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Review article

Influences of prenatal and postnatal stress on cognitive function and fear memory consolidation

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ABSTRACT

Stress can be defined as the brain response to any demand. Maternal exposure to stress during pregnancy may have negative effects on fetal and infant neurodevelopment, including delayed mental and motor development, difficult temperament, and impaired cognitive performance. Some of these effects are seen on brain structure and function and in the risk for later depression and posttraumatic stress disorder. Stress in adolescence appears to have lasting effects on brain regions such as the hippocampus and alters mood and anxiety-related behaviors in animal models, as well as cognitive function. The brain is the key organ of the response to stress because it determines what is threatening and, therefore, potentially stressful, as well as the physiological and behavioral responses which can be either adaptive or damaging. Stressors in adult life alter neuronal morphology in brain regions such as the hippocampus, amygdala, and prefrontal cortex and influence learning, anxiety, executive function, and somatic-visceral functions. Exposure to stress and stress hormones during the prenatal period, infancy, childhood, adolescence, adulthood or aging, has an impact on brain structures involved in cognition and mental health. As demonstrated in the above, generally stress can

have wide ranging effects on emotions, mood and behavior. Equally important but often less appreciated are effects on various systems, organs and tissues in all over the body. Recent studies and progress in neuroscience and biomedicine related to stress is providing a better understanding of mechanisms and pathways for these effects. Therefore, this article will provide an overview by discussing about influences of prenatal and postnatal stress on cognitive function and fear memory consolidation.

1. Introduction

Stress during pregnancy has been shown to be associated with cognitive impairments in the offspring. Prenatal stress is considered as a risk factor for psychiatric disorders such as schizophrenia and autism. Many of the endocrine and immune factors that play key roles in growth and development are also centrally involved in the stress response. This may be one reason why stress has the potential to impact intrauterine development. The role of stress and stress biology in development is common across all species and underlies evolutionary adaptations to external circumstances, such as food availability and challenges that threaten survival and reproduction. Glucocorticoids play a prominent role in the development of neural system during fetal period as it is shown that HPA axis is reprogrammed by the stressors during pregnancy (Szuran et al., 2000; Weinstock, 2008). Markham et al. (2010) reported the effects of prenatal stress on cognitive function of male and female rats. These researchers also reported that the spatial learning and memory and passive avoidance learning and memory were negatively affected by prenatal stress. Exposure to excessive stress hormones during the fetal period leads to the delayed development of the nervous system and inhibition of neurogenesis in different parts of the brain, which might provide an explanation for the cognitive deficits observed in the offspring (Noorlander et al., 2008; Lupien et al., 2009). Prenatal physical or psychological stress leads to impairments in learning and memory of adult male offspring in both spatial and contextual fear memory paradigms (Markham et al., 2010). Yang et al. (2006) have demonstrated that prenatal physical stress (footshock) alters synaptic plasticity in the hippocampus of the offspring. These researchers reported that the prenatal stress in the rats decreased long-term potentiation (LTP) and increased long-term depression (LTD) in the male offspring and also impairment of spatial learning. Several studies reported that prior exposure to moderate or high intensity stress is capable of enhancing associative learning and memory processing (Rau and Fanselow, 2009; Cordero et al., 2003). Rats exposed to physical restraint or footshock stress prior to contextual fear conditioning subsequently exhibited increased levels of conditioned fear behavior, namely freezing. In the previous studies, the researchers reported that the exposure to stressors during the early life has long-lasting neurobiological effects and puts one at increased risk for anxiety and mood disorders, aggressive dyscontrol problems, medical morbidity and structural changes in the CNS (Schneiderman et al., 2005; Schneiderman et al., 2005). It is previously demonstrated that prenatal stress increases the anxiety-like behaviors and depression in postnatal period (Koenig et al., 2005). Several studies have attempted to assess the anxiety-like behaviors and cognitive function of the prenatally stressed rats, there is still a lack of evidence for the effect of different prenatal stressors on the adolescent offspring cognitive functions (Bowman et al., 2004; Mueller and Bale, 2007). Adult hippocampal neurogenesis (AHN) is involved in learning and memory, stress and plays a significant role in neurodegenerative and psychiatric disorders. Prenatal stress (PS) and postnatal stress (PTS)-mediated modulations of AHN are correlated with impairments in adult brain functions, such as memory or behavior. The hypothesis of double neurogenic niche postulates that each kind of stress, PS and PTS, influences a specific neurogenic pool, developmental or postnatal (Ortega-Martínez, 2015). Stress during pregnancy has a wide variety of negative effects in both human and animal offspring. These effects are especially apparent in various forms of learning and memory such as object recognition and spatial memory. The cognitive effects of prenatal stress (PNS) may be mediated through epigenetic changes such as histone acetylation and DNA methylation (Kofman, 2002; Cabrera et al., 1999; Mesquita et al., 2009). Rats exposed to stress during the last week of gestation have significantly decreased dendritic spine density in the anterior cingulate gyrus and orbitofrontal cortex. Furthermore, prenatal exposure to glucocorticoids leads to increased adult corticotropin-

releasing hormone (CRH) levels in the central nucleus of the amygdala, a key region in the regulation of fear and anxiety (Schneiderman et al., 2005). Chronic exposure to stress hormones, whether it occurs during the prenatal period, infancy, childhood, adolescence, adulthood or aging, has an impact on brain structures involved in cognition and mental health. However, the specific effects on the brain, behavior and cognition emerge as a function of the timing and the duration of the exposure. In this review we will provide an overview by discussing about influences of prenatal and postnatal stress on cognitive function and fear memory consolidation.

2. Stress hormones and brain function

Stressful experience triggers the activation of two modes of operation; consist of autonomic nervous system and hypothalamus–pituitary–adrenal (HPA) axis. Actually these two systems play important role in restoring homeostasis following exposure to stress, and also modulate important physiological responses that are essential to cope with stress such as glycogenolysis, immune response, memory and cognition (Lupien et al., 2007; Finsterwald and Alberini, 2014). The primarily and fast mode of response initiates with the secretion of CRH (corticotropin releasing hormone) from hypothalamus, leaded to activation of locus coeruleus (LC) which has the majority of noradrenergic neurons in the brain (Kandel et al., 2000a; Smith and Vale, 2006). LC has widespread projection to other brain areas, such as the prefrontal cortex, amygdala cerebellum, and hippocampus and innervate these areas with noradrenergic signals via α and β adrenoceptors (Tsigos and Chrousos, 2002; Eysenck, 2004; Smith and Vale, 2006).

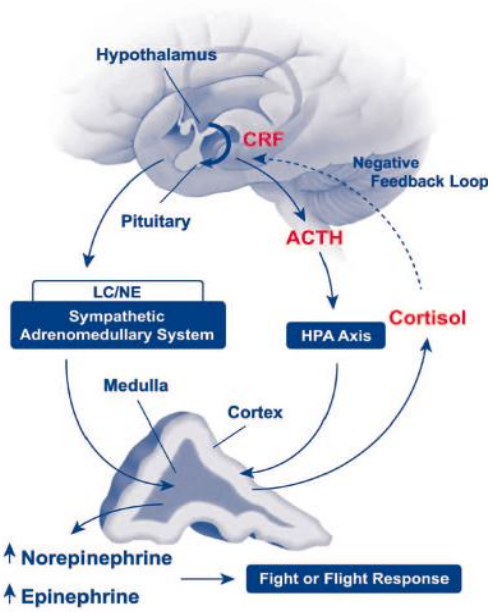

Fig. 1. Schematic representation of the HPA axis and stress response system. (Atsak, 2012).

On the other hand the second way is HPA axis triggered also with the releasing CRH from the hypothalamus. CRH causes subsequent secretion of adrenocorticotropin (ACTH) from the anterior pituitary gland. In turn, ACTH reaches the adrenal glands located above the kidneys through the blood vessels, and stimulates releasing of two main classes of stress hormones including glucocorticoids (called corticosterone in animals, and cortisol in humans), and the catecholamines (adrenaline and noradrenaline) (Lupien et al., 2007). It has been shown that there is a difference in the kinetic properties of exposure to stress between these two hormones. For instance, in vivo microdialysis studies have reported that noradrenaline levels rapidly increase fallowing stress, but return to its baseline within an hour (Quirarte et al., 1998). While, a delay of approximately 20 min observe for arising in corticosteroid hormone levels in the brain (compared to the rise observed in plasma; Droste et al., 2008) and decline to its normal level after 1–2 h. Differential time course of actions of these hormones, doesn't mean that there is no overlapping presence of noradrenaline and corticosteroids in time and space, but even they have important interactions with each other in different brain areas such as amygdala (Joels et al., 2011). It has been

proposed that the dissimilarity seen in the kinetic properties maybe as a result of special mechanisms and signaling pathways related to each hormones that we will explain more about them. In fact catecholamines principally act through G-protein coupled receptors activated second messengers and due to altering the functionality of ion channels. So rapid-onset changes in electrical properties of neurons occur, which generally are also quickly reversible fallowing reduction of noradrenaline levels in the synaptic cleft. Besides to these rapid proceedings, a secondary, delayed response to noradrenaline may develop through gene- mediated events, for e.g. via CREB, which last for hours (Krugers et al., 2012). In contrast Glucocorticoids are steroid hormones synthesized from cholesterol in the adrenal cortex. Because of their lipophilic nature, they can easily cross plasma membranes and activate two different intracellular receptors: mineralocorticoid receptors (MRs) and glucocorticoid receptors (GRs), known to be transcriptional regulators (Duma et al., 2006; de Kloet et al., 2000; Finsterwald and Alberini, 2014). In absence of ligand, cytoplasmic MRs and GRs are bound to protein complexes, called heat shock proteins such as hsp 70, hsp 90 (Grad and Picard, 2007). Upon binding of ligand, some conformational changes occur in these receptors that cause to their dissociation from the chaperone molecules and translocate to the nucleus. Then both MRs and GRs directly trigger transcription of target genes as a result of binding to specific sequences of 15 nucleotides in the promoter of target genes called glucocorticoid response elements (GREs) (Zalachoras, Houtman and Meijer, 2013). So in spite of catecholamines, the effect of glucocorticoids initiate in a delay phase. On the other hand, there is a growing body of evidence to propose that glucocorticoids hormones also induce rapid effects through nongenomic signaling pathway which are independent of nuclear translocation and gene expression regulation (Orchiniketal, 1991; Venero and Borrell, 1999; Di etal., 2003; Karst et al., 2010; Groc et al., 2008, Groeneweg et al., 2011; Prager and Johnson, 2009).

One notable characteristic about these two receptor is that, MRs have a tenfold higher affinity for glucocorticoids than GRs and are mostly saturated by the ligand in basal situation, while GRs occupation related to increasing in glucocorticoid levels following stress response (de Kloet et al., 2005; Lupien et al., 2007). Studies also suggest that the ratios of MR/GR occupancy can significantly influence the outcomes of the glucocorticoids' actions (Lupien and Lepage, 2001; Lupien et al., 2007). Actually it has been shown that cognitive performance can improve when most of the MRs are saturated and only part of the GRs are occupied with ligand (top of the inverted-U shape; enhanced MRs/GRs ratio). However, when circulating levels of glucocorticoids are significantly declined or enhanced (extremes of the inverted-U shape function; low MRs/GRs ratio), cognitive impairments will occur (Lupien et al., 2007). Another distinct difference between them is about their dispersion in the brain. The MRs are exclusively expressed in limbic structures. In contrast the GRs are not limited only to the limbic structure and dispersed over the whole brain. Notably, MRs and GRs are extensively distributed throughout the brain in both in the hippocampus and amygdala, two areas which have critical roles in memories of fear and stressful experiences. (de Kloet et al., 2005; Lupien et al., 2007).

3. Interactions of stress hormones and involvement of noradrenergic activation in the amygdala

Evidence from studies indicates that adrenaline and glucocorticoids not only alter transmission independent from each other but also the interaction between them may be essential in mediating stress effects on neural plasticity and memory enhancement (Joëls et al., 2011; Pu Krugers and Joëls, 2009; Roozendaal et al., 2006b). For example, fallowing administration of meytrapone, as a corticosterone-synthesis inhibitor, the elevation of circulating corticosterone reduces that cause to attenuate the memory-enhancing effects of epinephrine administered shortly after training (Roozendaal and McGaugh, 1996a). So researches have shown that the synergistic actions of epinephrine and corticosterone may be essential in mediating stress effects on memory enhancement. On the other hand in a study that was conducted by Roozendaa, et al, co-administration of propranolol (β-adrenoceptor antagonist) with the corticosterone immediately after object recognition training blocked the corticosterone-induced memory enhancement (Roozendaal, et al., 2006a). Additionally, others have demonstrated that administration of a β-adrenoceptor antagonist in to the BLA and other brain region block the memory enhancement by concurrently administered corticosteroids (Barsegyanetal, 2010). Therefore adrenergic activation is critical in enabling glucocorticoid enhancement of memory performance. Moreover, considerable evidence have indicated that the noradrenergic activation within the BLA is critically contributed in mediating the memory-modulating effects of corticosterone and epinephrine (McGaugh et al., 2000; McGaugh and Roozendaal 2002; Roozendaal, 2002). In the other word drugs and hormones that enhance memory performance should increase the release of norepinephrine within the amygdala (Roozendaal and McGaugh, 2011). So the amygdala

act as a major site where the two stress hormone can collaborate and interact to make their effects on memory activity. But as an important question, how catecholamine and glucocorticoid can trigger the activation of noradrenergic system in the basolateral complex of the amygdala (BLA)? It is well established that peripherally released adrenalin doesn't easily pass the blood brain barrier but also can stimulate ascending vagal afferents terminating in the nucleus of solitary tract. NTS has extensive noradrenergic projection to the basolateral complex of the amygdala (BLA) and LC. So the brain is one of the most important target for subsequent releasing of catecholamines upon exposure to stressful and arousing experiences (Lupien et al., 2007).

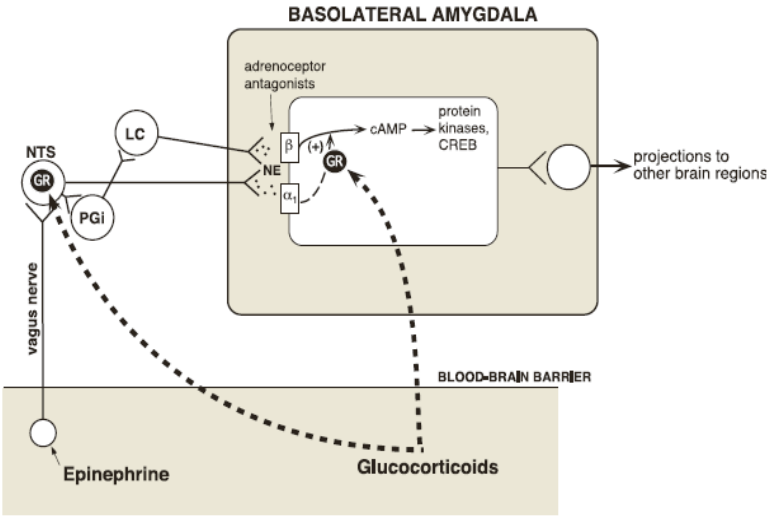

Fig. 2. The noradrenergic and glucocorticoid systems interact within the amygdala to mediate memory modulating effects. (Roozendaal, 2002).

On the other hand, as it has been found with epinephrine, glucocorticoid can also influence on memory consolidation via directly activation of GRs presented in brain stem nuclei, such as NTS that send noradrenergic projections to the BLA (Roozendaal and McGaugh, 2011). Interestingly some studies which have been conducted to understanding the mechanism of glucocorticoid interactions with the noradrenergic system, reported that within 15 min after the corticosterone administration, norepinephrine levels in the amygdala elevate and these events are consistent with rapid nongenomic effect of glucocorticoids and maybe activation of GRs in the BLA, facilitate memory performance by potentiating the norepinephrine-induced signaling cascade via an interaction with G-protein-mediated effects. Other recent researches propose that such rapid effects of glucocorticoids on the increase of norepinephrine in the BLA might related to endocannabinoid signaling pathway (Campolongo et al., 2009b; Hill and McEwen, 2009). As shown in fig.3 there is a model that explain clearly the role of the endocannabinoid system in mediating glucocorticoid effects on norepinephrine release in the BLA in regulating memory performance (Atsak et al., 2012).

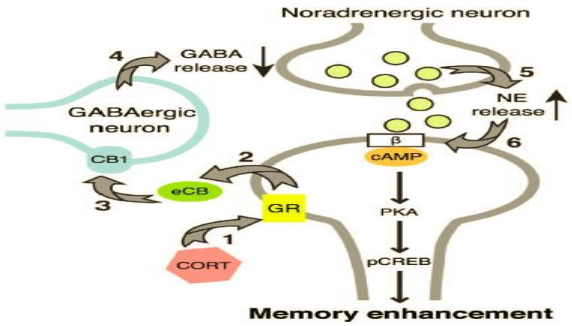

Fig. 3. Role of the endocannabinoid system in the BLA in mediating glucocorticoid effects on norepinephrine release.

Corticosterone (CORT) is secreted during emotionally arousing conditions and binds to a membrane-bound glucocorticoid receptor (GR) (1), which initiates a pathway to trigger endocannabinoid (eCB) synthesis (2). Then endocannabinoids are secreted into the synapse where they attach to CB1 receptors on GABAergic terminals (3), and cause to inhibit the release of GABA from GABAergic terminals (4). So the suppression of GABA release leads to disinhibit norepinephrine (NE) release (5), and subsequently the intracellular signaling pathway of the postsynaptic β adrenoceptor initiates (Hill and McEwen, 2009).

Actually two windows of time have been suggested that may occur after exposure to a stressful condition. Shortly after exposure to stress, rapid non-genomic actions of corticosteroids concur with initial effects of noradrenaline within 1 h after stress. In the second phase corticosterone might also act via its slow genomic pathway that cause to alter the noradrenergic actions which take place hours after exposure to stress. So the amygdala is a major site where the two hormone systems can interact and collaborate to deliver their regulation of memory activity, in consistency with the experience of stress being perceived (Krugers et al., 2012).

4. Prenatal stress

Prenatal stress is exposure of a pregnant female to physical or psychological tensions which may occur as results of stressful life events or environmental hardships. What is more, stressed mother's hormonal and immune system can cause dysfunction or retardation in fetus's immune system and brain development (Ruiz and Avant, 2005, Charil et al., 2010). Prenatal stress is shown to have determining role in fetal nervous system development in animal and increasingly in human. Although both prenatal and postnatal stress may have long lasting consequences, prenatal stress alters brain structure and function so that it does influence the offspring's cognitive function (Del Cerro et al., 2010). Such alterationsin nervous system can oftenbe mimicked by administrating the stress hormone to the pregnant animal (Afadlalet et al., 2010). Inmonkeys,offspring's anxiety increased when attention span was lessened (Schneider et al., 2002), as well as reduced hippocampalvolume (Coe et al., 2003) and poorly developed corpus callosum (Lulbachand, 2002). Anxiety and depression as major outcomes of stress have been showed to be associated with fetal and child development (O'Connor et al., 2002; Field et al., 2003; Hay et al., 2008; Laplante et al., 2008). Based on previous studies if a pregnant mother experience a term of stress, the child is at a high risk of anxiety, (O'Connor et al., 2003; Van Den Bergh and Marcoen, 2004), attention deficit hyperactivitydisorder(ADHD), (O'Connor et al., 2003; Huizinket et al., 2007) and conduct disorder (O'Connor et al., 2003; Barker and Maughan, 2009) as well as dysfunction of the HPA axis (Glover et al., 2009). In animal models, hippocampus of adult male ratslost its strength to properly proliferate and cellular death occurred in the hypothalamus-pituitary axis.García-Cáceres et al., (2010), showed that prenatal stress decreases cell turnover and proliferation in the hypothalamus of adult rats, which reduces structural plasticity and reduces the response to stress in adulthood. This study also showed that when prenatally stressed rats were stressed in adulthood the females showed an increase in corticotropin-releasing hormone suggesting it to be an up-regulation in the hypothalamic-pituitary adrenal axis. Males showed no elevation of corticosterone levels. Increase in adrenocorticotropic hormone with no effect of adult stress and a decrease in the corticotropinreleasing hormone mRNA in the hypothalamus showed a down-regulation(García-Cáceres et al., 2010).

5. Prenatal stress and complications of pregnancy

The HPA axis and the reproductive system are in a strong association in both pregnant and non-pregnant women (Chrousos, 1998). What is more, CRH and cortisol receptors are abundant in the endometrium, myometrium, and the ovaries. Therefore,psychological and physical stress influencesreproductive activities.It is observed during IVF therapies that the chance to achievesuccess is smaller if the mother asserts she is experiencing more stress or anxiety at the onset of pregnancy (Miladet et al., 1998; Demyttenaereet et al., 1994). Well-controlled studies in humans show a direct relationship between prenatal maternal stress and pregnancy complications listed below.

1-Spontaneous abortion

Spontaneous abortion is commonly found in unpleasant life event including death of a relative or being victim of criminality (Neugebauer et al., 1996)and work place stressors (Fensteret et al., 1995).

2- Structural malformations

Craniofacial malformations and heart defects are in a strong association with a number of life events like death of an older child during early pregnancy (Hansenet et al., 2000). Other structural malformations can manifest with psychosocial problems like inappropriate behavior with members of the family (Nimbyet et al., 1999).

3- Preeclampsia

Depression and anxiety (Kurkiet et al., 2000) and also some forms of work stress (Landbergis and Hatch, 1996) that are experienced during the first trimester seem to be associated with an increased risk for developing preeclampsia in a later phase of pregnancy. Patients who eventually develop preeclampsia often have increased serum concentrations of placental CRH (pCRH) from 18 to 20 weeks of gestation (Hobelet et al., 1999; Perkinset et al., 1995).

4- Preterm delivery

The relationship between stressful experiences during pregnancy and an increased risk of preterm delivery has been a consistent finding of independent studies for several decades (Paarlberget et al., 1995). It has been suggested that preterm uterine activity and shortened length of pregnancy result from stress during the third trimester. Remarkably, serum concentrations of placental CRH are already raised at 15–20 weeks of pregnancy in women who deliver preterm (Leunget et al., 1999).

5- Birth weight

Recent well-controlled research has documented that high anxiety and depression result in reduced birth weight and smaller head size (a measure of brain development). This effect of prenatal stress is of the same magnitude as the effect of smoking (Louet et al., 1994). The chance of delivering a low birth weight baby is higher if exposure to stress, daily hassles in particular, occurs during the first 3 months of pregnancy (Paarlberget et al., 1999). This may explain why others found a normal birth weight in infants of women whose husband died after the fourth month of pregnancy (Cepicky and Mandys, 1989).

6. Prenatal stress and cognitive function

Several studies have found an association between prenatal stress and children performing less well in cognitive tests. The prenatal stresses studied include life events (Bergman et al., 2007), exposure to a Canadian ice storm (Laplante et al., 2008), increased state anxiety (Menneset et al., 2006) and exposure to pregnancy-specific anxiety and increased daily hassles (Huizink et al., 2003). We do not know to what extent the cognitive impairment detected after prenatal stress is a side effect of readily distracted attention, or other behavioral changes.Some studies in humans show long-term associations between prenatal stress and altered basal cortisol levels, or cortisol responses to stress (O'Connor et al., 2005; Yehuda et al., 2005; Guttelinget et al.,2005; Huizink et al., 2008; Van den Bergh et al., 2008; Entringer et al., 2009).

7. Early life stress and cognitive function

When one is challenged in an emotional or physical situation thatis not able to adapt with, stresswill be the consequent (Gunnar and Quevedo, 2007). Early life stress(ELS) isresult of exposure to events during childhood by which child's primary needs are not met or those events are accounted as threats for child's age. Therefore, child may experience prolonged phases of stress. Childhood major stressors are usually categorizedas physical irritations, neglect, socialconformity, witnessing of violence,parental separation, parental death or illness, poverty (Brown et al., 2009). It is impossible to estimate the exact prevalence of ELS. Though,in 2007, 3.5 million (22.5%) children were observed by Child Protective Services in the United States alone. Abuse and neglect rate reached 10.6 % in 2007 (U.S.Department of Health and Human Services 2009).Moreover, these records likely underestimate the incidence of childhood trauma (Finklehor, 1994). ELSimpacts either behaviorally or physically. Although activation of stress response systems as a defensive responsehelps to cope with tough situations, very intensive or chronic levels of stress can inhibit brain development and affect mental health. (Andaet et al., 2006; De Belliset et al., 1999a; De Bellis et al., 1999b).Although it has been studiedwidely on neurobiological aspects of ELS (De Bellis, 2005; Teicher et al., 2003) less attention has been paid to cognitiveand emotional outcomes of

ELS.Exposure to ELS also impacts the function of the NAc. It alters dopamine (Brenhouseet et al., 2013) and serotonin pathways in the NAc of rodent's brain (Oreland et al., 2011). In humans, reduced NAc reactivity is attributed to ELS (Goffet et al., 2013). ELS enhances estrogen, oxytocin and serotonin-1A receptor expression after maternal separation in female rodents (Oreland et al., 2011). These three receptors are thought to be responsible of the development of anxiety and depression disorders (Skalkidouet et al., 2012).In contrast, in some other studies (Groeneweg et al., 2011) although ELS affected adult hippocampal-dependent memory, inconsistent effects on anxiety-like behaviors were detected (Simms et al., 2014). Raineki et al. showed that ELS causes a number of social behavioral deficits in preweaned rodents but later depressive-like symptoms in adolescent rodents (Vengelieneet et al., 2008). Finally, we assess the quality of ELS sequels in tow major etiologies based on human and animal literatures. The first one introduces ELS as a fear regulation modifier that is able to suppress fear responses in favor of goal oriented behavior. On the other side, the second one attributes alterations of behavior to amygdala.

8. ELS effects on synaptic plasticity and behavior

Unlike MS pattern ,neurogenesis rate in the sub ventricular zone of the hippocampus increases in the early post-partumstage while it decreases during late adulthood .what is more , specific proteins associated withsynaptic plasticity such as neural cell adhesion molecule1 (NCAM1)and synaptophysin are down regulated during adulthood after MS.Finally, behavioral outcome of the mentioned alterations in the nervous system including memory impairments, reduced social interaction,anhedonia, and anxiety appear(Nikolaos et al.,2015). Children experiencing ELS may have an impaired intellectual abilityincluding early institutionalization, neglect, or various forms of maltreatment (Cohen et al., 2008; De Bellis et al., 2009).Smaller intracranial volume, reduced hemispheric integration, and asmaller corpus callosum are some of the neural correlates of impaired global cognitivefunctioning following ELS (Noble et al., 2005; Teicher et al., 2004).DeBelliset al (2009) used abattery of standardized tests to observe neurocognitive functioning in neglected childrenwith and without PTSD compared to non-traumatized controls. Regardless of their PTSDdiagnosis, neglected children scored significantly lower on IQ than controls. Even whendifferences in IQ were statistically controlled, significant differences between neglected andnon-neglected children were found in a range of cognitive functions including language,memory/learning, and attention/executive functioning (De Bellis et al., 2009). Therefore, events inducing ELS are highly likely to affect intellectual performance of children.As the largest white matter structure inthe brain, the corpus callosum is composed of myelinated axons allowing an interhemispheric integration of diverse cognitive, motor, and sensory processes. In healthy samples, increased growth patterns were found for the anterior part of the corpus callosum between the ages of 3–6, assisting in vigilance and planning of new actions (Thompson et al., 2000). As language functions and associative memory functions become more prevalent, a sharp increase in posterior corpus callosum growth was noted around puberty (6–13 years). (Thompson et al., 2000). In both non-human and human research, exposure to ELS has been associated with decreases in corpus callosum size. In a study by Sanchez and colleagues (1998), primates separated from their mother from 2–12 months of age were later characterized by a reduced volume of the corpus callosum, loss of WM in prefrontal and parietal region, and impairments in recognition memory and reversal learning. In line with these preclinical data,reduced hemispheric integration and a smaller size corpus callosum, particularly in the medial and posterior regions, has been described in adults maltreated as children (Navalta et al., 2006), with the corpus callosum in neglected children being 17% smaller than in controls, and 11% smaller than in non-abused, psychiatric children (Teicheret et al., 2004).These findings have been strengthened by diffusion tensor imaging techniques, which have uncovered reduced fractional anisotropy in medial and posterior regions of the corpus callosum in maltreated children with PTSD (Jackowski et al., 2008) and in the genu of the corpus callosum in non-clinical adults with a history of ELS (Paul et al., 2008). Yet, more investigations are needed to assess how great ELS affects the size of corpus callosum. The anterior corpuscallosum develops and assists with functions needed earlier in life (e.g., vigilance, approachbehavior) while the posterior growth is more significant laterin development (e.g., language, associative memory). In conclusion, since development of corpus callosum lasts to the third decade of life, it maybe vulnerable to effects of ELS. Although postnatal neuronal proliferation in thehippocampus begins at a very early age, it continues into adulthood (Gogtay et al., 2006). In general, the anterior portion of the hippocampus is associated with anxiety-related behavior, associative memory, and emotional processing that decrease in dimensions with age. Several similar studies failed to show reduction in the hippocampal volumein animal offspring with ELS (De Bellis et al., 2002b; Teicher et al.,

2003; Karl et al., 2006).Besides, some other studies were not able to find any link between reduced hippocampal volumeand memory impairments following maltreatment (Pederson et al., 2004).

9. Pavlovian fear conditioning

Stressful events and threats lead to make strong memories that are essential for adapting and survival response. At first they are rapidly acquired but exist in an unstable state. It has been shown that during consolidation process, the acquired information became stable and transform in to long-term memory. Pavlovian fear conditioning is a useful behavioral task to study the neural mechanisms underlying fear learning and memory (Johnson et al., 2011). Moreover, classical fear conditioning (CFC) can be a model for psychological disorders such as PTSD. In classical fear conditioning, presentation of an initially biologically insignificant conditioned neutral stimulus (CS; for example an auditory sound or light) that is paired with the presentation of an unconditioned aversive stimulus (US; for example an electric foot shock) (Candace, 2015). Freezing behavior, as a measurement of fear learning, is generally defined as suppression all of the animal movements except respiration. These responses are rapidly formed; therefore fear conditioning has become a popular model and can be use to studying learning and memory mechanisms (Kim and Jung, 2006). There are different types of fear conditioning models, such as standard delay fear conditioning, in which the CS and US co-terminate; contextual fear conditioning, in which the US occurs in the absence of a discrete CS; and trace fear conditioning, in which the CS and US onset are separated by a stimulus-free interval. In summary, fear conditioning paradigm is useful for PTSD modeling and understanding molecular mechanism underlying fear learning.

10. The influence of stress on pavlovian fear acquisition and consolidation

We all experience stress in daily life in different forms and stressors can affect our learning and memory. Destructive effects of chronic and acute stress on learning and memory processes are particularly well documented. Stress has different effects on memory performance, especially aversive memories such as fear response. So we briefly review these effects separately. It should be noted that effects of stress is focused mainly on acute stress.

11. Effect of stress on fear memory acquisition

We pointed earlier the important role of amygdala in the acquisition and storage of pavlovian fear conditioning. Moreover, amygdale modulates expression of aversive responses to stress and stress hormones in a highly sensitive manner. However, based on different studies in animals, it has been shown that exposure to stress facilitates the acquisition of cued fear learning (Candace, 2015). This facilitating needs to noradrenaline so that blocking noradrenaline in the amygdala before training has defective effects on acquisition of cued fear conditioning (Bush et al., 2010). Inversely glucocorticoid does not affect the initial fear acquisition performance. This finding arised from the result that blocking there receptors has the opposite effect comparing with noradrenaline receptors. On the other hand, blocking glucocorticoid release does not affect the initial fear acquisition performance which proves that their release does not involve in the initial fear acquisition performance (Jin et al., 2007; Rodrigues and Sapolsky, 2009). These effects not only restricted to acquisition, but also evidence from human studies showed that stress can reduce memory retrieval of conditioned fear (Bentz et al., 2013). In all, it should be pointed that stress hormones have different effects on memory processing.

12. Effect of stress on fear memory consolidation

Considerable evidence raised from both human and rodent studies indicates that glucocorticoids (corticosterone in animals and cortisol in humans) released from the adrenal cortex in response to stressful stimuli, play a key role in learning and memory. Interestingly, during acute stress noradrenalin release and has enhancing effect on amygdale function (Tully et al., 2007). On the other hand, dose- dependently enhancement effects of glucocorticoids on consolidation of new fear memoires has been established, so glucocorticoid hormones have a key role in consolidation of long-term memories especially arousing experiences. Pharmacological blockade of corticosterone or cortisol synthesis with metyrapone (a glucocorticoid receptor antagonist) results in memory

consolidation impairment in both animals and humans (Blundell, 2011). A large body of results obtained from both animals and humans suggests that moderate density of glucocorticoid receptors (GRs) in basolateral complex of the amygdala (BLA), have critical role in mediating aversive and emotional memories, therefore glucocorticoid agonist or antagonist infusion into this area can affect memory consolidation (Roozendaal et al., 2009). Similar results obtained from infusion of glucocorticoids into the hippocampus or medial prefrontal cortex (mPFC), therefore, these findings suggest that enhancement effect of glucocorticoids on fear memory consolidation occurs with the participation of several areas of brain (Barsegyan et al., 2010). It is important to note that disruptive effect of stress hormones on prefrontal cortex function is well documented (Gärtner et al., 2014). Since the many behaviors which influenced by both stress and glucocorticoids is depend to mPFC, thus, pathophysiology of stress-related disorders such as PTSD, may related to stress- induced morphological and chemical changes in prefrontal cortex, so understanding how stress influences prefrontal structure and function will be helpful to recognized the mechanisms underlying PTSD. Generally, glucocorticoids can enhance consolidation of aversive memories in dose-dependent manner and work beside noradrenaline to facilitate it.

13. The neural circuitry underlying classical fear conditioning

Considerable body of researches had proved the involvement of medial prefrontal cortex (mPFC) in the regulation of a broad range of behaviors including emotional behaviors and psychiatric conditions such as post-traumatic stress disorders (PTSD) will be created after dysfunction of the mPFC (Shin et al., 2010; Pitman et al., 2012). This area of brain also modulates the stress effects on behavior. As discussed above, Amygdala is required to form CS- US association while the hippocampus is involved in contextual dependent learning in fear conditioning (Zovkic et al., 2013). In rodents, based on cytoarchitectonic and hodologic criteria, the mPFC can be devided in four distinct areas which, from dorsal to ventral, are the medial precentral cortex (PrCm) or medial agranular cortex (AGm), the anterior cingulate cortex (AC, dorsal and ventral parts), the prelimbic (PL) and the infralimbic (IL) cortices. PL and IL areas of the mPFC regulated suppression or expression of fear memory respectively This fact comes from differential connectivity of mPFC with the amygdale (Fig. 1) .Therefore IL and PL have opposite effects on fear expression.

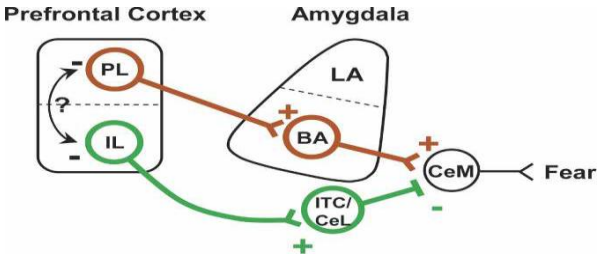

Fig. 4. Model of prelimbic (PL) and infralimbic (IL) interactions with the amygdala.

During PL mi.crostimulation, feedforward excitation activates (plus sign) the basal amygdala (BA) which in turn activates the medial division of the central nucleus (CeM) to produce conditioned fear responses. In contrast, IL microstimulation excites GABAergic cells in the intercalated (ITC) region as well as the lateral division of the central nucleus (CeL). Excitation of both of these nuclei inhibits (minus sign) the output of CeM and reduces fear. Adapted from Ivan Vidal-Gonzalez et al., 2006.

According to different studies about PL cortex it is established that PL is contribute in using higher-order information, such as contextual cues, goal value, or the associative history of a stimulus to modulate responding. For instance manipulation of PL cortex impairs goal directed animal responses (Sharpe and Killcross, 2014). Fear related behaviors deal with IL and PL cortex and reciprocal interactions between these areas with amygdale and hippocampus. GABAergic intercalated cell masses (ITC) and lateral division of the central nucleus (CeL) of amygdale receives projections from IL cortex. The output of this circuit is inhibition amygdala output neurons of the medial division of the central nucleus (CeM), so it is important to refer the critical role for the IL of the vmPFC in the retention of extinction learning and contextual modulation of extinction learning which is mediated by hippocampus (Francisco et al., 2010). Reduction in expression of conditioned fear to contextual and auditory stimuli will be happened if inactivation merely limit to PL (Corcoran and Quirk, 2007). Such finding pointed to this

fact that activation of PL cortex is necessary for fear expression. IL, indirectly projects to BLA via GABAergic cells in the lateral subdivision of the central nucleus (CeL) and intercalated (ITC) cell masses of the amygdale (Vertes, 2004).

14. Conclusion

Overall from the overview of this paper it can be concluded that the prenatal and postnatal exposure to stress may have negative effects on brain structure and function and in the risk for later depression and posttraumatic stress disorder. Exposure to stress and stress hormones during the prenatal period, infancy, childhood, adolescence, adulthood or aging, has an impact on brain structures involved in cognition, learning and mental health. Generally stress can have wide ranging effects on emotions, mood and behavior. Finally stress as a risk factor for mental health needs to more attention.

References

Afadlal, S., Polaboon, N., Surakul, P., Govitrapong, P., Jutapakdeegul, N., 2010. Prenatal stress alters presynapticmarker proteins in the hippocampus of rat pups. NeurosciLett. 470, 24-27.

Anda, R., Croft, J.B., Felitti, V., Nordenberg, D., Giles, W., Wiliamson, D.F., 1999. Adverse childhood experiences and smoking during adolescence and adulthood. JAMA. 228, 1652-1658.

Anda, R., Felitti, V., Bremner, J., Walker, J., Whitfield, C., Perry, B., 2006. The enduring effects of abuse and related adverse experiences in childhood. Eur. Arch. Psych. Clin. Neurosci., 256, 174-186.

Anda, R.F., Brown, D.W., Felitti, V.J., Bremner, J.D., Dube, S.R., Giles, W.H., 2007. Adverse childhood experiences and prescribed psychotropic medications in adults. Am. J .Prev. Med., 32, 389-394.

Atsak, P., Roozendaal, B., Campolongo, P., 2012. Role of the endocannabinoid system in regulating glucocorticoid effects on memory for emotional experiences. Neurosci., 204, 104-116.

Barker, E.D., Maughan, B., 2009. Differentiating early- onset persistent versus childhood-limited conductproblem youth. AM. J. Psychiat., 166, 900-908.

Barsegyan, A., Mackenzie, S.M., Kurose, B.D., McGaugh, J.L., Roozendaal, B., 2010. Glucocorticoids in the prefrontal cortex enhance memory consolidation and impair working memory by a common neural mechanism, Proc Nat AcadSci USA, 107, 16655-16660.

Bentz, D., Michael, T., Wilhelm, F.H., Hartmann, F.R., Kunz, S., von Rohr, I.R., de Quervain, D.J., 2013. Influence of stress on fear memory processes in an aversive differential conditioning paradigm in humans, Psychoneuroendocrinol., 38(7), 1186-1197.

Bergman, K., Sarkar, P., O'Connor, T.G., Modi, N., Glover, V., 2007. Maternal stress during pregnancypredicts cognitive ability and fearfulness in infancy. J. Am. Acad. Child. Adolesc. Psychiatry., 46, 1454-1463.

Blundell, J., Blaiss, C.A., Lagace, D.C., Eisch, A.J., Powell, C.M., 2011. Block of glucocorticoid synthesis during re-activation inhibits extinction of an established fear memory. Neurobiol. Learn. Mem., 95, 453-460.

Bos, KJ., Fox, N., Zeanah, C.H., Nelson, C.A., 2009. Effects of early psychosocial deprivation on the development of memory and executive function. Frontiers in Behavioral Neuroscience. 3.

Bowman, R.E., MacLusky, N.J., Sarmiento, Y., Frankfurt, M., Gordon, M., Luine, V.N., 2004. Sex- ually dimorphic effects of prenatal stress on cognition, hormonal responses, and central neurotransmitters, Endocrinol., 145, 3778–3787.

Bremner, J.D., Vythilingam, M., Vermetten, E., Southwick, S.M., McGlashan, T., Nazeer, A., 2003a. MRI and PET study of deficits in hippocampal structure and function in women with childhood sexual abuse and Posttraumatic Stress Disorder. Am. J. Psychiatry., 160, 924-932.

Bremner, J.D., Vythilingam, M., Vermetten, E., Southwick, S.M., McGlashan, T., Staib, L.H., 2003b. Neural correlates of declarative memory for emotionally valenced words in women with posttraumatic stress disorder related to early childhood sexual abuse. Bio. Psychiatry., 53, 879-889.

Brenhouse, H.C., Lukkes, J.L., Andersen, S.L., 2013. Early life adversity alters the developmentalprofiles of addiction-related prefrontal cortex circuitry. Brain. Sci., 3, 143-158.

Brown, D.W., Anda, R.F., Tiemeier, H., Felitti, V.J., Edwards, V.J., Croft, J.B., 2009. Adverse childhood experiences and the risk of premature mortality. Am. J. Prev. Med., 37, 389-396.

Bush, D.A., Caparosa, E.M., Gekker, A., LeDoux, J.E., 2010. Beta-adrenergic receptors in the lateral nucleus of the amygdala contribute to the acquisition but not the consolidation of auditory fear conditioning. Behav. Neurosci., 4, 1-7.

Cabrera, R., Rodriguez-Echandia, E., Jatuff, A., Foscolo, M., 1999. Effects of prenatal expo- sure to a mild chronic variable stress on body weight, preweaning mortality and rat behaviour. Braz. J. Med. Biol. Res., 32, 1229-37.

Campolongo, P., Roozendaal, B., Trezza, V., Hauer, D., Schelling, G., McGaugh, J.L., Cuomo, V., 2009b. Endocannabinoids in the rat basolateral amygdala enhance memory consolidation and enable glucocorticoid modulation of memory. Proc. Natl. Acad. Sci., USA, 106(12), 4888-4893.

Cepicky, P., Mandys, F., 1989. Reproductive outcome in women who lost their husbands in the course of pregnancy. Eur. J. Obstet. Gynecol. Reprod. Biol., 30, 137-140.

Charil, A., Laplante, D.P., Vaillancourt, C., King, S., 2010. Prenatal stress and brain development. Brain. Res. Rev., 10, 1016-1028.

Chrousos, G.P., 1998. Stressors, stress, and neuroendocrine integration of the adaptive response. In: CsermelyP, editor. Stress of life: from molecules to man. Ann. NY. Acad. Sci., 311-335.

Coe, C.L., Kramer, M., Czeh, B., Gould, E., Reeves, A.J., Kirschbaum, C., 2003. Prenatal stress diminishesneurogenesis in the dentate gyrus of juvenile rhesus monkeys. Biol. Psychiat., 54, 1025-1034.

Coe, C.L., Lulbach, G.R., Schneider, M.L., 2002. Prenatal disturbance alters the size of the corpus callosumin young monkeys. Dev. Psychobiol., 41, 178-185.

Cohen, N.J., Lojkasek, M., Zadeh, Z.Y., Pugliese, M., Kiefer, H., 2008. Children adopted from China: a prospective study of their growth and development. J. Child. Psychol. Psychiatry., 49, 458-468.

Corcoran, K.A., Quirk, G.J., 2007. Activity in prelimbic cortex is necessary for the expression of learned, but not innate, fears. J. Neurosci., 27, 840-844.

Cordero, M.I., Venero, C., Kruyt, N.D., Sandi, C., 2003. Prior exposure to a single stress session facilitates subsequent contextual fear conditioning in rats. Evidence for a role of corticosterone. Horm. Behav., 44, 338-45.

De Bellis, M,D., Hooper, S.R., Spratt, E.G., Woolley, D.P., 2009. Neuropsychological findings in childhood neglect and their relationships to pediatric PTSD. J. Int. Neuropsychol. Soc., 15, 868-878.

De Bellis, M.D,. 2005. The psychobiology of neglect. Child. Maltreat., 10, 150-172.

De Bellis, M.D., Baum, A.S., Birmaher, B., Keshavan, M.S., Eccard, C.H., Boring, A.M., 1999a. Developmental traumatology part I: biological stress systems. Biol. Psychiatry., 45, 1259-1270.

De Bellis, M.D., Keshavan, M.S., Clark, D.B., Casey, B.J., Giedd, J.N., Boring, A.M., 1999b. Developmental traumatology part II: brain development. Biol. Psychiatry., 45, 1271-1284.

De Bellis, M.D., Keshavan, M.S., Shifflett, H., Iyengar, S., Beers, S.R., Hall J., 2002b. Brain structures in pediatric maltreatment-related posttraumatic stress disorder: a sociodemographically matched study. Biol. Psychiatry., 52, 1066-1078.

De Kloet, E.R., Joëls, M., Holsboer, F., 2005. Stress and the brain: from adaptation to disease. Nat. Rev. Neurosci., 6(6), 463-475.

De Kloet, E.R., Meijer, O.C., Vreugdenhil, E., Joëls, M., 2000. The Yin and Yang of nuclear receptors: symposium on nuclear receptors in brain, Oegstgeest, The Netherlands, Trend. Endocrinol. Metab., 11(6), 245-248.

Del Cerro, M.C., Perez-Laso, C., Ortega, E., Martin, J.L., Gomez, F., Perez-Izquierdo, M.A., 2010. Maternalcare counteracts behavioral effects of prenatal environmental stress in female rats. Behav. Brain. Res. 208, 593-602.

Demyttenaere, K., Nijs, P., Evers-Keibooms, G., Koninckx, P., 1994. Personality characteristics, psychoneuroendocrinologicalstress and outcome of IVF depend upon the etiology of infertility. Gynecol. Endocrinol., 8, 233-240.

Di, S., Malcher-Lopes, R., Halmos, K.C., Tasker, J.G., 2003. Non genomic glucocorticoid inhibition via endocannabinoid release in the hypothalamus: a fast feedback mechanism. J. Neurosci., 23(12), 4850-4857.

Droste, S.K., de Groote, L., Atkinson, H.C., Lightman, S.L., Reul, J.M., Linthorst, A.C., 2008. Corticosterone levels in the brain show a distinct ultradian rhythm but a delayed response to forced swim stress. Endocrinol., 149(7), 3244-3253.

Duma, D., Jewell, C.M., Cidlowski, J.A., 2006. Multiple glucocorticoid receptor isoforms and mechanisms of post-translational modification. J. Steroid. Biochem. Mol. Biol., 102(1), 11-21.

Entringer, S., Kumsta, R., Hellhammer, D.H., Wadhwa, P.D., Wust, S., 2009b. Prenatal exposure to maternalpsychosocial stress and HPA axis regulation in young adults. Horm. Behav., 55, 292-298.

Eysenck, M.W., 2004. Psychology: An international perspective. Taylor and Francis.

Fenster, L., Schaefer, C., Mathur, A., Hiatt, R.A., Pieper, C., Hubbard, A.E., 1995. Psychologic stress in the workplace andspontaneous abortion. Am. J. Epidemiol., 142, 1176-1183.

Finklehor, D., 1994. The international epidemiology of child sexual abuse. Child. Abuse. Negl., 18, 409-417.

Finsterwald, C., Alberini, C.M., 2014. Stress and glucocorticoid receptor-dependent mechanisms in long-term memory: from adaptive responses to psychopathologies. Neurobiol. Learn. Mem. 112, 17-29.

García-Cáceres, C., Lagunas, N., Calmarza-Font, I., Azcoitia, I., Diz-Chaves, Y., García-Segura, L.M., Baquedano, E., Frago, L.M., Argente, J., Chowen, J.A., 2010. Gender differences in the long-term effects of chronic prenatal stress on the HPA axis and hypothalamic structure in rats. Psychoneuroendocrinol., 1525–1535.

Gärtner, M., Rohde-Liebenau, L., Grimm, S., Bajbouj, M., 2014. Working memory-related frontal theta activity is decreased under acute stress. Psychoneuroendocrinol., 43, 105-13.

Glover, V., O'Connor, T.G., O'Donnell, K., 2009. Prenatal stress and the programming of the HPA axis. Neurosci. Biobehav. Res., 35, 17 22.

Goff, B., Gee, D.G., Telzer, E.H., Humphreys, K.L., Gabard-Durnam, L., Flannery, J., Tottenham, N., 2013. Reduced nucleus accumbens reactivity and adolescent depression following early-life stress. Neurosci., 249, 129-38.

Gogtay, N., Nugent, T.F., Herman, D.H., Ordonez, A., Greenstein, D., Hayashi, K.M., 2006. Dynamic mapping of normal human hippocampal development. Hippocam., 16, 664-72.

Gonzalez, I.V., Gonzalez, B.V., Rauch, S.L., Quirk, g.J., 2006. Microstimulation reveals opposing influences of prelimbic and infralimbic cortex on the expression of conditioned fear. Learn. Mem., 13(6), 728-33

Grad, I., Picard, D., 2007. The glucocorticoid responses are shaped by molecular chaperones. Mol. Cell. Endocrinol., 275, 2–12.

Groc, L., Choquet, D., Chaouloff, F., 2008. The stress hormone corticosterone conditions AMPAR surface trafficking and synaptic potentiation. Nat. Neurosci., 11(8), 868–870.

Groeneweg, F.L., Karst, H., de Kloet, E.R., Joels, M., 2011. Rapid non-genomic effects of corticosteroids and their role in the central stress response. J. Endocrinol., 209(2), 153–167.

Gunnar, M., Quevedo, K., 2007. The neurobiology of stress and development. Ann. Rev. Psychol., 58, 145-173.

Gutteling, B.M., de Weerth, C., Buitelaar, J.K., 2005. Prenatal stress and children's cortisol reaction to thefirst day of school. Psychoneuroendocrinol., 30, 541-549.

Hansen, D., Lou, H.C., Olsen, J., 2000. Serious life events and congenital malformations: a national study withcomplete follow-up. Lancet., 356, 875-80.

Hay, D.F., Pawlby, S., Waters, C.S., Sharp, D., 2008. Antepartum and postpartum exposure to maternaldepression: Different effects on different adolescent outcomes. J. Child. Psychol. Psyc., 49, 1079-1088.

Heim, C., Nemeroff, C.B., 2001. The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. Biol. Psychiatry., 49, 1023-1039.

Hill, M.N., McEwen, B., 2009. Endocannabinoids: the silent partner of glucocorticoids in the synapse. Proc. Natl. Acad. Sci. USA, 106(12), 4579-4580.

Hobel, C.J., Dunkel-Schetter, C., Roesch, S.C., Castro, L.C., Arora, C.P., 1999. Maternal plasma corticotropin-releasinghormone associated with stress at 20 weeks' gestation in pregnancies ending in preterm delivery. Am. J. Obstet. Gynecol., 180, S257-63.

Huizink, A.C., Bartels, M., Rose, R.J., Pulkkinen, L., Eriksson, C.J., Kaprio, J., 2008. Chernobyl exposureas stressor during pregnancy and hormone levels in adolescent offspring. J. Epidemiol. Commun. Hum., 62, e5.

Huizink, A.C., Dick, D.M., Sihvola, E., Pulkkinen, L., Rose, R.J., Kaprio, J., 2007. Chernobyl exposure as stressorduring pregnancy and behaviour in adolescent offspring. Acta. Psychiat. Scand., 116, 438-446.

Huizink, A.C., Robles de Medina, P.G., Mulder, E.J., Visser, G.H., Buitelaar, J.K., 2003. Stress duringpregnancy is associated with developmental outcome in infancy. J. Child. Psychol. Psyc., 44, 810-818.

Jackowski, A.P., Douglas-Palumberi, H., Jackowski, M., Win, L., Schultz, R.T., Staib, L.W., 2008. Corpus callosum in maltreated children with posttraumatic stress disorder: A diffusion tensor imaging study. Psychiatry Res: Neuroimaging., 162, 256-261.

Jin, X.C., Lu, Y.F., Yang, X.F., Ma, L., Li, B.M., 2007. Glucocorticoid receptors in the basolateral nucleus of amygdala are required for postreactivation reconsolidation of auditory fear memory. Eur. J. Neurosci., 25, 3702-3712.

Joels, M., Fernandez, G., Roozendaal, B., 2011. Stress and emotional memory: a matter of timing. Trend. CognSci., 15(6), 280-288.

Johnson, L.R., McGuire, J., Lazarus, R., Palmer, A.A., 2011. Pavlovian fear memory circuits and phenotype models of PTSD. Neuropharmacol.

Kandel, E.R., Schwartz, J.H., Jessell, T.M. (Eds.), 2000a. Principles of neural science. 4, 1227-1246.

Karl, A., Schaefer, M., Malta, L.S., Dörfel, D., Rohleder, N., Werner, A., 2006. A meta-analysis of structural brain abnormalities in PTSD. Neurosci. Biobehav. Rev., 30, 1004-1031.

Karst, H., Berger, S., Erdmann, G., Schütz, G., Joëls, M., 2010. Metaplasticity of amygdalar responses to the stress hormone corticosterone. Proc. Natl. Acad. Sci. U.S.A., 107(32), 14449–14454.

Kim, J.J., Jung, M.W., 2006. Neural circuits and mechanisms involved in Pavlovian fear conditioning: A critical review. Neurosci. Biobehav. Rev., 30, 188-202.

Koenig, J.I., Elmer, G.I., Shepard, P.D., Lee, P.R., Mayo, C., Joy, B., 2005. Prenatal exposure to a repeated variable stress paradigm elicits behavioral and neuroendocrinological changes in the adult offspring: potential relevance to schizophrenia, Behav. Brain. Res., 156, 251–261.

Kofman, O., 2002. The role of prenatal stress in the etiology of developmental behavioural disorders. Neurosci. Behav. Rev. 26, 457–70.

Krugers, H.J., Karst, H., Joels, M., 2012. Interactions between noradrenaline and corticosteroids in the brain: from electrical activity to cognitive performance. Front. Cell. Neurosci., 6.

Kurki, T., Hiilesmaa, V., Raitasalo, R., Mattila, H., Ylikorkala, O., 2000. Depression and anxiety in early pregnancy andrisk for preeclampsia. Obstet. Gynecol., 95, 487-90.

Landbergis, P.A., Hatch, M.C., 1996. Psychosocial work stress and pregnancy-induced hypertension. Epidemiol., 7, 346-51.

Laplante, D.P., Brunet, A., Schmitz, N., Ciampi, A., King, S., 2008. Project Ice Storm: Prenatal maternal stressaffects cognitive and linguistic functioning in 5½-yearold children. J. Am. Acad. Child. Adol. Psychiatry., 47, 1063-1072.

Leung, T.N., Chung, T.K.H., Madsen, G., McLean, M., Chang, A.M.Z., Smith, R., 1999. Elevated mid-trimester maternalcorticotrophin-releasing hormone levels in pregnancies that delivered before 34 weeks. Br. J. Obstet. Gynaecol., 106, 1041-6.

Lou, H.C., Hansen, D., Nordentoft, M., Pryds, O., Jensen, F., Nim, J., 1994. Prenatal stressors of human life affectfetal brain development. Dev. Med. Child. Neurol., 36, 826-32.

Lupien, S.J., Lepage, M., 2001. Stress, memory, and the hippocampus: can't live with it, can't live without it. Behav. Brain. Res., 127(1), 137-158.

Lupien, S.J., Maheu, F., Tu, M., Fiocco, A., Schramek, T.E., 2007. The effects of stress and stress hormones on human cognition: Implications for the field of brain and cognition. Brain. Cognition., 65(3), 209-237.

Lupien, S.J., McEwen, B.S., Gunnar, M.R., Heim, C., 2009. Effects of stress throughout the lifespan on the brain, behaviour and cognition, Nat. Rev. Neurosci., 10, 434–445.

Markham, J.A., Taylor, A.R., Taylor, S.B., Bell, D.B., Koenig, J.I., 2010. Characterization of the cognitive impairments induced by prenatal exposure to stress in the rat, Front. Behav. Neurosci., 4.

McGaugh, J.L., 2000. Memory: a century of consolidation. Science, 287(5451), 248–51.

McGaugh, J.L., Roozendaal, B., 2002. Role of adrenal stress hormones in forming lasting memories in the brain. Curr. Opin. Neurobiol., 12(2), 205–210.

Mennes, M., Stiers, P., Lagae, L., Van den Bergh, B., 2006. Long-term cognitive sequelae of antenatal maternalanxiety: Involvement of the orbitofrontal cortex. Neurosci. Biobehav. Res., 30, 1078-1086.

Mesquita, A., Wegerich, Y., Patchev, A., Oliveira, M., Leao, P., Sousa, N., 2009. Glucocor- ticoids and neuro- and behavioural development. Semin. Fetal. Neonatal. Med., 14, 130–5.

Milad, M.P., Klock, S.C., Moses, S., Chatterton, R., 1998. Stress and anxiety do not result in pregnancy wastage. Hum. Reprod., 13, 2296–300.

Mueller, B.R., Bale, T.L., 2007. Early prenatal stress impact on coping strategies and learning performance is sex dependent. Physiol. Behav., 91, 55-65.

Navalta, C.P., Polcari, A., Webster, D.M., Boghossian, A., Teicher, M.H., 2006. Effects of childhood sexual abuse on neuropsychological and cognitive function in college women. J. Neuropsychiatry. Clin. Neurosci., 18, 45-53.

Neil, S., Gail, I., Scott, D.S., 2005. Stress and health: psychological, behavioral, and biological determinants. Ann. Rev. Clin. Psychol., 1, 607-628.

Neugebauer, R., Kline, J., Stein, Z., Shrout, P., Warburton, D., Susser, M., 1996. Association of stressful life events withchromosomally normal spontaneous abortion. Am. J. Epidemiol., 143, 588-96.

Nikolaos, P.D., Edo, R.D., Rachel, Y., Dolores, M., Thorsten, M.K., 2015. Early Life Stress Effects on Glucocorticoid BDNF Interplayinthe Hippocampus. Front. Mol. Neurosci., 10.3389.

Nimby, G.T., Lundberg, L., Sveger, T., McNeil, F., 1999. Maternal distress and congenital malformations: do mothersofmalformed fetuses have more problems? J. Psychiatr. Res., 33, 291-301.

Noble, K.G., Tottenham, N., Casey, B.J., 2005. Neuroscience perspectives on disparities in school readiness and cognitive achievement. Futu. Child., 15, 71-89.

Noorlander, C., Visser, G., Ramakers, G., Nikkels, P., De Graan, P., 2008. Prenatal corticosteroid exposure affects hippocampal plasticity and reduces lifespan, Dev. Neurobiol., 68, 237-246.

O'Connor, T.G., Ben-Shlomo, Y., Heron, J., Golding, J., Adams, D., Glover, V., 2005. Prenatal anxiety predictsindividual differences in cortisol in pre-adolescent children. Biol. Psychiat., 58, 211-217.

O'Connor, T.G., Heron, J., Golding, J., Glover, V., 2003. Maternal antenatal anxiety and behavioural/emotionalproblems in children: A test of a programming hypothesis. J. Child. PsycholPsyc., 44, 1025-1036.

Orchinik, M., Murray, T.F., Moore, F.L., 1991. A corticosteroid receptor in neuronal membranes. Science. 252(5014), 1848–1851.

Oreland, S., Raudkivi, K., Oreland, L., Harro, J., Arborelius, L., Nylander, I., 2011. Ethanol-inducedeffects on the dopamine and serotonin systems in adult wistar rats are dependent on early-lifeexperiences. Brain. Res., 1405, 57-68.

Paarlberg, K.M., Vingerhoets, A.J., Passchier, J., Dekker, G.A., Heinen, A.G., van Geijn, H.P., 1995. Psychosocial factors andpregnancy outcome: a review with emphasis on methodological issues. J. Psychosom. Res., 39, 563-95.

Paarlberg, K.M., Vingerhoets, A.J., Passchier, J., Dekker, G.A., van Geijn, H.P., 1999. Psychosocial predictors of low birthweight: a prospective study. Br. J. Obstet. Gynaecol., 106, 834-41.

Paul, R.H., Henry, L., Stuart, M.G., Guilmette, T., Niaura, R., Bryant, R., 2008. The relationship between early life stress and microstructural integrity of the corpus callosum in a non-clinical population. Neuropsychiatr. Dis. Treat., 4, 193–201.

Payne, J., Jackson, E., Hoscheidt, S., Ryan, L., Jacobs, W., Nadel, L., 2007. Stress administered prior to encoding impairs neutral but enhances emotional long-term episodic memories. Lern. Mem., 17, 861-868.

Pederson, C.L., Maurer, S.H., Kaminski, P.L., Zander, K.A., Peters, C.M., Stokes-Crowe, L.A., 2004. Hippocampal volume and memory performance in a community-based sample of women with Posttraumatic Stress Disorder secondary to child abuse. J. Trauma. Stress., 17, 37-40.

Pereda, N., Guilera, G., Forns, M., Gómez-Benito, J., 2009. The international epidemiology of child sexual abuse: A continuation of Finkelhor. Child. Abuse. Negl., 33, 331-342.

Perkins, A.V., Linton, E.A., Eben, F., Simpson, J., Wolff, C.D.A., Redman, C.W.G., 1995. Corticotrophin-releasing hormone and corticotrophin-releasing hormone binding protein in normal and pre-eclamptic human pregnancies. Br. J. Obstet. Gynaecol., 102, 118-22.

Pitman, R.K., Rasmusson, A.M., Koenen, K.C., Shin, L.M., Orr, S.P., Gilbertson, M.W., Milad, M.R., Liberzon, I., 2012. Biological studies of post-traumatic stress disorder. Nat. Rev. Neurosci., 13, 769-787.

Prager, E.M., Johnson, L.R., 2009. Stress at the synapse: Signal transduction mechanisms of adrenal steroids at neuronal membranes. Sci. Signal., 2(86), re5-re5.

Pu, Z., Krugers, H.J., Joëls, M., 2009. Beta-adrenergic facilitation of synaptic plasticity in the rat basolateral amygdala in vitro is gradually reversed by corticosterone. Learn. Memory., 16(2), 155–160.

Quirarte, G.L., Galvez, R., Roozendaal, B., McGaugh, J.L., 1998. Norepinephrine release in the amygdala in response to footshock and opioid peptidergic drugs. Brain. Res. 808(2), 134–140.

Raio, C.M., Phelps, E.A., 2015. The influence of acute stress on the regulation of conditioned fear. Neurobiology of Stress, 1, 134-146.

Rau, V., Fanselow, M.S., 2009. Exposure to a stressor produces a long lasting enhancement of fear learning in rats. Stress, 12, 125–33.

Roozendaal, B., 2002. Stress and memory: opposing effects of glucocorticoids on memory consolidation and memory retrieval. Neurobiol. Learn. Mem., 78(3), 578–95.

Roozendaal, B., Hui, G.K., Hui, I.R., Berlau, D.J., McGaugh, J.L., Weinberger, N.M., 2006b. Basolateral amygdala noradrenergic activity mediates corticosterone-induced enhancement of auditory fear conditioning. Neurobiol. Learn. Mem., 86(3), 249–255.

Roozendaal, B., McEwen, B.S., Chattarji, S., 2009. Stress, memory and the amygdala. Nature. Rev. Neurosci., 10, 423-433.

Roozendaal, B., McGaugh, J.L., 1996a. Amygdaloid nuclei lesions differentially affect glucocorticoid-induced memory enhancement in an inhibitory avoidance task. Neurobiol. Learn. Mem., 65(1), 1–8.

Roozendaal, B., McGaugh, J.L., 2011. Memory modulation. Behav. Neurosci., 125(6), 797.

Roozendaal, B., Okuda, S., Van der Zee, E.A., McGaugh, J.L., 2006a. Glucocorticoid enhancement of memory requires arousal-induced noradrenergic activation in the basolateral amygdala. P. Natl. Acad. Sci., USA. 103(17), 6741–6746.

Ruiz, R.J., Avant, K.C., 2005. Effects of maternal prenatal stress on infant outcomes: a synthesis of the literature. ANS. Adv. Nurs. Sci., 28(4), 345–55.

Rutter, M., O'Connor, T.G., 2004. Are there biological programming effects for psychological development? Findings from a study of Romanian adoptees. Dev. Psychol., 40, 81-94.

Schneider, M.L., Moore, C.F., Kraemer, G.W., Roberts, A.D., DeJesus, O.T., 2002. The impact of prenatalstress, fetal alcohol exposure, or both on development: Perspectives from a primate model. Psychoneuroendocrinol., 27, 285–298.

Sharpe, M.J., Killcross, S., 2014. The prelimbic cortex contributes to the down- regulation of attention towards redundant cues. Cerebral. Cortex., 24, 1066-1074.

Shin, L.M., Liberzon, I., 2010. The neurocircuitry of fear, stress, andanxiety disorders. Neuropsychopharmacol., 35, 169-191.

Simms, J.A., Nielsen, C.K., Li, R., Bartlett, S.E., 2014. Intermittent access ethanol consumption.

Smith, S.M., Vale, W.W., 2006. The role of the hypothalamic-pituitary-adrenal axis in neuroendocrine responses to stress. Clin. Neurosci., 8(4), 383-395.

Spanagel, R., Noori, H.R., Heilig, M., 2014. Stress and alcohol interactions: Animal studies and clinicalsignificance. Trend. Neurosci., 37, 219-227.

Stamatakis, A., Kalpachidou, T., Raftogianni, A., Zografou, E., Tzanou, A., Pondiki, S., Stylianopoulou, F., 2015. Rat dams exposed repeatedly to a daily brief separation from the pups exhibitincreased maternal behavior, decreased anxiety and altered levels of receptors for estrogens(eralpha, erbeta), oxytocin and serotonin (5-ht1a) in their brain. Psychoneuroendocrinol., 52, 212-228.

Sylvia Ortega-Martínez, 2015. Influences of prenatal and postnatal stress on adult hippocampal neurogenesis: The double neurogenic niche hypothesis. Behav. Brain. Res., 281, 309-317.

Szuran, T.F., Pliška, V., Pokorny, J., Welzl, H., 2000. Prenatal stress in rats: effects on plasma corticosterone, hippocampal glucocorticoid receptors, and maze performance, Phys- iol. Behav. 71, 353–362.

Teicher, M., Andersen, S., Polcari, A., Anderson, C., Navalta, C., Kim, D., 2003. The neurobiological consequences of early stress and childhood maltreatment. Neurosci. Biobehav. Rev., 27, 33-44.

Teicher, M., Dumont, N., Ito, Y., Vaituzis, C., Giedd, J., Andersen, S., 2004. Childhood neglect is associated with reduced corpus callosum area. Biol. Psychiatry., 56, 80-85.

Thompson, P.M., Giedd, J.N., Woods, R.P., MacDonald, D., Evans, A.C., Toga, A.W., 2000. Growth patterns in the developing brain detected by using continuum mechanical tensor maps. Nature., 404, ,190-193.

Tsigos, C., &Chrousos, G. P. (2002).Hypothalamic–pituitary–adrenal axis, neuroendocrine factors and stress.J Psychosom. Res. 53(4), 865-871.

Tully, K., Li, Y., Tsvetkov, E., Bolshakov, V.Y., 2007. Norepinephrine enables the induction of associative long-term potentiation at thalamo-amygdala synapses. Proc. Natl. Acad. Sci., U.S.A., 104, 14146-14150.

Van Den Bergh, B.R., Marcoen, A., 2004. High antenatal maternal anxiety is related to ADHD symptoms, externalizingproblems, and anxiety in 8- and 9-year-olds. Child. Dev., 75, 1085–1097.

Van den Bergh, B.R., Van Calster, B., Smits, T., Van Huffel, S., Lagae, L., 2008. Antenatal maternal anxiety isrelated to HPA-axis dysregulation and self-reported depressive symptoms in adolescence: A prospective study on the fetal origins of depressed mood. Neuropsychopharmacol., 33, 536-535.

Venero, C., Borrell, J., 1999. Rapid glucocorticoid effects on excitatory amino acid levels in the hippocampus: a microdialysis study in freely moving rats. Eur. J. Neurosci., 11(7), 2465–2473.

Vengeliene, V., Bilbao, A., Molander, A., Spanagel, R., 2008. Neuropharmacology of alcohol addiction. Br. J. Pharmacol., 154, 299-315.

Vertes, R.P., 2004. Differential projections of the infralimbic and prelimbic cortex in the rat. Synapse, 51, 32-58.

Weinstock, M., 2005. The potential influence of maternal stress hormones on development and mental health of theoffspring BRAIN BEHAV IMMUN, 19, 296–308. Weinstock, M., 2008.The long-term behaviouralconsequencesof prenatal stress. Neurosci. Biobehav. Res., 32, 1073-1086.

Weinstock, M., 2008. The long-term behavioural consequences of prenatal stress, Neurosci. Biobehav. Rev., 32, 1073–1086.

Yang, J., Han, H., Cao, J., Li, L., Xu, L., 2006. Prenatal stress modifies hippocampal synaptic plas- ticity and spatial learning in young rat offspring, Hippocampus, 16, 431–436.

Yehuda, R., Engel, S.M., Brand, S.R., Seckl, J., Marcus, S.M., Berkowitz, G.S., 2005. Transgenerationaleffectsof posttraumatic stress disorder in babies of mothers exposed to the World Trade Center attacks during pregnancy. J. Clin. Endocr. Metab., 90, 4115–4118.

Zalachoras, I., Houtman, R., Meijer, O.C., 2013. Understanding stress-effects in the brain via transcriptional signal transduction pathways. Neurosci., 242, 97–109.

Zovkic, I.B., Sweatt, J.D., 2013. Epigenetic mechanisms in learned fear: implications for PTSD. Neuropsychopharmacol., 38, 77-93.

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