questionnaires

Life events questionnaire. Overall, the perceived mean severity rating for the life events ranged between ‘somewhat negative’ to ‘moderately negative’ (Table 4). Moved or looked for a new home was the most common life event experienced by the mothers during the prenatal period and the postnatal period, 39% and 52% respectively. However, overall, it was not perceived as highly stressful during either period. On the other hand, unusually big pressures or conflict at work and starting a new job was perceived as the most stressful life events during the prenatal period. Postnatally, someone close (other than the participating child in this project) sustaining a serious physical injury, illness or hospitalisation, was perceived as the most stressful life event. Due to the small sample size, data analysis on the effects of timing of life events occurring during pregnancy were not conducted.

Pregnancy complications. Items on the pregnancy complications questionnaire were given a severity rating of 1 for ‘mild’, 2 for ‘moderate’ or 3 for ‘severe’ (Table 5). One of the most common pregnancy complications experienced by the mothers were hypertension (19%) – with a group mean severity score of M = 2.5. Six of the mothers (19%) indicated experiencing a pregnancy complication not listed on the questionnaire with a group mean severity score of M = 1.8. These complications included, a large ovarian cyst, underactive thyroid, large fibroid, and coccyx (pelvic) pain – all of which were rated as being 'mild' in severity. One mother experienced low iron levels throughout pregnancy and indicated it as being 'moderate' in severity. One mother experienced preeclampsia and rating severity as 'severe'. Three of the mothers experienced hyperemesis gravida (severe nausea and vomiting), with a mean severity score of M = 2.7. While only one mother indicated poor foetal growth and only one mother indicated experiencing premature rupture of membranes, both were rated as being 'moderate' in severity.

Table 4.

Most Frequent Life Events Experienced by Mothers During the Prenatal and Postnatal Period and Mean Severity Rating

Life Event	Number		Percentage		Mean severity score*	
	Pre-natal	Post-natal	Pre-natal	Post-natal	Pre-natal	Post-natal
Moved or looked for a new home	12	16	39	52	0.6	1.0
Unusual financial pressure or money troubles	8	11	26	35	1.6	1.3
Looked for work for 3 weeks or more	3	10	10	32	0.6	1.0
Started a new job	5	8	16	26	2.1	0.3
Lived apart from spouse/partner due to job, travel or other practical reasons	8	7	26	23	1.0	1.3
Someone close sustained a serious physical injury, illness or hospitalization	7	5	23	16	1.7	1.8
Unusually big pressures or conflicts at work	7	3	23	10	2.1	2.0

Note. *Maximum total = 3, where 0 = Not at all negative, 1 = Somewhat negative, 2 = Moderately negative, 3 = Very much negative

Table 5.

Pregnancy Complications Experienced by Mother and Mean Severity Score

	Number	Severity*
Diabetes	2	1.5
Placenta previa/abruption/haemorrhage	2	1.5
Hypertension	6	2.5
Hyperemesis gravida	3	2.7
False labour	3	1.7
Poor foetal growth	1	2.0
Premature rupture of membranes	1	2.0
Maternal infection	1	1.0
Other condition(s) of foetus	0	
Other condition(s) of mother	6	1.8

Note. *Maximum score = 3, where 1 = mild, 2 = moderate, 3 = severe

Infant questionnaires

Infants' mental state. The infant mental state questionnaire provides an indication of the infants' stress levels during the instrumental learning task. The minimum score that can be obtained = 8, and the maximum score = 40. A high score is indicative of high stress and a low score is indicative of low stress. As a group, the infants' stress level was relatively low with a group mean score of M = 13, SD = 5, range = 8-27.

Bayley behaviour observation inventory. Each of the seven items on the Bayley behaviour questionnaire were given a rating of 0 if the caregiver rated the behaviour as 'not at all typical of the child', 1, if, 'is somewhat typical of the child' or 2, if, 'is very typical of the child'. Overall, as a group, the mean scores for each behaviour item indicate that the infants were 'very typical' in displaying positive affect (M = 1.9), enthusiasm (M = 1.9), exploration (M = 2.0), and ease of engagement (readily taking part in activities) (M = 1.8). Cooperativeness was rated as 'somewhat typical of the child' with a group mean of M = 1.5, while distractibility, and fear/anxiety (approaches new tasks with apprehension) were not at all typical of the infants: *M* = 0.6 and *M* = 0.4, respectively.

Instrumental learning task

We first analysed the infants' behaviour in the instrumental learning task at a group level. In the first (learning) phase, the mean number of demonstrations (one demonstration equals three times producing the light and sound effect) required by the experimenter before the infants pushed the respective buttons themselves was *M* = 1.32, *SD* = 1.04 for the blue button and *M* = 1.13, *SD* = 0.56 for the red button. In the second (habituation) phase, the mean number of times the infants pushed the button was *M* = 24.74, *SD* = 23.56, range = 1-101. In the test phase, to determine the infants' behaviour across time, the phase was divided into three 10 second intervals: 0-10 s, 10-20 s, 20-30 s. Then, the proportion of times the infants touched the habituated button relative to touching both buttons was calculated for each interval. For example, during the 0-10 s time interval, infant "Jack" touched the habituated button once and the non-habituated button three times. The total number "Jack" touched each button is then combined to give a total of four. Since "Jack" touched the habituated button once out of a total of four, this would give him a proportion score of: 0.25 or 25%. A repeated measures ANOVA test revealed that, as a group, the infants displayed a significant change in the infants' pushing behaviour over time: $F(4, 120) = 4.38$, $p = 0.002$ (Figure 6). Follow-up t-tests reveal that relative to touching both buttons, the infants touched the habituated button significantly more often during the first (0-10 s) interval than the second interval: $t(30) = 3.58$, $p = 0.001$. However, there was no significant difference in infants touching the habituated button during the first and last interval: $t(30) = 1.70$, $p = 0.094$. There was also no significant difference in the infants touching the habituated button during the second and last interval: $t(30) = 1.62$, $p = 0.110$. The infants' means for touching each button during the test phase are displayed in Table 6.

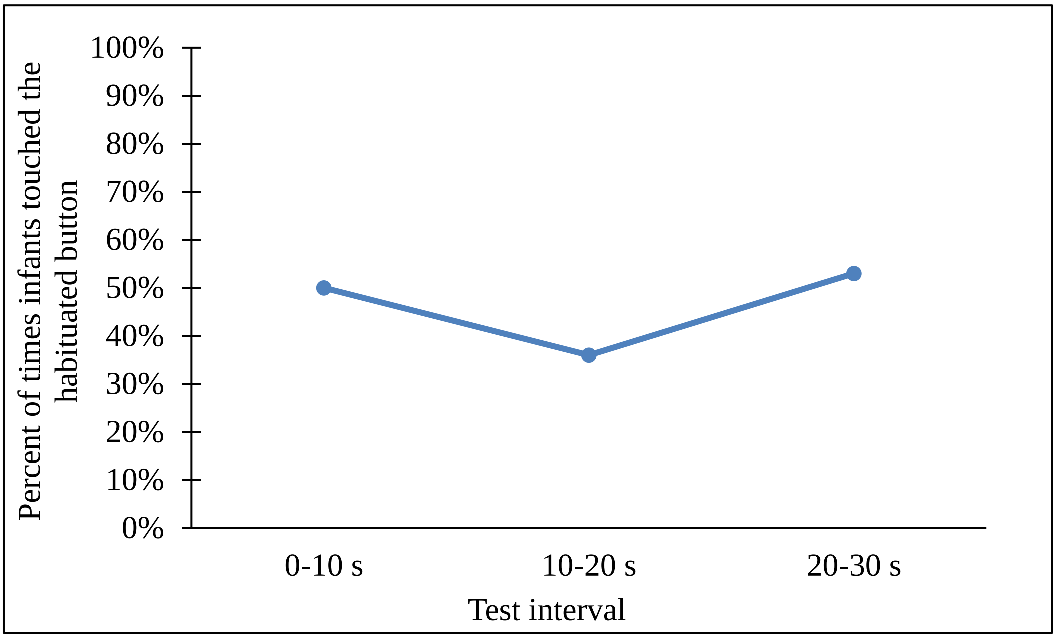

Figure 6: Percentage of times infants touched the habituated button relative to touching both buttons during test phase.

Table 6.

Mean Number of Times (SDs in parentheses) Infants Touched Buttons During Test Phase of Instrumental Learning Task

Test interval	Habituated button	Non-habituated button
0-10 s	2.29 (1.37)	2.48 (1.60)
10-20 s	1.30 (1.18)	1.32 (1.11)
20-30 s	1.68 (1.47)	1.74 (2.16)

Relations between life events and infants' behaviour during test phase

Our main question of interest was how the infants' behaviour in the instrumental learning task was related to exposure to stressful life events. In addition, we wanted to determine whether there was a difference between exposure to stressful life events in the prenatal period and the postnatal period and each period's relation to the infants' behaviour in the learning task. Thus, we conducted correlation analyses for each period (prenatal and postnatal) separately to determine whether there were significant relations between the infants' behaviour during the test phase of the instrumental learning task and: a) the number of life events experienced, b) the total sum severity score of life events and c) the total sum severity of pregnancy complications. To do this, first the test phase was, once again, divided into three 10 second time intervals: 0-10 s, 10-20 s, and 20-30 s.

Next, the proportion of the number of times each infant touched the habituated button relative to touching both buttons across each time interval was calculated. Finally, to assess the infants' engagement with the habituated button relative to both buttons across the 30 second test phase, a difference score was calculated for each infant. To do this, the proportion score during the first 10-second interval (0 – 10 s) was subtracted from the last 10-second interval (20-30 s). If the difference score is positive, this indicates that relative to touching both buttons, the infant touched the habituated button more in the first 10 seconds than they did in the last 10 seconds of the test phase. If the difference score is negative, the reverse is true – the infant touched the habituated button more during the last 10 seconds than the first 10 seconds. A positive correlation between x and y would indicate that the higher the number of life events or the higher the severity of life events experienced, the higher the difference score would be. This would indicate a decrease in engagement with the habituated button (relative to both buttons) over time as the number or severity of life events increases. On the other hand, a negative correlation would indicate that the higher the number of life events or the higher the severity of life events experienced, the lower the difference score would be, indicating *increasing* engagement with the habituated button (relative to both buttons) over time as the number or severity of life events experienced, increases. We would expect the latter to be true: the higher the stress (number or severity of life events) experienced, the lower the difference score.

There was no significant correlation between the number of life events during the prenatal period (Figure 7) or the postnatal period (Figure 8) and infants' engagement with the habituated button relative to both buttons in the test phase: $r = 0.05$, $p = 0.76$, and $r = 0.10$, $p = 0.60$, respectively. There was no significant correlation between the severity of life events in the prenatal (Figure 9) or the postnatal period (Figure 10) and infants' engagement with the habituated button in the test phase: $r = 0.197$, $p = 0.288$ and $r = 0.032$, $p = 0.862$, respectively. There was also no significant correlation between severity of pregnancy complications and infants' touching of the habituated button relative to touching both buttons during the test phase, $r = 0.190$, $p = 0.306$ (Figure 11).

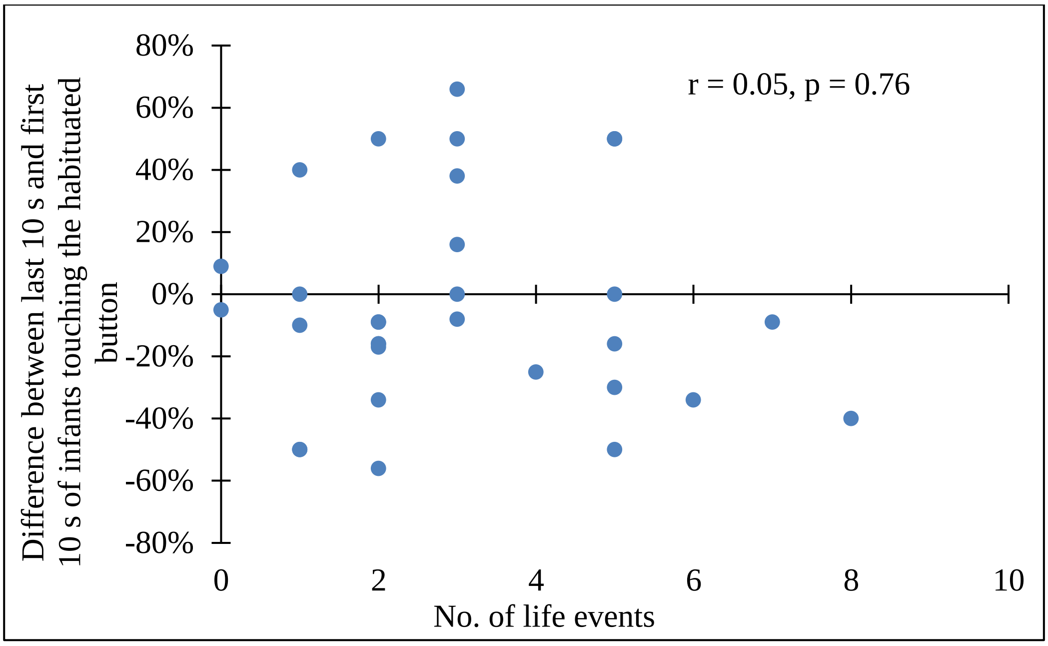

Figure 7: Number of prenatal life events and difference between infants touching habituated button during 0-10 s and 20-30 s interval of learning task

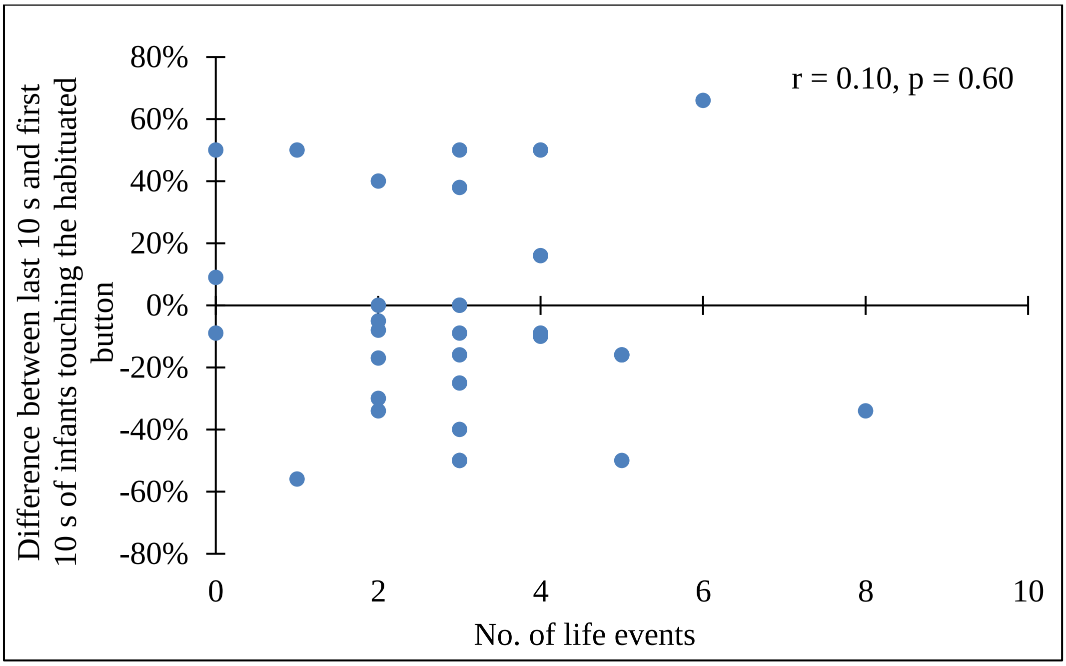

Figure 8: Number of postnatal life events and difference between infants touching habituated button during 0-10 s and 20-30 s interval of learning task

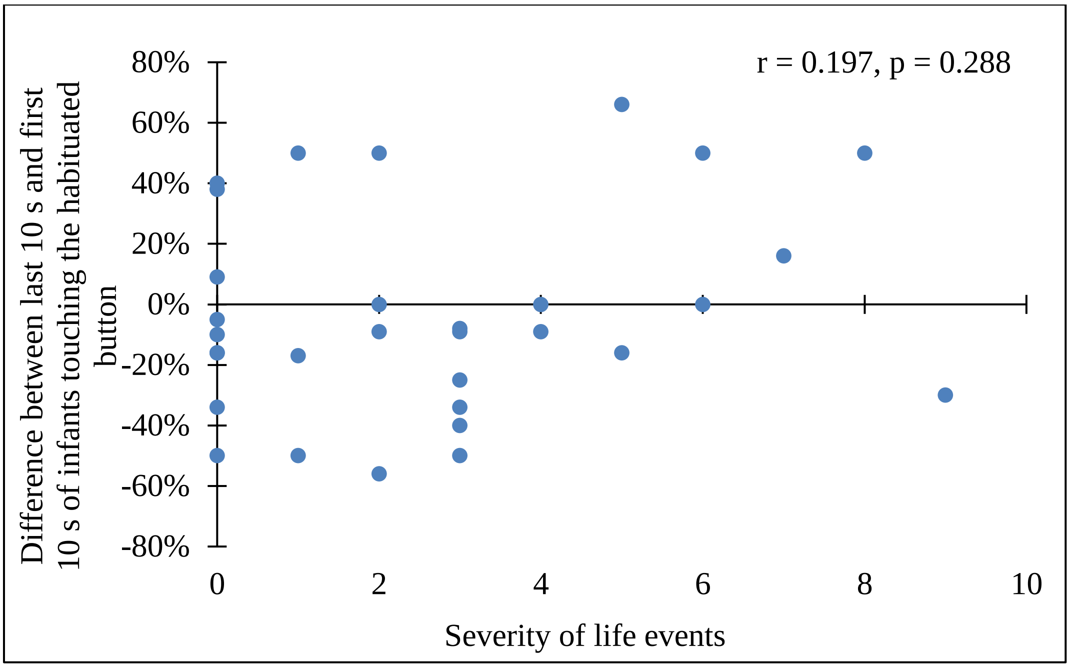

Figure 9: Severity of life events during prenatal period and difference between infants touching habituated button during 0-10 s and 20-30 s of learning task

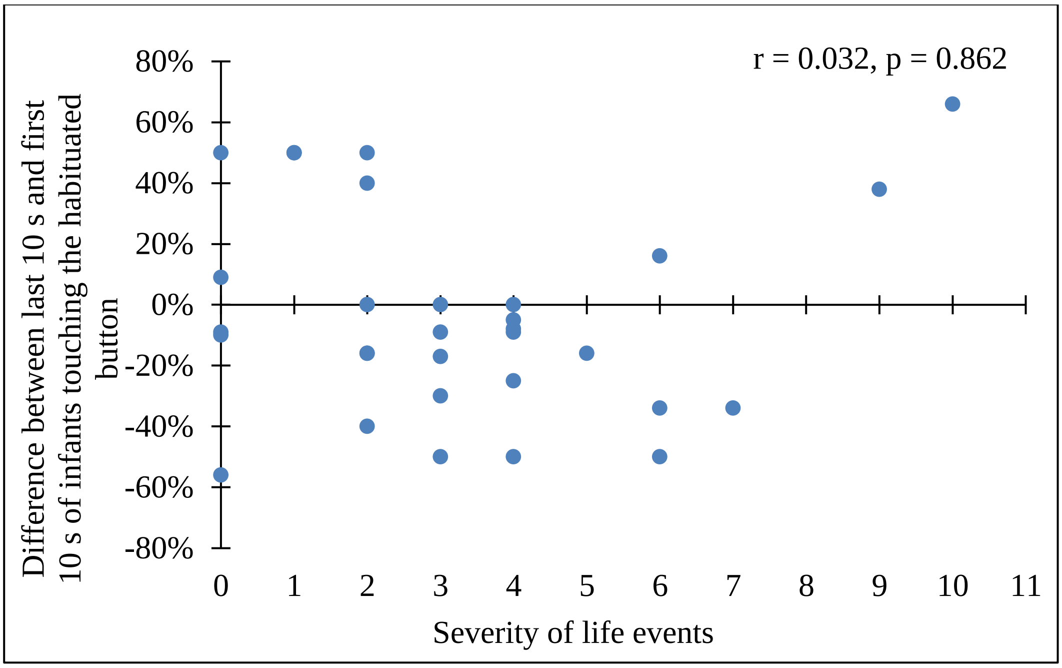

Figure 10: Severity of life events during postnatal period and difference between infants touching habituated button during 0-10 s and 20-30 s of learning task

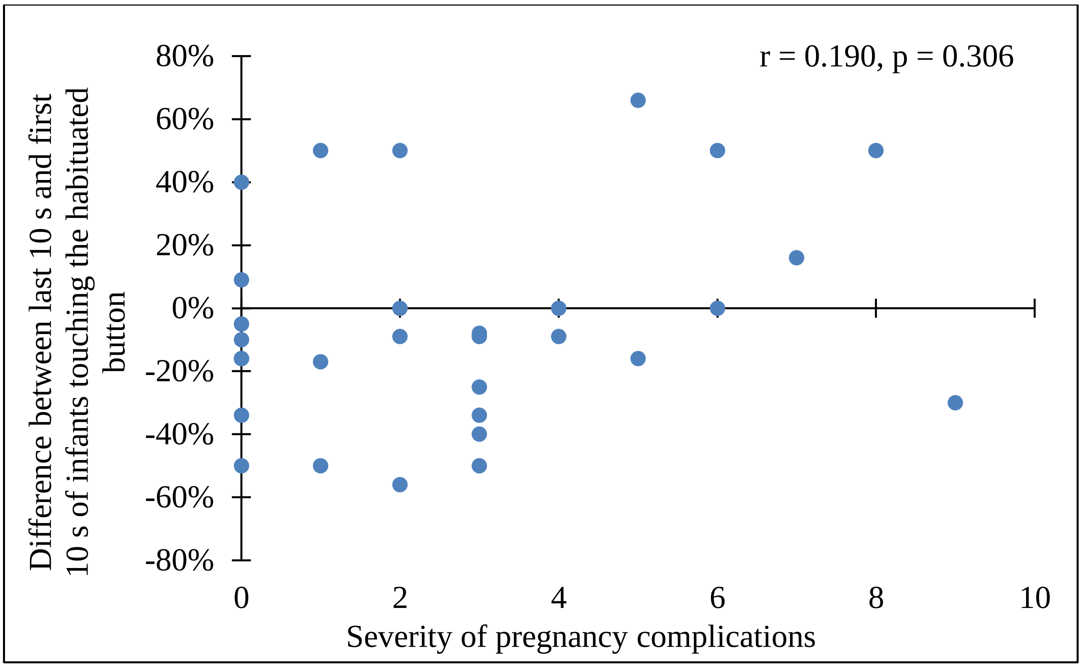

Figure 11: Severity of pregnancy complications and difference between infants touching habituated button during 0-10 s and 20-30 s of learning task

Maternal stress and infants' behaviour during instrumental learning task

To further determine whether there were any relations between the number of life events and infants' behaviour across the phases of the instrumental learning task, the infants were divided into two groups: high-stress and low-stress. In addition, again, because we wanted to determine also whether there was any difference between exposure to stressful life events in the prenatal period and the postnatal period on infants' behaviour in the learning task, the procedure to determine groups was performed for each period (prenatal and postnatal) separately. To do determine groups, first the total number of life events for each participant in the prenatal period was calculated. Then a median split was used to divide the infants into the two groups. The same procedure to determine groups was then repeated for the severity of life events in the prenatal period. Then, the procedure was repeated for the postnatal period. Finally, the procedure was repeated for the *overall* number of life events (i.e. during the prenatal and postnatal period) and *overall* severity of life events. Given stress' role in promoting rigid response strategies not just in adults but also in 15-month-old infants as Seehagen et al., (2015) have demonstrated, we would expect an interaction effect between infants' behaviour across the 30-s test phase and stress group. Specifically, we would expect that infants in the high stress group would either increase or maintain their pushing of the habituated button over the test phase, despite this action no longer leading to the production of the effects. On the other hand, we would expect that infants in the low stress group would disengage from pushing of the habituated button and explore the non-habituated button.

Prenatal period

Number of life events. In the learning phase of the instrumental learning task, the number of times the experimenter demonstrated pushing each button three times before infants pushed the respective buttons themselves was compared. There was not a significant difference between the groups for the number of required demonstrations. For the blue button, $M_{high\text{-}stress}$ = 1.60, $M_{low\text{-}stress}$ = 1.06, $t(29) = 1.41$, $p = 0.17$. For the red button: $M_{high\text{-}stress}$ = 1.06, $M_{low\text{-}stress}$ = 1.18, $t(29) = -0.60$, $p = 0.55$. In the habituation phase, the number of times infants pushed the button and produced the effect was compared between the groups. There was not a significant difference between the groups, $M_{high\text{-}stress}$ = 26.53, SD = 25.13, $M_{low\text{-}stress}$ = 23.06, SD = 19.76, $t(29) = 0.40$, $p = 0.69$. In the test phase, the overall engagement with both buttons was compared. There was not a significant difference between the groups in the number of times infants touched both buttons overall, $M_{high\text{-}stress}$ = 9.46, SD = 4.53, $M_{low\text{-}stress}$ = 11.50, SD = 6.26,

$t(29) = -1.05$, $p = 0.30$. To assess cognitive flexibility, the infants' engagement with the habituated button relative to both buttons across the test phase was analysed. We controlled for pushing times in phase II for the following analyses to account for any interaction this may have had on infants' behaviour during the test phase. To do this analysis, the test phase was divided into three 10 second intervals and a 3 (time interval: 0-10 s, 10-20 s, 20-30 s) x 2 (group: low stress, high-stress) mixed-model ANCOVA (covariate: number of times button pushed during habit-acquisition phase) was conducted. There was a significant effect of time interval, $F(2,56) = 5.07$, $p = 0.009$, $\eta_p^2 = 0.153$. There was no significant effect of group: $F(1,28) = 3.358$, $p = 0.078$, $\eta_p^2 = 0.107$. There was no significant interaction effect of time and group: $F(2,56) = 0.217$, $p = 0.806$, $\eta_p^2 = 0.008$. There was also no main effect of, or interaction with, the covariate: $F(1,28) = 0.089$, $p = 0.768$, $\eta_p^2 = 0.003$. Post hoc analyses for significant main effect of time interval revealed that relative to touching both buttons, the infants touched the habituated button significantly less often during the second interval (10-20-s) than during the first and last interval: $t(29) = 1.95$, $p = 0.030$ and $t(14) = 1.78$, $p = 0.042$, respectively.

Severity of life events. In the learning phase, there was not a significant difference between the high-stress and low-stress group in the number of times the experimenter demonstrated each button before infants pushed the respective buttons themselves: for the blue button: $M_{high\text{-}stress} = 1.33$, $M_{low\text{-}stress} = 1.37$, $t(29) = -0.11$, $p = 0.91$, for the red button: $M_{high\text{-}stress} = 1.0$, $M_{low\text{-}stress} = 1.25$, $t(29) = -1,29$, $p = 0.21$. In the habituation phase, there was not a significant difference between the groups in the number of times they produced the effect:

$M_{high\text{-}stress}$ = 24.46, *SD* = 25.44, $M_{low\text{-}stress}$ = 25.00, *SD* = 21.53, *t*(29) = -0.06, *p* = 0.95. In the test phase, there was not a significant difference between the groups in the number of times infants touched both buttons overall, $M_{high\text{-}stress}$ = 9.46, *SD* = 4.32, $M_{low\text{-}stress}$ = 11.50, *SD* = 6.52, *t*(29) = -1.05, *p* = 0.30. To assess cognitive flexibility, the infants' engagement with the habituated button relative to both buttons across the test phase was analysed. We controlled for pushing times in phase II for the following analyses to account for any interaction this may have had on infants' behaviour during the test phase. Again, to do this analysis, the test phase was divided into three 10 second intervals and a 3 (time interval: 0-10 s, 10-20 s, 20-30 s) x 2 (group: low stress, high-stress) mixed-model ANCOVA (covariate: number of times button pushed during habit-acquisition phase) was conducted. There was a significant effect of time interval: *F*(2,56) = 5.00, *p* = 0.010, η_p^2 = 0.152. There was no significant effect of group: *F*(1,28) = 1.39, *p* = 0.248, η_p^2 = 0.047. There was no significant interaction of time and group: *F*(2,56) = 0.042, *p* = 0.959, η_p^2 = 0.001. There was also no main effect of, or interaction with, the covariate: *F*(1,28) = 0.204, *p* = 0.655, η_p^2 = 0.007. Post hoc analyses revealed that relative to touching both buttons, the infants touched the habituated button significantly less often during the second interval (10-20-s) than during the first and last interval: *t*(29) = -2.50, *p* = 0.022 and *t*(29) = -1.77, *p* = 0.043, respectively.

Postnatal period

Number of life events. In the learning phase, there was not a significant difference between the high-stress and low-stress group in the number of times the experimenter demonstrated each button before infants pushed the respective buttons themselves: for the blue: $M_{high\text{-}stress}$ = 1.46, $M_{low\text{-}stress}$ = 1.37, $t(29) = 0.21$, $p = 0.82$. For the red button: $M_{high\text{-}stress}$ = 1.00, $M_{low\text{-}stress}$ = 1.12, $t(29) = -1.46$, $p = 0.16$. In the habituation phase, there was not a significant difference between the groups in the number of times they produced the effect: $M_{high\text{-}stress}$ = 19.33, SD = 18.17, $M_{low\text{-}stress}$ = 26.81, SD = 28.18, $t(29) = -1.26$, $p = 0.21$. In the test phase, there was not a significant difference between the groups in the number of times infants touched both buttons overall: $M_{high\text{-}stress}$ = 9.26, SD = 4.41, $M_{low\text{-}stress}$ = 11.68, SD = 6.38, $t(29) = -1.26$, $p = 0.21$. To assess cognitive flexibility, the infants' engagement with the habituated button relative to both buttons across the test phase was analysed. Again, we controlled for pushing times in phase II for the following analyses to account for any interaction this may have had on infants' behaviour during the test phase. This analysis, again, involved dividing the test phase into three 10 second intervals and a 3 (time interval: 0-10 s, 10-20 s, 20-30 s) x 2 (group: low stress, high-stress) mixed-model ANCOVA (covariate: number of times button pushed during habit-acquisition phase) was conducted. There was a significant effect of time: $F(2,56) = 4.808$, $p = 0.012$, $\eta_p^2 = 0.147$. There was also a significant effect of group: $F(1,28) = 7.19$, $p = 0.012$, $\eta_p^2 = 0.204$. There was no significant interaction between time and group, $F(2,56) = 0.264$, $p = 0.769$, $\eta_p^2 = 0.009$. There was also no main effect of, or interaction with, the covariate: $F(1,28) = 0.019$, $p = 0.891$, $\eta_p^2 = 0.001$. Post hoc analyses for significant main effect of time interval revealed that relative to touching both buttons, the infants touched the habituated button significantly less often during the second interval (10-20-s) than during the first and last interval: $t(29) = -2.66$, $p = 0.008$ and $t(29) = -1.95$, $p = 0.030$, respectively. Follow-up tests for group effect also revealed that across the test phase, relative to touching both buttons, infants in the low stress group touched the habituated button significantly less often than infants in the high stress group: $t(29) = 2.10$, $p = 0.025$.

Severity of life events. In the learning phase, there was not a significant difference between the high-stress and low-stress group in the number of times the experimenter demonstrated each button before infants pushed the respective buttons themselves: for the blue button: $M_{high\text{-}stress} = 1.40$, $M_{low\text{-}stress} = 1.43$, $t(29) = -0.08$, $p = 0.92$. For the red button: $M_{high\text{-}stress} = 1.00$, $M_{low\text{-}stress} = 1.12$, $t(29) = -1.46$, $p = 0.16$. In the habituation phase, there was not a significant difference between the groups in the number of times they produced the effect: $M_{high\text{-}stress} = 18.86$, $SD = 16.58$, $M_{low\text{-}stress} = 30.25$, $SD = 28.07$, $t(29) = -1.38$, $p = 0.17$. In the test phase, there was not a significant difference between the groups in the number of times infants touched both buttons overall: $M_{high\text{-}stress} = 11.06$, $SD = 5.52$, $M_{low\text{-}stress} = 10.00$, $SD = 5.58$, $t(29) = 0.53$, $p = 0.59$. To assess cognitive flexibility, the infants' engagement with the habituated button relative to both buttons across the test phase was analysed. We, again, controlled for pushing times in phase II for the following analyses to account for any interaction this may have had on infants' behaviour during the test phase. To do this analysis, again, the test phase was divided into three 10 second intervals and a 3 (time interval: 0-10 s, 10-20 s, 20-30 s) x 2 (group: low stress, high-stress) mixed-model ANCOVA (covariate: number of times button pushed during habit-acquisition phase) was conducted. There was a significant effect of time interval: $F(2,56) = 4.690$, $p = 0.013$, $\eta_p^2 = 0.143$. There was also a significant effect of group: $F(1,28) = 4.843$, $p = 0.036$, $\eta_p^2 = 0.147$. There was no significant interaction of time and group: $F(2.56) = 1.29$, $p = 0.283$, $\eta_p^2 = 0.044$. There was also no main effect of, or interaction with, the covariate: $F(1,28) = 0.141$, $p = 0.710$, $\eta_p^2 = 0.005$. Post hoc analyses for significant main effect of time interval revealed that relative to touching both buttons, the infants touched the habituated button significantly less often during the second interval (10-20-s) than during the first and last interval: $t(29) = -2.67$, $p = 0.007$ and $t(29) = -1.78$, $p = 0.042$, respectively. Follow-up tests of group effect revealed that across the test phase, relative to touching both buttons, infants in the low stress group touched the habituated button significantly less often than infants in the high stress group: $t(29) = 4.00$, $p = 0.001$.

Overall

To determine whether there was a relation between the number of life events overall and infants' behaviour across the phases in the instrumental learning task, the *combined* total number of life events for *both* the prenatal and postnatal period both was calculated for each participant. Then the group median was again used to divide the sample into a high-stress and a low-stress group. The same procedure was repeated for the severity of life events.

Number of life events. In the learning phase, there was no significant difference between the groups in the number of demonstrations required. For the blue button: $M_{high\text{-}stress} = 1.26$, $M_{low\text{-}stress} = 1.37$, $t(29) = -0.29$, $p = 0.77$. For the red button: $M_{high\text{-}stress} = 1.00$, $M_{low\text{-}stress} = 1.25$, $t(29) = -1.29$, $p = 0.22$. In the habituation phase, there was not a significant difference in the number of times infants produced the effect: $M_{high\text{-}stress} = 21.60$, $SD = 15.22$, $M_{low\text{-}stress} = 27.68$, $SD = 29.52$, $t(29) = -0.72$, $p = 0.47$. In the test phase, there was a not significant difference between the groups in the number of times the infants touched both buttons overall: $M_{high\text{-}stress}$ = 9.53, *SD* = 4.29, $M_{low\text{-}stress}$ = 11.44, *SD* = 6.45, *t*(29) = -0.98, *p* = 0.33. To assess cognitive flexibility, the infants' behaviour across the test phase was analysed. Pushing times in phase two was controlled for to account for any interaction this may have had on infants' behaviour during the test phase. To do this analysis, again, the test phase was divided into three 10 second intervals and a 3 (time interval: 0-10 s, 10-20 s, 20-30 s) x 2 (group: low stress, high-stress) mixed-model ANCOVA (covariate: number of times button pushed during habit-acquisition phase) was conducted. There was a significant effect of time: $F(2,56) = 5.104$, $p = 0.009$, $\eta_p^2 = 0.154$. There was also a significant effect of group: $F(1,28) = 5.705$, $p = 0.024$, $\eta_p^2 = 0.169$. There was no significant interaction of time and group, $F(2,56) = 0.154$, $p = 0.857$, $\eta_p^2 = 0.005$. There was also no main effect of, or an interaction with, the covariate: $F(1,28) = 0.147$, $p = 0.704$, $\eta_p^2 = 0.005$. Post hoc analyses for significant main effect of time interval revealed that relative to touching both buttons, the infants touched the habituated button significantly less often during the second interval (10-20-s) than during the first and last interval: $t(29) = -2.00$, $p = 0.028$ and $t(29) = -1.72$, $p = 0.046$, respectively (Figure 12). Follow-up tests of group effect revealed that across the test phase, relative to touching both buttons, infants in the low stress group touched the habituated button significantly less often than infants in the high stress group: $t(29) = 2.66$, $p = 0.008$.

Severity of life events. In the learning phase, there was no significant difference between the groups in the number of demonstrations required. For the blue button: $M_{high\text{-}stress}$ = 1.33, $M_{low\text{-}stress}$ = 1.31, *t*(29) = 0.05, *p* = 0.95. For the red button: $M_{high\text{-}stress}$ = 1.00, $M_{low\text{-}stress}$ = 1.25, *t*(29) = -1.29, *p* = 0.22. In the habituation phase, there was not a significant difference in the number of times infants produced the effect: $M_{high\text{-}stress}$ = 17.53, *SD* = 14.25, $M_{low\text{-}stress}$ = 31.50, *SD* = 28.79, *t*(29) = -1.73, *p* = 0.09. In the test phase, there was not a significant difference between the groups in the number of times the infants touched both buttons overall: $M_{high\text{-}stress}$ = 9.46, *SD* = 5.07, $M_{low\text{-}stress}$ = 11.50, *SD* = 5.96, *t*(29) = -1.04, *p* = 0.30. To assess cognitive flexibility, the infants' behaviour across the test phase was analysed. Once again, pushing times in phase two was controlled for to account for any interaction this may have had on infants' behaviour during the test phase. To do this analysis, the test phase was divided into three 10 second intervals and a 3 (time interval: 0-10 s, 10-20 s, 20-30 s) x 2 (group: low stress, high-stress) mixed-model ANCOVA (covariate: number of times button pushed during habit-acquisition phase) was conducted. In assessing cognitive flexibility, there was a significant effect of time: $F(2,56) = 5.205$, $p = 0.008$, $\eta_p^2 = 0.157$ (Fig.). There was no significant effect of group: $F(1,28) = 0.197$, $p = 0.661$, $\eta_p^2 = 0.007$. There was no significant interaction between time and group: $F(2,56) = 0.329$, $p = 0.721$, $\eta_p^2 = 0.012$. There was no main effect of, or an interaction with, the covariate: $F(1,28) = 0.033$, $p = 0.857$, $\eta_p^2 = 0.001$. Post hoc analyses for significant main effect of time interval revealed that relative to touching both buttons, the infants touched the habituated button significantly less often during the second interval (10-20-s) than during the first interval: *t*(29) = -1.77, *p* = 0.043 (Figure 13).

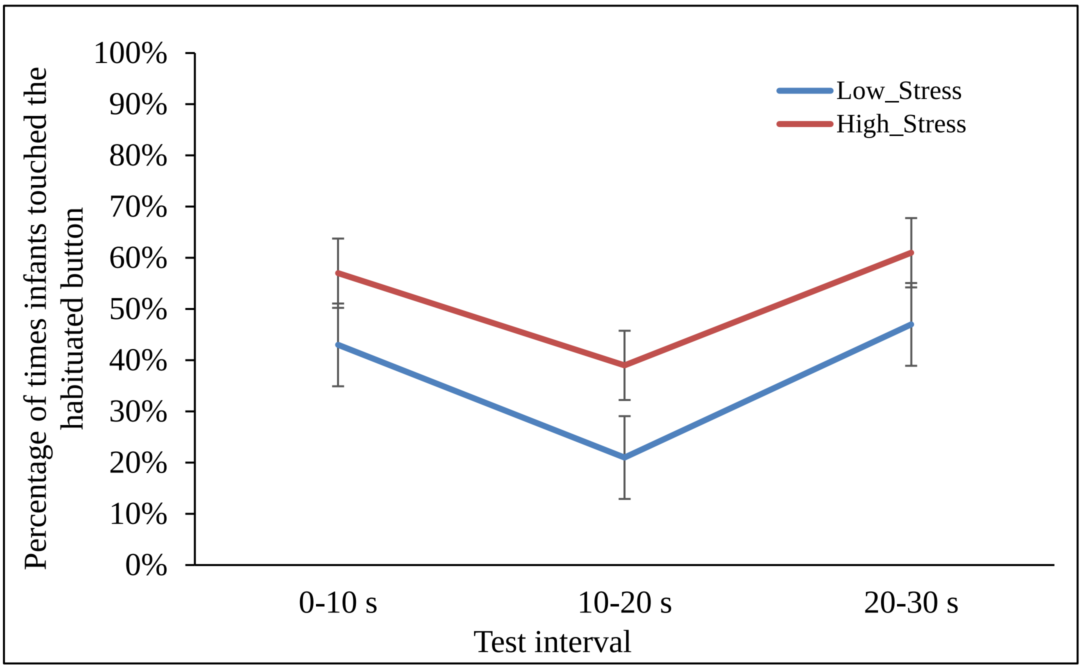

Figure 12: Percentage of times infants touched the habituated button relative to touching both buttons in the instrumental learning task. Error bars represent SEM

Note: Groups determined using combined total number of life events for both the prenatal and the postnatal period for each participant

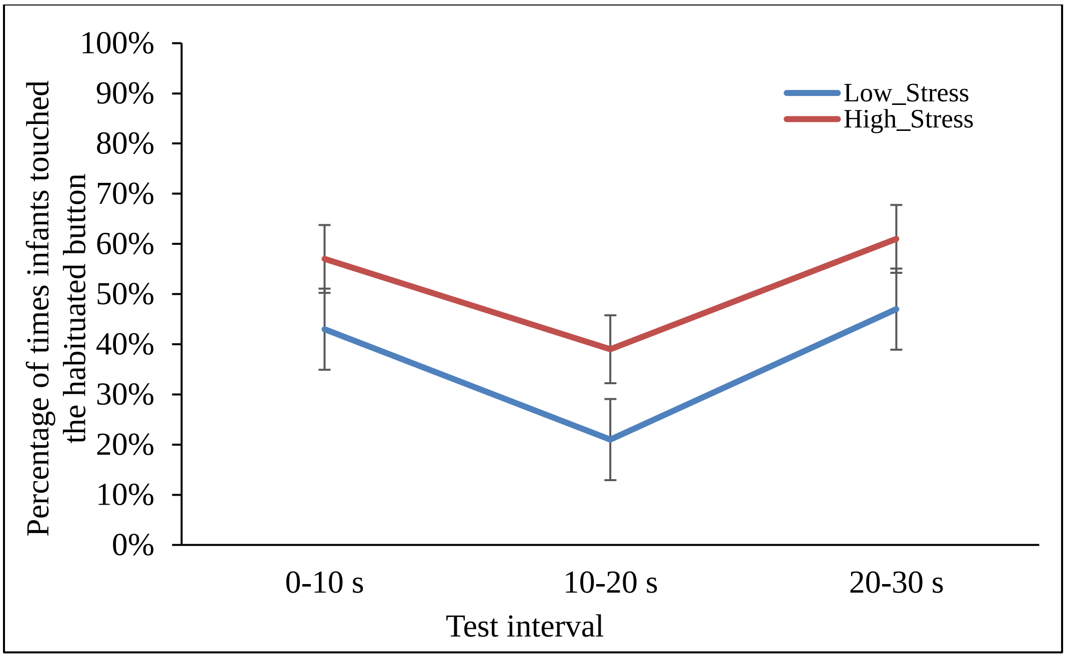

Figure 13: Percentage of times infants touched the habituated button relative to touching both buttons in the instrumental learning task. Error bars represent SEM

Note: Groups determined using combined total severity score of life events for both the prenatal and the postnatal period for each participant

Discussion

The present study explored the relationship between early life stress and cognitive flexibility in 14-16-month-old infants. The first main aim was to determine whether there was any relation between infant cognitive flexibility and: a) the *number* of life events, and b) the *severity* of life events experienced pre- and postnatally. Specifically, we asked whether infants who had experienced a higher number of life events and/or life events with high severity would display more rigid behaviour patterns than infants who experienced fewer life events and/or life events of low severity. A second aim was to determine whether there was a difference between exposure to stressful life events in the prenatal period and exposure to stressful life events in the postnatal period in their relationship to infant cognitive flexibility.

Recall that we predicted there would be a positive relation between the frequency and severity of potentially stressful early life events and infants' tendency to engage in rigid habitual behaviour.

Factors influencing infants' behaviour during instrumental learning task

As a group, the infants did not continue to decrease in their engagement with the habituated button in the instrumental learning task, even though pushing no longer produced the effects of light and sound. The infants did disengage from the habituated button during the second 10-s interval before increasing again in the final interval of the test phase. Further analysis revealed that the infants touched the habituated button significantly less often during the second interval than during the first and last interval. The infants' behaviour during the test phase of the task is somewhat surprising given that the infants were not under current stress, in that no stress manipulation was implemented prior to the task. Yet, the infants' behaviour in the test phase of the task differs from Seehagen and colleagues' (2015) findings of their infants in the no-stress condition. In the Seehagen et al. study, infants in this condition displayed steady disengagement from the habituated button over the course of the 30-s test phase, opting to explore the non-habituated button instead. It is unclear why the infants in the present study, as a group, did not continue to disengage from the habituated button despite extinction of effects and despite the absence of acute stress. It is possible that differences in procedure, particularly in the duration of the warm-up period, between Seehagen and colleagues' study and the present study might, in part, explain the infants' behaviour. Prior to the instrumental learning task, infants in the no-stress condition of Seehagen and colleagues' study initially engaged in free-play with their caregiver only in the laboratory room for a period of 30-minutes to acclimatize to the novel environment. Then the infants continued to engage in free-play with their caregiver only for further 18-minutes. The experimenter then re-entered the laboratory room and the infants then engaged in free-play with both the caregiver and the experimenter for a final 12-minute period. In the present study, time constraints meant the warm-up period lasted on average between just 10-15-minutes. In addition, half of this time was spent conversing with the caregiver regarding the procedure for the instrumental learning task, answering any questions about the study and obtaining informed consent, rather than interacting with the infant. Zmyj, Schneider and Seehagen (2017) found that after a warm-up period of 30-minutes, 15-month-old infants displayed a significant decrease in cortisol levels. This suggests that an extended warm-up period might be necessary for infants to acclimatize to a test environment. Although infants in the present study were tested in their own familiar home environment as opposed to an unfamiliar laboratory room, an encounter with a strange or novel event/person or stimulus has been found to contribute in inducing elevated cortisol levels in infants (Goldberg, et al., 2003; Gunnar et al., 2009; Nachmias, Gunnar, Mangelsdorf, Parritz, & Buss, 1996). It is possible that the infants' continued engagement with the habituated button was a reflection of elevated cortisol levels in response to the presence of a stranger (the experimenter). It is also possible that differences in both samples such as in socioeconomic status and number (and severity) of exposure to stressful life events, might have contributed to the differences in behaviour between the two groups. These variables were not assessed, or at least not reported, in previous studies.

Mediating factors in early stress exposure and cognitive functioning

In the present study, there was no significant correlation between the number or severity of potentially stressful life events (experienced during either the prenatal period, or the postnatal period) and infants' behaviour in the test phase of the instrumental learning task. It is important to consider that it is likely that an interaction or mix of factors could account for the findings. Possible factors that might have influenced the findings are discussed. These include the nature of stress exposure, parental and/or environmental, and developmental influences.

Nature of stress exposure. It is possible that the number and/or severity of life events experienced during the prenatal period and/or the postnatal period by the present sample as a group, was not high and/or severe enough to significantly inhibit cognitive flexibility. It is well known that not all stress is created equal. The National Scientific Council on the Developing Child (NSCDC) (2005) identifies three types of stress; positive stress, tolerable stress and toxic stress. In young children, positive stress are situations such as dealing with frustration, getting an immunisation, or meeting new people. These types of stressful situations tend to be short-lived and provoke a mild stress response such as brief elevations in heart rate or mild increases in stress hormones (Gunnar et al., 2009). Importantly, positive stress is stress that the child, with support from caring and warm adults, can learn to manage and control (Albers, Riksen-Walraven, Sweep, & de Weerth, 2008; Nachmias, et al., 1996). Tolerable stress are stressful events that evoke stress responses that have the *potential* to adversely affect the development of the brain (NSCDC, 2005). However, this type of stress tends to generally occur over limited time periods and as such, allow the brain to recover and prevent potentially deleterious effects. The types of stressful events that fall under this category are much like the life events identified in the present study such as, death or serious illness of a loved one, parental separation or divorce, hospitalisation or natural disaster. The NSCDC (2005) notes that, again, as with positive stress, an important factor in tolerable stress for stress to be indeed tolerable, is the presence of a supportive, caring and warm caregiver during these stressful events. Toxic stress on the other hand, are chronic and uncontrollable stressful life events that lead to frequent, elevated and/or prolonged activations of the stress response. Moreover, unlike positive stress and tolerable stress this type of stress is often experienced in the absence of supportive and caring caregivers. On the basis of the definitions of these stress categories, presumably the life events used in the present study fall under the tolerable stress category in that this type of stress has only the *potential* not certainty, to exert deleterious effects on cognitive functioning. Findings of previous studies in this area reflect this potentiality. For example, Entringer, et al. (2009b), Schwabe et al., (2002) and Zhu et al. (2014) all utilised life events – that is, stress that would constitute as moderate or tolerable stress – as indicators of degree of prenatal stress exposure. The authors found relations between this type of stress exposure and later working memory performance and cognitive flexibility in young adults, and scores on the MDI in infants. Furthermore, Entringer et al. (2009b) did not include in their assessment retrospective stress appraisals of life events, only the presence or absence of – yet, yielded significant results. Gutteling and colleagues (2006) also included life events as a measure of prenatal stress exposure in 6-year-old children. As mentioned in the introduction, the authors found a relation between life events and the attention/concentration index only of the TOMAL. Although the relation was relatively weak, the overall low-modest stress levels experienced by the mothers is noted. Similarly, in the present sample, in the prenatal period, looking at only the severity rating of the life events, the highest mean severity score of a life event (started a new job) reported by the group was 2.1. That is, only *moderately* negative. It is possible that the severity of stress exposure in the group was relatively low for the instrumental learning task to detect.

In addition to severity of stress, the timing of stress exposure may also play an important part in determining offspring cognitive functioning. There is a general trend in the literature toward stress exposure during the earlier stages rather than mid-late stages as the crucial point in gestation that exerts negative influences on cognitive functioning (Brouwers et al., 2001; Davis & Sandman, 2010; Gutteling et al., 2006; King & Laplante, 2005, & Van den Bergh et al., 2005). However, others have not found this to be the case. For example, Loomans et al. (2012) and Zhu et al. (2014) found prenatal stress exposure during the mid-stages and late stages, respectively, of pregnancy, to be related to cognitive functioning. However, although Zhu et al. (2014) found that infants exposed to prenatal stress scored lower than non-stress infants in the MDI, their scores were within the normal range. Loomans et al. (2012) found only greater intra-individual variability in performance on a cognitive control task in children who experienced greater maternal stress than children who experienced lower maternal stress. Furthermore, maternal stress explained only 1% of the variance in intra-individual variability. As mentioned in the introduction, the early stages of pregnancy are a time of major neuronal developments including, proliferation, differentiation and migration of neurons (Van den Bergh, 2005; Zhu et al., 2014). As such, during this stage naturally occurring increases in the enzyme 11ß-HSD2 protect the developing foetus from elevated levels of stress hormones (Davis & Sandman, 2010). The relatively small size of the present sample meant investigation in this area could not be conducted. However, it is possible, that in the present sample, the mothers' degree of stress exposure during pregnancy was not only relatively mild, but also relatively mild at crucial stages of development during pregnancy to significantly alter cognitive flexibility in the infants.

At the moment, studies on the cognitive implications for moderate <u>post</u>natal stress exposure during early life, such as life events, are rare. As noted in the introduction, commonly studied types of postnatal stress exposure include those that fall under the toxic stress category such as, child maltreatment, parental separation in the form of foster care placement(s) and institutionalisation. Nevertheless, as with the prenatal period, studies on stress exposure during the early postnatal period also indicate that timing – or more specifically, duration of stress exposure – plays a part in later cognitive functioning. For example, recall the Romanian orphans. Infants who had longer duration in the institutions displayed poorer outcomes in cognitive functioning than infants who spent less than six-months, when tested at follow up sessions (Nelson et al., 2007; 2009; Rutter & Connor, 2004). Other authors also observed longer duration in orphanages to be associated with generally lower scores on cognitive tasks than shorter duration when tested at ages between five and 11-years (Noble, Tottenham, & Casey, 2005), and between 12-months and 2-years (Cohen, Lojkasek, Zadeh, Pugliese, & Kiefer, 2008). This suggests that, in the postnatal period, chronicity of stress exposure – that is, severity as well as duration may impact on the trajectory of later cognitive functioning. In the present sample, in the postnatal period, again the highest mean severity rating of a life event reported by the group was "only" *moderately* negative (2.0) (unusually big pressures or conflicts at work). In addition to the low severity of postnatal stress exposure of the mothers, it is possible that the duration of stress exposure was also insufficient in length to establish an association with the infants' cognitive flexibility.

However, when divided into low-stress and high-stress groups, it is surprising to note a main effect of group when looking at both, the number and severity of life events during the postnatal period, and when looking at the number of life events overall. In each instance, infants in the low-stress group touched the habituated button significantly less often than infants in the high-stress group throughout the test interval. Seehagen et al., (2015) posits two mechanisms of how the habit-acquisition phase might explain infants' behaviour during the test phase. The first being that, pushing of the available button becomes increasingly automatic with repeated practice of button pushing. Second, it is possible that, outcome devaluation of button pushing occurs through repeated exposure to the light and sound effect. As with the infants in Seehagen and colleagues' study, it is likely that the behaviour of the high-stress and low-stress infants in the present study was due to automation rather than outcome devaluation. This is because, despite extinction of effects (and therefore presumably, appeal of habituated button), the infants did not disengage from the habituated button immediately once the non-habituated button was made available. It was not until the second interval that the infants disengaged from the habituated button before increasing engagement again in the final interval. Unlike the infants in the no-stress condition of the Seehagen and colleagues' study, the fact that the infants did not continue to disengage from the habituated button given the absence of acute stress, may indeed be due to the possible reasons discussed above. However, it may also imply that even moderate early stress exposure might be associated with reduced cognitive flexibility – albeit perhaps not at the same level as acute stress, such as that experienced by infants of the stress-condition in the Seehagen et al. study. Infants in the stress-condition of the Seehagen et al. study displayed an increasing upward linear pattern of engagement with the habituated button over time, indicating interference of current stress experience on the infants' ability to alter automated behaviour in response to the changes in the value of the outcome. On the other hand, infants in the present sample, increased engagement with the habituated button from the second interval to a similar rate observed in the first interval during the final interval. While the direction of engagement with the habituated button was similar for both the low-stress and high-stress group of the present study, the significant difference in proportion of engagement with the habituated button between the two groups throughout the test interval, might also allude to the possibility that higher levels of ELS exposure may be associated with increased automated behaviour even in the absence of acute stress.

As discussed above, the mechanisms through which stressful life events can impact on cognitive functioning and indeed, on the development of the child, is believed to be the persistent exposure to excess levels of glucocorticoids. However, parental/caregiver factors are instrumental in determining the extent of the impact of persistent exposure to elevated levels of stress hormones.

Parental factors. As mentioned, a key factor separating positive stress and tolerable stress from toxic stress is the ongoing presence of at least one supportive caregiver. Studies in both animals and humans have shown that the effects of stressful early life experiences can in large part be mediated by parental/caregiver factors (Champagne, Bagot, van Hasselt, Ramakers, Meaney, de Kloet, Joëls, & Krugers, 2008; Essex, Boyce, Hertzman, Lam, Armstrong, Neumann, & Kobor, 2013; Gunnar & Quevado, 2007; Hutchinson, McLaughlin, Wright, Ortiz, Anouti, Mika, Diamond, & Conrad, 2012; Liu, Diorio, Tennenbaum, Caldji, Francis, Freedman, Sharma, Pearson, Plotsky, & Meaney, 1997; Maccari et al., 1995; Meaney, 2001; Nachmias et al, 1996). In this way, caregiver behaviour may serve as a moderator for the potential implications early life stress/environmental adversity can have on development – including on cognitive functioning. For example, Bergman et al. (2010) observed that maternal cortisol levels at 17-weeks gestation were associated with cognitive ability in infants at 17-months of age. Importantly, the association was found in <u>in</u>secure attachment mother-child dyads but not in secure attachment dyads. Stams, Juffer, and van IJzendoorn, (2002) also found that higher attachment security and maternal sensitivity in early mother-infant relationship of adopted children, uniquely predicted better socioemotional and cognitive adjustment in middle-school. In another study, Lewis-Morrarty et al. (2012) observed foster parents who underwent an intervention program to learn behaviours that enhance and promote young children's self-regulatory capacities. Taught behaviours included sensitivity and following the child's lead in times of distress. The authors found that preschool-aged children of parents who participated in the intervention program exhibited stronger cognitive flexibility and theory of mind skills compared to foster children who had received a control intervention. Furthermore, the results were comparable to that of a control group who had never been in foster care. This suggests that the mere presence of a caregiver alone is insufficient for healthy socioemotional and cognitive development of a child. The quality of the relationship between child and caregiver is key in moderating the implications of early life stress in cognitive development. Because the present study did not carry out a measure(s) of parent-child interactions, we can only speculate about the nature of the relationship between the mother and infant dyads in the present sample. Nevertheless, it is plausible to posit that perhaps positive mother-infant relationships might, in part, contribute to the findings of the present study by way of moderating any potential adverse influences of early life stress exposure on the infants' cognitive functioning.

Environmental factors. One factor that may influence parental behaviour and the nature of the relationship with the child is socioeconomic status (SES). Indicators of SES that are typically studied include parental education, income and occupation. The general consensus in the child development literature is that SES may influence not only the health and wellbeing of the child but also cognitive, socioemotional and behavioural development as well (Esminger, Fothergill, Bornstein, & Bradley, 2003; Bradley & Corwyn, 2002; Hackman, Farah, & Meaney, 2010; Hoff, Laursen, & Tardif, 2002; Mistry, Biesanz, Chien, Howes, & Benner, 2008; Raviv, Kessenich, & Morrison, 2004). Two pathways have been proposed as to how SES impacts on child development. The first being access to resources (such as stimulating material such as books) and experiences (reading with the child, visits to the museum and library, attending a good school etc) that promote cognitive functioning (Conger & Donnellan, 2007; Gershoff, Aber, Raver, & Lennon, 2007, Hackman et al., 2010; NICHD Early Childcare Research Network, 2005). It is posited that lower-SES parents, given their economic hardships, need to invest more in meeting basic and immediate needs and less in resources and experiences that will benefit the development of the child (Conger & Donnellan, 2007). The second pathway proposed, posits that, the psychosocial stress associated with lower SES environments adversely affects parents' emotions, behaviours and relationships, and hence parenting behaviours towards the child (Conger & Donnellan, 2007; Hoff et al., 2002). In general, higher SES parents tend to employ child-centred and authoritative parenting styles whereas lower-SES parents tend to be associated more with inconsistent, strict or punitive authoritarian styles that might stem from stress associated with lower-SES (Hoff et al., 2002). This in turn, elevates the child's *risk* for developmental problems (Conger & Donnellan, 2007; Mistry et al., 2008). In the present sample, 71% of the mothers and 62% of the fathers attained a tertiary level qualification, while a further 16% of the mothers completed a higher postgraduate qualification. Given the varied opportunities acquisition of tertiary level qualifications presents, occupation was diverse in the present sample. Assuming that educational level and income are positively correlated, it is rational to posit that the current sample might be skewed towards higher-SES. Recruiting samples of lower-SES is a common problem faced by (developmental) researchers (Ejiogu, Norbeck, Mason, Cromwell, Zonderman, & Evans, 2011; Nielson, Haun, Kärtner, & Legare, 2017). Practical restraints (economic, lack of transport or unable to take time off work), lack of real-time benefit for participation, fear of exploitation, and unfamiliarity with research, have been cited as some significant barriers to participation from populations of lower-SES (Ejiogu et al., 2011). It is worth pointing out that the mediating role of parental factors applies only to the postnatal period and therefore does not account for stress exposure in the prenatal period. The low mean severity of life events reported by the mothers in the present sample may serve as a sufficient explanation as to the lack of significant findings in the prenatal period. Although the potential impact of stressful early life experiences – including during the prenatal period – on cognitive flexibility were not observed in the present study, it is not to say that that will remain the case. It is also important to consider the role developmental factors play in how stressful early life events impact on cognitive functioning.

Developmental factors. Although the infants in the present study did not evidence any reduction of cognitive flexibility in relation to early life stress experiences, it is premature to infer that moderate stress exposure during early life does not adversely impact on cognitive flexibility in infants, due to a lack of studies in this area. Neither can we rule out with certainty possible delayed effects. Although many cognitive skills are evident in early life, they may not be fully functional until later childhood or adolescence (Anderson, 2002; Diamond, 2002). As mentioned, while many developmental processes such as proliferation, differentiation and neuronal migration of the human brain occur during gestation (Keunen, Counsell, & Benders, 2017; Casey, Giedd & Thomas, 2000), other important processes such as myelination and synaptic pruning occur from early childhood and continue through to adolescence (Blakemore & Choudhury, 2006; Steinberg, 2005). Age-related changes in the human brain suggest that different cognitive processes may come ‘on-line’ at different ages (Anderson, 2002; Blakemore & Choudhury, 2006; Diamond, 2002). For example, lower-order cortices such as the sensorimotor cortex and the occipital poles – areas associated the senses and basic language and attention – develop and mature first within the first few years of life (Casey, Tottenham, Liston, & Durston, 2005; Pechtal & Pizzagalli, 2011). Whereas, higher-order cortices such as the prefrontal cortex are the last to develop and do not fully mature till early adulthood (Casey et al., 2005; Pechtel & Pizzagalli, 2011). Cognitive processes associated with the prefrontal cortex are selective attention, decision-making, inhibition, working memory and cognitive flexibility (Anderson, 2002, Blakemore & Choudhury, 2006; Diamond, 2002). Neuroimaging studies show correlations between development in neural processes and performance on different aspects of cognitive functioning (Casey, Trainor, Giedd, Vauss, Vaituzis, Hamburger, Kozuch, & Rapoport, 1997; Casey et al., 2000; Sowell, Delis, Stiles, & Jernigan, 2001). For example, increased activity of myelination and synaptic pruning during late childhood and adolescence increases conductivity and information processing (Sowell, Trauner, Gamst, & Jernigan, 2002). However, exposure to elevated levels of glucocorticoids during early life may adversely influence brain structure by either delaying and/or modifying the developmental trajectory of the brain and thereby, cognitive functioning (Lupien et al., 2009). As such, the functional implications of altered brain structure on cognitive functioning may not necessarily be evident until later in life when structural processes are complete (Anderson, 2002; Lupien et al., 2009). As we have seen, cognitive deficits have been observed in children (for example, Bos et al., 2009; Colvert et al., 2008; Lewis et al., 2007; Lewis-Morrarty et al., 2012;) as well as in adolescents (for example, Mezzacappa et al., 2001; Mueller et al., 2010; Spann et al., 2012) and young adults (for example, Entringer et al., 2009b; Navalta et al., 2006; Pesonen et al., 2011; Schwabe et al., 2012) with histories of early life stress exposure. Human neuroimaging (Anderson, Tomada, Vincow, Valente, Polcari, & Teicher, 2008; Mueller et al., 2010; Cohen, Grieve, Hoth, Paul, Sweet, Tate, Gunstad, Stroud, McCaffery, Hitsman, Niaura, Clark, McFarlane, Bryant, Gordon, & Williams, 2006; Teicher et al., 2003) and experimental animal studies (Lemaire et al., 2000; Radley, Rocher, Miller, Janssen, Liston, Hof, McEwen, & Morrison, 2006; Salm, Pavelko, Krouse, Webster, Kraszpulski, & Birkle, 2004; Spinelli, Chefer, Suomi, Higley, Barr, & Stein, 2009) show relations between abnormal brain structures in areas related to cognitive functioning and early stress exposure. For example, early exposure to maltreatment has been found to be associated with overall reduced volumes in the hippocampus, corpus callosum and the prefrontal cortex in adolescents and young adults (Teicher, Tomoda, & Anderson, 2006). More studies are necessary to clarify whether cognitive deficits in later life are due to brain abnormalities in structure and function following early stress exposure that persist into adolescence and adulthood or, whether they increase or emerge with age as a function of development (Hedges & Woon, 2011). In addition, it is likely that genetic predisposition, foetal programming, gender, the nature of stress exposure, including frequency and chronicity as well as timing of exposure, play a role in determining the nature and severity of the adverse influence stress exposure can have on brain development (Anderson et al., 2008). Nevertheless, taken together, these studies allude to the possibility of delayed influences of early stress exposure on cognitive functioning in the present sample. In other words, cognitive deficits may become apparent as structural and functional brain development occur throughout different stages in childhood and adolescence.

Strengths and limitations

Given the lack of studies that assessed moderate or tolerable stress and its impact on cognitive flexibility – and indeed, on cognitive functioning in general – in young children, it is perhaps a strength of the present study to use this type of stress as an indicator of stress exposure. Much of the studies on the impact of stress exposure during early life, focus on events or experiences in the chronic stress category such as child maltreatment, foster care placements and institutionalisation – stress that would also constitute as *direct* stress exposure. However, there is a gap in the literature on studies of the impact on young children of *indirect* stress exposure through more common events such as parental separation through divorce or for practical reasons, moving to a new house or starting a new job. In the present sample, all the infants had been exposed to at least one type of life event. Thus, assessing this type of stress is important because many young children are likely affected. At the same time, given that chronicity is a likely determinant for how stress influences cognitive functioning, the present study might have benefited from the inclusion of more severe types of stress exposure. However, the task of including more severe types of stressors is not without practical difficulties given the relative rarity of such cases.

Given also the lack of studies on the short-term, more immediate impact of early stress exposure on cognitive flexibility, observing relations between these variables with such a young sample within a very narrow age range might also be considered a strength of the present study. We have seen how the immediate effects of *acute* stress can inhibit cognitive flexibility in 15-month-old infants (Seehagen et al., 2015), however, little is known if the same observances can be said of accumulated early stress exposure in the absence of acute stress. Therefore, it made sense to start from a similar age range to the Seehagen et al. (2015) study. Furthermore, the narrow age range takes into account the rapid brain development occurring during the early years. As such, this allows the infants to use the same measure of cognitive flexibility, allowing for more accurate comparisons and interpretation of the results (Ellingson, 2016).

At the same time, the use of just one age group could be seen as a limitation of the present study. Given the possibility of delayed effects of early stress exposure, the inclusion of another age group might have been useful in alluding to this possibility. The small sample size is also another important limitation of the present study. This limited investigation into the role timing of stress exposure, particularly for during the prenatal period, might have played in differential outcomes of cognitive flexibility in the infants. Finally, the use of a single measure of cognitive functioning might also be considered a limitation of the present study. Multiple measures might have elucidated whether the lack of relation between early stress exposure and cognitive functioning is limited to cognitive flexibility but perhaps not in other measures.

Future directions

In light of the limitations of the present study, future studies in this area might consider the use of a larger sample size so as to allow for investigation into the timing of stress exposure during the prenatal period. Given the possibility that one of the reasons as to why the infants of the present sample did not display rigid, 'habit' behavioural tendencies may be due to the low-moderate severity and/or frequency of stress exposure in the mothers, future studies might also consider a more varied sample through the inclusion of high-risk populations. This might include the use of strategies during the recruitment process that are aimed at lower-SES settings. Future studies might also consider a follow-up session of the same sample to investigate the possibility of delayed effects. Alternatively, the inclusion of another, older age-grop may suffice. In either case, the use of a developmentally-appropriate instrumental learning task alternative as a measure of cognitive flexibility is an important consideration. In line with cognitive flexibility measures, future studies might also consider the use of more than one task when measuring cognitive flexibility to strengthen support for findings. The infants of the present study did not continue to disengage from the habituated button despite the absence of acute stress. As discussed, this may be due to elevated cortisol levels in response to the presence of a stranger (experimenter) that remained elevated throughout the learning task due to an insufficient duration of the warm-up period. Thus, in future, it is worth considering an extended warm-up period of at least 30-minutes to account for this. In addition, an objective measure of the infants' current stress levels might be of benefit. Future studies might consider taking cortisol samples of the infants on arrival prior to the instrumental learning task and post-task to supplement the subjective measure of the infants' mental state (infant mental state questionnaire). Finally, in addition to assessing specific cognitive abilities, future studies in this area might consider assessment of the short-term impact of early life stress on general development of cognitive functioning in infants and young children as well. This might include assessment in the areas of, problem solving, attention, working memory and even declarative memory through the use of deferred imitation paradigms.

Conclusion

Stress is ubiquitous. It is not limited to the severe forms often studied. While severe forms of stress exposure are indeed significant, they are rare in comparison to the prevalence of exposure to potentially stressful life events such as separation from a spouse or even moving to a new house. Life events that, despite their prevalence, we often may not associate with any significant negative effects on infants and young children. Yet, the emerging evidence on a) the negative associations between prenatal maternal stress exposure in the form of life events, and child development, b) how, postnatally, infants can indirectly experience the physiological manifestations of stressful events their caregiver experience, c) the negative effects of acute stress on cognitive functioning in infants, and finally the signficant findings from further analyses of the present study, suggests the relevance of further investigations into this area of research.

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Appendices

Appendix A: Recruitment poster

A matter of habit?

Take part in an exciting study with your child!

Are you fascinated by how babies and young children learn? Are you a parent/caregiver of a child between the ages of 14-16 months?

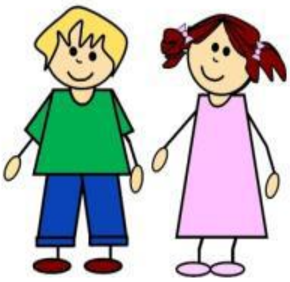
Then you may be interested in taking part with your child in a current research project that explores the relation between early life events and flexible learning in babies.

What will I have to do?
Participation will involve:
- completing a brief questionnaire and
- your child doing a fun learning task

Where?
Both activities are conducted in your own home where we visit you.

How long will it take?
The whole process will take one session lasting approximately 30 minutes. At the end of the session your child will receive a small gift and a certificate.

This project is part of the *Waikato Early Development Studies* at the *School of Psychology* at the *University of Waikato.* If you would like to find out more about this study, go to www.waikato.ac.nz/fass/weds to register your interest. Alternatively, you can contact:



Catherine Taylor (Masters student)
cbt6@students.waikato.ac.nz
Phone: 027 333 5041 or 07 544 3421

This research project has been approved by the School of Psychology Research and Ethics Committee of the Faculty of Arts and Social Sciences, University of Waikato. Any questions about the ethical conduct of this research may be sent to the convenor of the Research and Ethics Committee (currently Dr Rebecca Sargisson, phone 07 557 8673, email: rebeccas@waikato.ac.nz

Appendix B: Parent information sheet

A matter of habit? Flexibility of learning in infants

Thank you for your interest in this project which is part of the Waikato Early Development Studies at the University of Waikato. Please read this information sheet carefully before deciding whether or not to participate.

What is the aim of the study?
In this study we investigate how flexible infants are in their learning behaviour. In particular, we explore the relationship between experiences of potentially negative early life events and flexibility of learning.

How old does my child need to be?
This specific project involves infants between the ages of 14 and 16 months.

What will my child be asked to do?
Should you agree to take part in this project, we would like to visit you and your child in your home on a single occasion. We will show your child some specific actions to copy with a box that has two buttons on it which light up and make a noise when pushed. Then, your child will get to play with one of the buttons as long as he or she likes. Lastly, your child can play with both buttons again. But at this time, the buttons will not light up or make a noise anymore. Overall, these activities will take a few minutes. We know from previous research that most infants find playing with the buttons enjoyable. We will video-record your child playing so that we can later have a close look at what each infant in the study did when playing with the buttons.

What will I be asked to do?
We would like to ask you to complete a brief questionnaire about a list of life events that you may have experienced during your pregnancy and/or after you gave birth. In the questionnaire, you will be asked if you have experienced any of these events and to rate their impact on you. We would also like you to complete a brief questionnaire that asks about how your pregnancy and labour went. Lastly, we would like to ask you to rate your child's calmness during the button task on a very brief questionnaire and also about your child's typical everyday behaviour on another brief questionnaire

How long will the session take?
The whole session should take approximately 30 minutes altogether.

If I change my mind, can I withdraw myself and my child from the study?
Yes. If for any reason, you don't want to participate anymore and wish to withdraw yourself and your child from the study, you can do so at any time without any negative consequences.

What data or information will be collected and what use will be made of it?

The data (questionnaires, video-records) are collected and used for the research purposes outlined in this information sheet only. They will be securely stored in such a way that only the researchers directly involved in the study will have access to them. Data will be stored for a maximum of 10 years and then be destroyed. The published results of the study will not be linked to a particular child or participants thus you and your child's anonymity will be preserved.

What if I have questions?

You can contact:

Catherine Taylor (Masters student)
Ph: 07 544 3421 or 027 333 5041
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Dr Sabine Seehagen (Supervisor)
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This research project has been approved by the School of Psychology Research and Ethics Committee of the Faculty of Arts and Social Sciences, University of Waikato. Any questions about the ethical conduct of this research may be sent to the convenor of the Research and Ethics Committee (currently Dr Rebecca Sargisson, phone 07 557 8673, email: rebeccas@waikato.ac.nz

Appendix C: Consent form

School of Psychology

THE UNIVERSITY OF WAIKATO
Te Whare Wānanga o Waikato

CONSENT FORM

Research Project: Early life events and cognitive flexibility in infants

Please complete the following checklist. Tick (□) the appropriate box for each point.	**YES**	**NO**
I have read the Participant Information Sheet (or it has been read to me) and I understand it.		
I have been given sufficient time to consider whether or not to participate in this study		
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet		
I understand that taking part in this study is voluntary (my choice) and that I may withdraw myself and/or my child from the study at any time without penalty		
I have the right to decline to participate in any part of the research activity		
I know who to contact if I have any questions about the study in general.		
I agree to my child being video recorded during participation. Video records will be stored using a non-identifying code.		
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.		
I wish to receive a copy of the findings via an annual newsletter. If yes, please provide a convenient email address: (Please print): ______________________________		

Declaration by participant:

I agree to participate in this research project and I understand that I may withdraw at any time. If I have any concerns about this project, I may contact the convenor of the Psychology Research and Ethics Committee (Dr Rebecca Sargisson, phone 07 557 8673, email: rebeccas@waikato.ac.nz)

Participant's name (Please print):

Signature: Date:

Declaration by member of research team:

I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it. I believe that the participant understands the study and has given informed consent to participate.

Researcher's name (Please print):

Appendix D: Pregnancy complications questionnaire

The following are questions about your pregnancy and labour or delivery of your child.

Did you have any pregnancy complications? Tick all that apply:			
Condition	**Mild**	**Moderate**	**Severe**
Diabetes			
Placenta Previa/abruption/haemorrhage			
Hypertension			
Hyperemesis gravida			
False labour			
Multiple gestation			
Poor Foetal growth			
Premature rupture of membranes			
Maternal Infection			
Other condition(s) of mother:			
Other condition(s) of foetus:			

How would you rate your experience and care with your LMC during your pregnancy? Please circle the one that applies best: a. Excellent b. Good c. Fair d. Poor e. Very poor		
Were any of the following necessary during labour or after birth? Tick all that apply:		
	Yes	**No**
Emergency caesarean		
Forceps or ventouse		
Incubator		
Oxygen tent		
Extended stay in hospital		
Other		

Appendix E: Prenatal life events questionnaire

This questionnaire asks about events that may have happened **during your pregnancy.** For each event, please tick “yes” if the event happened during your pregnancy or “no” if the event did not happen during your pregnancy. If you tick “yes,” then, please also indicate in which trimester (first, second or third) the event happened. In addition, please also indicate ***how negative or undesirable*** the event was for you.

During your pregnancy:	**No**	**Yes**	**1st Tri**	**2nd Tri**	**3rd Tri**	**0 Not at all negative**	**1 Some what negative**	**2 Moderately negative**	**3 Very much negative**
Did you get married or start living with someone as if married?									
Did you live apart from your spouse or partner because of job, travel, or other practical reasons?									
Did you separate from your spouse or partner because of not getting along?									
Did you get divorced?									
Did someone important move out of your home?									
Did someone move in with you?									

Did someone important to you other than your spouse or partner move away so you didn't see the person as much?									
Did you have extra home or family responsibilities such as caring for an older relative or someone's child?									
Did someone close to you sustain a serious physical injury, illness or hospitalization?									
Did anyone close and important to you die? • If yes, please specify relationship:									
Did you lose your job?									
Did you look for work for 3 weeks or more?									
Did you start a new job?									
Did you have unusually big pressures or conflicts at work?									

Did you move or look for a new home?									
Did you experience a loss of your house, car, or something else important to you?									
Were you burglarized or robbed?									
Did you have unusual financial pressures or trouble with money?									
Were you arrested by the police, had problems with the law or immigration, or went to jail?									
Did you have trouble with CYFS?									
Did you have a serious physical injury, illness or were hospitalized?									
Did you have a problem with alcohol or drugs?									
Did you have a serious nervous or emotional problem besides drinking or drugs?									

Did you experience discrimination or harassment because of your race, gender, ethnicity or religion?									
Were you threatened with physical harm by anyone?									
Were you mugged, or personally assaulted?									
Were you in a hurricane, fire, or other major disaster?									
Were you involved in a serious motor vehicle accident?									

Appendix F: Postnatal life events questionnaire

This questionnaire is about events that may have happened **after you gave birth**. For each event, please tick “yes” if the event happened after you gave birth or “no’” if the event has not happened after you gave birth. If you tick “yes,” then, also please indicate ***how negative*** or ***undesirable*** the event was for you.

After you gave birth:	**No**	**Yes**	**0** **Not at all negative**	**1** **Some what negative**	**2** **Moderately negative**	**3** **Very much negative**
Have you gotten married or started living with someone as if married?						
Have you lived apart from your spouse or partner because of job, travel, or other practical reasons?						
Have you separated from your spouse or partner because of not getting along?						
Have you gotten divorced?						
Has someone important moved out of your home?						
Has someone moved in with you?						
Has someone important to you other than your spouse or partner moved away so you don’t see the person as much?						

Have you had extra home or family responsibilities such as caring for an older relative or someone's child?						
Has your child (that is participating) been severely ill or been diagnosed with an illness?						
Has someone close to you other than your child (that is participating) sustained a serious physical injury, illness or hospitalization?						
Has anyone close and important to you died? • If yes, please specify relationship:						
Have you lost your job?						
Have you looked for work for 3 weeks or more?						
Have you started a new job?						
Have you had unusually big pressures or conflicts at work?						
Have you moved or looked for a new home?						
Have you experienced a loss of your house, car, or something else important to you?						

Have you been burglarized or robbed?						
Have you had unusual financial pressures or trouble with money?						
Have you been arrested by the police, have problems with the law or immigration, or been to jail?						
Have you had trouble with CYFS?						
Have you had a serious physical injury, illness or been hospitalized?						
Have you had a problem with alcohol or drugs?						
Have you had a serious nervous or emotional problem besides drinking or drugs?						
Have you experienced discrimination or harassment because of your race, gender, ethnicity or religion?						
Have you been threatened with physical harm by anyone?						
Have you been mugged, or personally assaulted?						

Have you been in a hurricane, fire, or other major disaster?						
Have you been involved in a serious motor vehicle accident?						

Appendix G: Infant mental state questionnaire

Below, is a list of words that describe different moods. Please go through the list of words one by one and indicate how you perceived your child's mood for the specified situation. For each word, please tick the circle that you feel is most appropriate.

Example:
While participating in the learning task with the buttons, my child felt….

	Not at all				Very
Relaxed	1 O	2 O	3 O	4 O	5 O

Suppose you estimate that your child felt very relaxed while participating in the learning task with the buttons, you would tick the circle under number 5

	Not at all				Very
Relaxed	1 O	2 O	3 O	4 O	5 ✓O

Please note the following points:
The list contains several adjectives that describe different aspects of mood. Please give your answer for each adjective independent of your answer to another adjective.
If answering is difficult, please select the answer that is most applicable.
Please judge every word and do not omit any of the words.

While participating in the learning task with the buttons, my child felt….

	Not at all **1**	**2**	**3**	**4**	**Very** **5**
1. Restless	O	O	O	O	O
2. Placid	O	O	O	O	O
3. Agitated	O	O	O	O	O
4. Relaxed	O	O	O	O	O
5. Even-tempered	O	O	O	O	O
6. Tense	O	O	O	O	O

7. Nervous	O	O	O	O	O
8. Calm	O	O	O	O	O

Appendix H: Modified Bayley behaviour observation inventory

Below are some descriptions of behaviours. Please read the description of each behaviour and rate the degree to which each statement is typical of your child's everyday behaviour. Please indicate this by ticking the box that best describes your child.

Behaviour	Caregiver Rating		
	Is not at all typical; child rarely or never like this	Is somewhat typical; the child is like this some of the time	Is very typical; the child is like this most of the time
Positive Affect Smiles and laughs			
Enthusiasm Show enthusiasm and excitement			
Exploration Explores objects in the environment			
Ease of engagement Readily takes part in activities			
Cooperativeness Cooperates with adult requests			
Distractibility Unable to focus on task			
Fear/Anxiety Approaches new tasks with apprehension; looks to caregiver for reassurance			