Developmental Cognitive Neuroscience 19 (2016) 233–247

Contents lists available at ScienceDirect

Developmental Cognitive Neuroscience

journal homepage: http://www.elsevier.com/locate/dcn

Effects of early life stress on amygdala and striatal development

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ARTICLE INFO

Article history:
Received 27 March 2015
Received in revised form 28 March 2016
Accepted 27 April 2016
Available online 29 April 2016

Keywords:
Amygdala
Striatum
Early life stress
Affective valuation
Learning

ABSTRACT

Species-expected caregiving early in life is critical for the normative development and regulation of emotional behavior, the ability to effectively evaluate affective stimuli in the environment, and the ability to sustain social relationships. Severe psychosocial stressors early in life (early life stress; ELS) in the form of the absence of species expected caregiving (i.e., caregiver deprivation), can drastically impact one's social and emotional success, leading to the onset of internalizing illness later in life. Development of the amygdala and striatum, two key regions supporting affective valuation and learning, is significantly affected by ELS, and their altered developmental trajectories have important implications for cognitive, behavioral and socioemotional development. However, an understanding of the impact of ELS on the development of functional interactions between these regions and subsequent behavioral effects is lacking. In this review, we highlight the roles of the amygdala and striatum in affective valuation and learning in maturity and across development. We discuss their function separately as well as their interaction. We highlight evidence across species characterizing how ELS induced changes in the development of the amygdala and striatum mediate subsequent behavioral changes associated with internalizing illness, positing a particular import of the effect of ELS on their interaction.

Contents

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http://dx.doi.org/10.1016/j.dcn.2016.04.005

1. Introduction

The ability to navigate the world is dependent upon evaluating affective stimuli in terms of their relative danger/safety and their potential for reward (e.g., appraising someone as trustworthy, avoiding unhealthy foods). While extensive research indicates that affective valuation relies heavily on the amygdala and ventral striatum in adulthood, early life may be a time during which such processes are critical for learning environmental contingencies and understanding how to interact with the world. A robust literature highlights important normative structural and functional changes in the amygdala and striatum during the early years of life (i.e., childhood, adolescence), which facilitate approach and avoidance behaviors. One key factor in the normative development of affective valuation is a stable rearing environment characterized by the presence of species expected caregiver availability (Tottenham, 2012). Caregivers provide developing organisms not only a means by which to meet basic survival needs, but they also provide a regulatory base from which to explore and learn about the world (Hofer, 2006).

Across species, severe psychosocial stressors early in life (early life stress; ELS), particularly in the form of the *absence* of species expected caregiving (i.e., caregiver deprivation) can profoundly influence affective valuation and the establishment of stable relationships with caregivers and others. Caregiver deprivation is frequently associated with a host of developmental concerns, including the onset of both internalizing (anxiety and depressive disorders) and externalizing behaviors (e.g., impulsivity, conduct disorders) later in life (Ellis et al., 2004; Zeanah et al., 2009). These behavioral phenotypes critically involve alterations in the ability to evaluate and appropriately respond to rewarding/aversive stimuli, suggesting that ELS induces alterations in the functional development of the amygdala and striatum. In this review we will examine the effects of ELS on neural and socio-affective development, largely from on the perspective of caregiver deprivation. We propose that the association between ELS and subsequent behavioral consequences associated with internalizing illness are mediated by changes effected on amygdala and striatal function and their interaction. We will begin by operationalizing ELS and its downstream behavioral consequences. We will next detail anatomical and functional considerations of the amygdala and ventral striatum in maturely developed organisms, with respect to their role in affective valuation, with a particular spotlight on examining their interaction. Next we will review extant findings on the normative structural and functional development of these structures. We will then highlight the role of ELS in the structural and functional development of these regions and related behavioral effects. We will conclude with a proposal for how ELS may affect amygdala-striatal interactions and discuss limitations and future directions for the field.

A recent framework for conceptualizing ELS posits that adverse early experiences fall along dimensions of threat and deprivation (McLaughlin et al., 2014; Sheridan and McLaughlin, 2014). Here, threat is conceptualized as an atypical experience posing a direct physical danger to a developing organism (e.g., physical/sexual abuse), whereas deprivation is operationalized as the absence of expected social, cognitive and affective environmental inputs and enrichment during development (e.g., neglect). Consideration of the nature of adversities experienced is an important step forward in the field. We would add that caregiver deprivation (i.e., emotional neglect or institutional care) also poses a direct threat to a (semi-)altricial organism's survival: caregiver deprivation involves a lack of protection from outside threats and a lack/absence of physiological and affective regulation from a caregiver. Caregiver deprivation can take many forms across species––e.g., removing a maternal figure from a nest, rearing in isolation from the rest of a group, or institutionalization in humans (i.e., being reared in orphanage care). We will focus largely on ELS in the form of caregiver deprivation in this review, because it allows for the ability to draw parallels across non-human and human literatures.

ELS is often associated with the development of a host of cognitive, social and affective deficits, which precede the development of mental illness later in life (Gee and Casey, 2015; Green et al., 2010; Gunnar and Quevedo, 2007; Masten and Cicchetti, 2010). Most frequently, caregiver deprivation is linked with the development of social withdrawal, poor regulatory abilities, and higher risk for internalizing illness such as depression and anhedonia, anxiety disorders, as well as externalizing disorders and behavioral problems (Conti et al., 2012; Corcoran et al., 2012; Ellis et al., 2004; Gee and Casey, 2015; Gunnar and Quevedo, 2007; Lupien et al., 2009; Pechtel and Pizzagalli, 2011; Romeo et al., 2003; Sánchez et al., 2001; Tottenham and Sheridan, 2009; Zeanah et al., 2009). The link between caregiver deprivation and downstream mental health consequences may be mediated by ELS induced changes in the functional development of the amygdala and striatum and their interaction, both of which undergo massive change throughout childhood and adolescence, lending them to be plastic and subject to environmental influence (Gee and Casey, 2015; Masten and Cicchetti, 2010).

2. Amygdala and striatum: anatomical considerations

The amygdala and striatum are two subcortical structures critical for affective valuation and learning across species. The amygdala is comprised of approximately thirteen nuclei and subnuclei (rodents: LeDoux, 2000 non-human primates: Pitkänen and Amaral, 1998; Pitkänen et al., 1997). The basolateral complex of the amygdala (the lateral nucleus, basal nucleus, accessory basal nucleus; BLA) and the central nucleus (CeA) are most often implicated in affective valuation, and relay information regarding associations between environmental stimuli and potential outcomes to connected regions (LeDoux, 2000; Pitkänen et al., 1997). The BLA receives sensory input from thalamic nuclei, auditory and sensory cortices as well as the hippocampus, and provides both direct and indirect signals to the central nucleus of the amygdala (Pitkänen et al., 1997). The majority of BLA neurons are excitatory glutamatergic cells which project to other amygdala nuclei including the CeA, the ventral hippocampus (anterior in humans), prefrontal cortex and importantly, to the ventral striatum (nucleus accumbens (NAcc)). The CeA is the major output structure of the amygdala, containing primarily inhibitory GABAergic neurons and controls autonomic responses to incentive-laden stimuli (Davis and Whalen, 2001; Phelps and LeDoux, 2005).

The striatum is the primary input region of the basal ganglia (Delgado, 2007) and receives input from a host of prefrontal cortical and subcortical structures including orbitofrontal cortex (OFC), ventromedial PFC (vmPFC), portions of anterior cingulate cortex (ACC), the hippocampus, and importantly, the amygdala (Alexander et al., 1986; Haber and Behrens, 2014; Haber and Knutson, 2010; Middleton and Strick, 2000; Pennartz et al., 2011; Sesack and Grace, 2010). The striatum can be segregated along a dorsal-ventral divide (though see Voorn et al., 2004) The dorsal striatum is comprised of the caudate nucleus and the putamen, whereas the ventral striatum is comprised of the nucleus accumbens (consisting of medial (core) and lateral (shell) divisions), and ventral portions of the caudate nucleus and putamen (Delgado, 2007; Haber and Knutson,

2010; Meredith and Pattiselanno, 1996; Zaborszky et al., 1985). The ventral striatum receives excitatory glutamatergic input from cortical regions, thalamus, ventral hippocampus (anterior in humans), and the BLA (Haber and Behrens, 2014; Tovote et al., 2015). Importantly, dopaminergic (DA) input from midbrain nuclei (e.g., ventral tegmental area) heavily innervate the ventral striatum, and these connections are thought to mediate ventral striatal function in appetitive behaviors (Haber et al., 2000; Haber and Knutson, 2010; Sesack and Grace, 2010)

3. Amygdala and striatum function in maturity

The amygdala's role in affective valuation has often been characterized from the point of view of aversive learning, and evaluating threats. Across species, the amygdala is strongly implicated in fear learning––i.e., associating stimuli or actions with aversive/threatening outcomes (e.g., shock)––and triggering a response to a threat (Davis, 1992; LeDoux, 2000; Pitkänen et al., 1997; Robbins and Everitt, 1996; Whalen et al., 2004, 1998, 2001). In both maturely developed rodents and humans, studies of fear learning can be conducted using mild electric shocks as an aversive unconditioned stimulus. During fear learning, current stimulus-value associations are relayed from the BLA to the CeA, leading to a putative physiological 'fear' response. Such a response is often characterized by heightened amygdala activation to threatening stimuli (e.g., predator), increased autonomic arousal, and behavioral responses aimed at avoiding or confronting a threat (e.g., freezing behavior in rats) (Groenewegen et al., 1999; LaBar et al., 1998; Olsson and Phelps, 2004; Phelps and LeDoux, 2005). Such physiological and behavioral outcomes can in turn facilitate avoidance learning (i.e., learning to avoid negative outcomes or threatening stimuli). Indeed, amygdala lesions are associated with an inability to demonstrate orienting behaviors and implicit learning of pairings between conditioned stimuli and aversive outcomes.

However, abundant evidence demonstrates that the amygdala also facilitates reward processing, suggestive of a broader evaluative role. Studies of reward processes in non-human animals typically employ food or juice as reinforcers, where as human studies typically employ monetary rewards. Non-human animal studies show dissociable roles for the BLA and CeA in reward processes. The BLA in part plays a role in linking environmental stimuli to their current biological value, thereby supporting goal-directed choice (Baxter and Murray, 2002). Lesions to the BLA impair an organism's ability to maintain and update value representations when an instrumental response is required (Baxter and Murray, 2002; Davis and Whalen, 2001). The CeA, on the other hand aids in the generation of physiological responses and behaviors during both reward-related learning and aversive learning. These responses tend to be directed toward conditioned stimuli, as opposed to valued outcomes (e.g., orienting responses to a tone that predicts a reward) (Davis and Whalen, 2001; Tovote et al., 2015). In fact, lesions to the CeA abolish stimulus oriented responses during reward learning, but leave the instrumental response to the reward intact (Baxter and Murray, 2002). Distinct populations of amygdala neurons in non-human primates flexibly represent the current state value of rewarding and aversive stimuli (Belova et al., 2008; Paton et al., 2006; Salzman et al., 2007) and code valence specific expectations regarding upcoming rewarding and aversive outcomes (Belova et al., 2007). Human fMRI work corroborates the amygdala's role in signaling the positive and negative value of affective stimuli in the environment that can inform behavior (O'Doherty et al., 2001, 2002), suggesting an evolutionarily conserved, broad and evaluative role for this region (Gottfried et al., 2003).

The striatum is broadly involved in motor, cognitive and hedonic aspects of affective valuation. The dorsal striatum is typically associated with cognitive and motor aspects of incentive-based behavior––e.g., linking actions with outcomes and action selection (Balleine et al., 2007; Tricomi et al., 2004). The ventral striatum is of particular interest to this review because of its role in the pursuit of appetitive stimuli, representing the subjective value of experienced and expected primary, secondary and more abstract social rewards (Bartra et al., 2013; Fareri and Delgado, 2014; Haber and Knutson, 2010; Kable and Glimcher, 2007; Knutson et al., 2001, 2005; Robbins and Everitt, 1996), and its function as an interface between limbic and motor structures, translating affective, motivational signals into action(Groenewegen et al., 1999; Hart et al., 2013). Similarly to the amygdala, however, emergent evidence suggests that the ventral striatum is also involved in processing of aversive stimuli in certain contexts (Delgado et al., 2008; Levita et al., 2009; Pohlack et al., 2012; Robinson et al., 2013). The ventral striatum's role in affective valuation and learning is related to input from midbrain DA nuclei, which facilitate learning and behavioral adaptation via prediction error signaling––i.e., coding for the difference between experienced and expected outcomes (Hollerman and Schultz, 1998; Niv and Schoenbaum, 2008; Schultz et al., 1997). However, we note that the nature of the specificity of this signal (i.e., unique to reward or more valence general) is currently debated in the literature (Fiorillo, 2013; Matsumoto and Hikosaka, 2009). The ventral striatum in humans thus aids affective learning via the computation of value-based signals that may be dopamine dependent.

4. Amygdala-striatal interactions in maturity

The unidirectional glutamatergic projections from the BLA to the ventral striatum (Everitt et al., 1991; Groenewegen et al., 1999; Robbins et al., 1989) facilitate the ventral striatum's role as an interfacing region able to translate evaluative signals into action. The basolateral amygdala encodes the sensory and affective properties of stimuli and outcomes (i.e., value) learned via Pavlovian or instrumental conditioning processes, which are then relayed to the ventral striatum to translate into value-based actions (e.g., pursue, avoid) (Everitt et al., 1991; Groenewegen et al., 1999; Hart et al., 2013; Robbins et al., 1989); thus, amygdala-ventral striatal connections may be critical for learning and updating stimulus value. We do note that the basolateral amygdala also projects to the dorsal striatum in rodents (Hart et al., 2013) and non-human primates (Cho et al., 2013), which may facilitate response-outcome learning (Balleine et al., 2007; Hart et al., 2013).

The rodent literature provides a useful base from which to examine the nature of amygdala-striatal interactions, particularly given that work on this in humans is limited. Studies of reward devaluation (Balleine and Dickinson, 1998; Yin et al., 2004) indicate that motivated responding for rewards can be influenced or controlled by representations of a response and a reward, and this process appears dependent upon the relationship between the BLA and NAcc. Reward devaluation involves either allowing an animal to consume a valued stimulus (i.e., food reward) to satiety or conditioning a previously rewarding stimulus with an aversive outcome (i.e., poison), and then testing in extinction whether the animal continues to choose that stimulus. Indeed, lesioning BLA-NAcc core projections eliminates reward devaluation effects, resulting in continued pursuit of devalued outcomes. BLA-NAcc shell lesions, on the other hand, leave intact the ability to detect changes in outcome value (Shiflett and Balleine, 2010). Studies involving a phenomenon known as Pavlovian-to-instrumental transfer (PIT) provide additional insight into the nature of amygdalostriatal interactions. PIT

studies measure a process by which instrumental approach or avoidance of incentives are mediated by Pavlovian associations between an environmental stimulus and the incentive (Balleine and Dickinson, 1998; Cardinal and Everitt, 2004 see also Lewis et al., 2013). Testing PIT in the laboratory involves classically conditioning organisms to associate a stimulus with a rewarding (or aversive) outcome and later testing in extinction if the organism increases instrumental responding for an incentive in the presence of only the classically conditioned cue (specific PIT) or in the presence of any cue (general PIT) (Balleine and Dickinson, 1998; Lewis et al., 2013). BLA-NAcc interactions are critical to both types of PIT (Corbit and Balleine, 2005), such that lesioning BLA-NAcc shell projections impairs specific PIT while lesioning CeA-NAcc core projections impair general PIT (Corbit and Balleine, 2011). This dichotomy suggests that the NAcc shell may be important for inhibiting responding to stimuli that were not paired with a reinforcing outcome (Corbit and Balleine, 2011). Reward devaluation and PIT studies thus highlight the importance of amygdalostriatal interactions in affective learning that may mimic real-life conditions, in which we come to associate certain behaviors (e.g., eating, drinking) with specific contexts (e.g., specific groups of people) or in which we have to rapidly learn about changing environmental contingencies.

Amygdalostriatal interactions originate from the amygdala. Recording of local field potentials (low frequency electrical signal fluctuation in a neuronal population likely reflecting synaptic input; (van der Meer, 2010)) from the basolateral amygdala and striatum in cats has revealed spontaneous preferential coupling of amygdala and striatal gamma oscillations, which is induced by the BLA (Popescu et al., 2009). Gamma oscillations are generally thought to be important for a variety of cognitive processes (van der Meer, 2010), and for broader homeostatic maintenance (Merker, 2013). Amygdalostriatal coupling was associated with improved reward-learning performance (Popescu et al., 2009). Amygdala-induced NAcc reward-related responses are further dependent upon glutamatergic BLA to NAcc projections (though see also Britt et al., 2012; Stuber et al., 2011), and optogenetic inactivation of the BLA reduces NAcc neural firing to reward predicting stimuli (Ambroggi et al., 2008). Taken together, amygdalostriatal interactions in affective valuation and learning appear based on excitatory amygdala-based signals sent to the ventral striatum, which then facilitates value-based decisions/actions.

While limited, an emergent human literature corroborates the importance of amygdalostriatal interactions in affective valuation and learning, though their precise nature and direction is less clear. For example, increased task-based functional connectivity between the amygdala and striatum is associated with better learning of reward predicting information when preceded by social cues (Watanabe et al., 2013). Conversely, fear conditioned stimuli inhibit both the ability to update the representation of that stimulus as a reward-predicting stimulus (i.e., reversal learning, which additionally involves the OFC (for exetnsive reviews see Kringelbach, 2005; Rolls, 2000)), which is reflected in the inhibition of activation in the striatum, among other regions (Wittmann, 2014). The implementation of computational approaches to fMRI––i.e., applying mathematically formulated models of psychological processes (Niv, 2009)––has facilitated more mechanistic and precise characterizations of amygdala and striatum function in valuation and learning which could inform thoughts regarding interactive functions. The ventral striatum is frequently implicated in the computation of prediction-error signaling in humans in a variety of contexts, both non-social and social, and in instrumental and pavlovian situations (Daw et al., 2011; Fareri et al., 2015a; Li et al., 2011; O'Doherty et al., 2004; Schonberg et al., 2007). Computational processes subserved by the amygdala also support varied roles in affective and associative learning. The amygdala has been implicated in performing prediction-error related computations during instrumental learning and decision-making (Prévost et al., 2011; Rutledge et al., 2010), which may be dissociable depending on incentive context: the BLA encodes action-value and uncertainty signals during reward-learning, whereas the CeA does so during avoidance learning (Prévost et al., 2011). Further, during Pavlovian learning contexts, the amygdala supports a more general associability signal––i.e., the strength of the association between a stimulus and outcome, agnostic to expectations (Rescorla and Wagner, 1972)––as compared to a prediction error computation, which instead relies on the ventral striatum (Li et al., 2011). A complex interplay between the amygdala and striatum thus appear important with respect to affective valuation and learning, performing dissociable computations as a function of varied contexts; however, initial signals regarding stimulus/action values is generated in the amygdala which may then be used by the ventral striatum in terms of updating expectations for learning.

5. Amygdala development

The early years of life require an ability to rapidly learn and assess environmental contingencies. Studies of structural and functional development of the amygdala indicate that early life is a time of dynamic change in the amygdala, which could facilitate affective learning (Tottenham and Sheridan, 2009). The rodent amygdala is largely structurally intact early in life (Bouwmeester et al., 2002; Chareyron et al., 2012), and extensive prenatal neurodevelopmental differentiation renders the human amygdala structurally present and developed by birth (Ulfig et al., 2003) as well, with rapid growth reported in the first year of life (Gilmore et al., 2012). While structural changes continue to occur within the amygdala into early adulthood (Giedd et al., 1996b; Goddings et al., 2013; Hu et al., 2013; Wierenga et al., 2014), evidence in non-human primates (Payne et al., 2010) and in humans (Hu et al., 2013; Ostby et al., 2009; Wierenga et al., 2014) indicates that the most rapid rates of structural change in the amygdala occur prior to adolescence. Massive changes in amygdala function emerge in these early years as well, impacting our ability to learn about the environment. During development, social and affective signals gleaned from the facial expressions of others provide a primary source of information about the world. As such, affective facial displays are typically employed as affective stimuli in studies of human amygdala development. For example, fearful faces provide cues as to an impending threat in the environment, while happy faces may signal social approval. The functional response profile of the amygdala to these important socio-affective signals significantly changes across the lifespan, though the nature of change tends to vary as a function of the question posed. Initial studies indicated that children and early adolescents (aged approximately 9–13) showed stronger amygdala reactivity to neutral compared to fearful faces, whereas adults showed the opposite pattern (Thomas et al., 2001 though see also Pagliaccio et al., 2013). Neutral expressions may thus be more ambiguous/threatening early in life, or alternatively, the amygdala may not be able to effectively evaluate aversive/threatening facial expressions early on. Peak amygdala reactivity has also been reported during adolescence when averaging activation across valence of affective facial expressions (Hare et al., 2008; Moore et al., 2012). However, isolating the response of the amygdala to threatening stimuli (i.e., fearful faces) in comparison to an implicit baseline condition reveals that threat-based amygdala reactivity is high early in life (i.e., childhood) and decreases throughout adolescence into adulthood (Gee et al., 2013b see also Vink et al., 2014). Similar linear age-related declines in amygdala reactivity emerge when: (1) considering faces of varied emotional expression (Swartz et al., 2014) and varied social value (i.e., mothers, strangers) com-

pared to baseline (Tottenham et al., 2012) (2) examining responses to others in pain (Decety and Michalska, 2009; Decety et al., 2011); (3) evaluating positive (e.g., food) stimuli (Silvers et al., 2014); and (4) comparing only adolescents to adults (Guyer et al., 2008; Monk et al., 2003). The overall pattern of increased amygdala reactivity during early life suggests an enhanced ability to detect affective stimuli early in life.

If the amygdala cues the ventral striatum to associations between valued stimuli/actions and outcomes in adult organisms in preparation for incentive-based responses, a highly reactive amygdala early in life may adaptively serve to develop this functional relationship with the ventral striatum. While there is not abundant human evidence for this, amygdala activation early in life could serve to 'train' other anatomically connected regions (e.g., mPFC) and foster the later development of additional connectivity (Cressman et al., 2010). The mPFC's roles in the regulation and extinction of fear (Hartley and Phelps, 2012, 2010; Motzkin et al., 2014; Phelps et al., 2004; Schiller and Delgado, 2010) typically do not emerge prior to adolescence (Callaghan and Richardson, 2013),consistent with adolescent development of mPFC to amygdala projections compared to the existence of amygdala to mPFC projections in pre-adolescent rodents (Cressman et al., 2010). Human fMRI studies support the later developmental emergence of mPFC-amygdala connectivity, with a regulatory profile (e.g., negative connectivity) during the viewing of fearful faces emerging only after age 10, and becoming linearly more negative with age (Gee et al., 2013b). Similar task-based connectivity patterns emerge when viewing images of pain administered to others (Decety et al., 2011) and during response inhibition tasks (Perlman and Pelphrey, 2011); supporting task-free resting-state evidence also shows that amygdala-mPFC connectivity emerges only after late childhood/early adolescence (Gabard-Durnam et al., 2014). Interpreted within this framework, high amygdala reactivity early in life may serve a normative function of training the connected regions (e.g., ventral striatum) to encode value-based stimuli, with regulatory mPFC function coming online at later developmental stages.

6. Striatal development

Striatal development has been a particular focus of investigations aiming to characterize oft observed adolescent specific increases in incentive-based behaviors––e.g., risky decision-making. Importantly, deficits in striatal responses to reward and the ability to sustain positive affect are one characteristic of internalizing illness such as depression (Heller et al., 2013; Pizzagalli et al., 2009; 2008) and as such it is critical to highlight the normative development of this region. Striatal subnuclei––caudate, putamen, nucleus accumbens––often exhibit linear age-related decreases in volume (Giedd et al., 1996a; Wierenga et al., 2014), in contrast to protracted prefrontal cortical development, which may reach peak gray matter volume at approximately onset of adolescence prior to declining into adulthood (Giedd, 2004; Somerville and Casey, 2010; Sowell et al., 1999) However, recent longitudinal work (Raznahan et al., 2014) reports an overall curvilinear trajectory of striatal volumetric maturation that is protracted compared to cortical volumetric maturation, with regionally heterogeneous patterns: age-related volumetric increases in the caudate and posterior lateral putamen emerged in conjunction with volumetric decreases in anterior ventral portions of the caudate and putamen (Raznahan et al., 2014). Raznahan and colleagues take these results to suggest the importance of accounting for more fine-grained structural developmental changes within a region, such as rate of change across age.

In contrast to the amygdala, peak functional reactivity in the ventral striatum is consistently observed during adolescence, as compared to childhood and adulthood, within the context of experiencing (monetary) rewards (Casey et al., 2010; Fareri et al., 2008; Richards et al., 2013; Somerville et al., 2010) (though see also Bjork et al., 2010; Ernst et al., 2005; Galván et al., 2006; Van Leijenhorst et al., 2010a,b). This effect tends to be exaggerated for rewards of greater magnitude (Galván et al., 2006). A heightened adolescent reward response enhances both computations of subjective value in the ventral striatum compared to adults (Barkley-Levenson and Galvan, 2014) and neurocomputational learning signals (i.e., prediction error) compared to children and adults (Cohen et al., 2010; though see also van den Bos et al., 2012). Similar adolescent specific effects persist across domains to experienced primary (Galván and McGlennen, 2012 though see also Silvers et al., 2014), and social (Jones et al., 2014; Somerville et al., 2011) rewards, concurring with the augmented influence of peers during adolescence (Crone and Dahl, 2012; Steinberg, 2008). Studies focusing on reward anticipation, on the other hand, reveal a less consistent picture of developmental change in the striatum, potentially as a function of varied task demands. For example, reaction time tasks requiring a button press to a cue often report a decreased ventral striatal response in adolescents (vs. adults) when anticipating the delivery of a reward (Bjork et al., 2010, 2004), while anticipation of making a response during an anti-saccade task is associated with increased ventral striatal recruitment in adolescence (Geier et al., 2010). In conjunction with mesolimbic dopaminergic changes during adolescence, increased ventral striatal reactivity to rewards in adolescence may be related to an increase in risk-taking behaviors (Galván, 2013)––i.e., greater sensitivity to experienced rewards drives the pursuit of such rewards, though a recent meta-analysis suggests adolescent risk-taking increases vary as a function of the immediacy of potential reward availability (Defoe et al., 2015)

Given the prominence of midbrain dopaminergic projections to the ventral striatum, as well as prefrontal cortex (Haber et al., 2000, 2006; Sesack and Grace, 2010), brief consideration of mesolimbic dopaminergic development is warranted. The concentration of dopamine receptors throughout the striatum increases during the transition to adolescence in rodents, but interestingly declines post adolescence across the striatum except in the NAcc, where levels remain high throughout adulthood (Teicher et al., 1995). Relatedly, pre-adolescent increases in dopaminergic synthesis decline between adolescence and early adulthood in the striatum except for in the NAcc (Andersen et al., 1997), and firing rates of VTA dopaminergic neurons are more rapid in adolescent than adult rats (McCutcheon et al., 2012). Less PFC, NAcc and amygdala innervation of the VTA in adolescent as compared to young adult rats (Yetnikoff et al., 2014), in conjunction with ventral striatal developmental patterns likely underlies oft observed increases in appetitive behaviors during adolescence across species (Casey et al., 2010; Spear, 2000).

7. Amygdalostriatal interactions during development

In spite of the fact that the relationship between the amygdala and striatum is critical in maturity, an important outstanding question pertains to the development of the interactions between the amygdala and striatum. Anatomical connectivity between these regions in the rodent is present at adult-like levels early in life, emerging by postnatal day 7 (corresponding roughly to human infancy), with no significant changes after that point (Bouwmeester et al., 2002). Human resting-state fMRI findings support the early emergence and importance of amygdalostriatal interactions across species, reporting the existence of positive functional connectivity between the amygdala and ventral striatum as early as age 4, which remains significantly positive into early adulthood (i.e., early 20 s) (Fareri et al., 2015b). However, there has been little characterization of the normative development of task-based amygdalostriatal

functional interactions and how they may relate to affective valuation.

Prominent dual systems models of human neurobehavioral development point to the relationship between the ventral striatum and prefrontal cortex, suggesting that regulatory abilities relying on prefrontal cortex are not maturely developed and efficient, underlying adolescent sensitivity to reward (reviewed in Crone and Dahl, 2012; Pfeifer and Allen, 2012). Others suggest a three-pronged model of affective behavior consisting of the ventral striatum, amygdala and vmPFC, corresponding to reward, avoidance and control systems, respectively (Ernst et al., 2006), hypothesizing that adolescent behavior is biased towards reward-seeking behavior due to increased influence of the ventral striatum and away from avoidance-based behaviors. Similarly to dual process models, however, this relationship is proposed to be mediated by the protracted development of PFC regulatory function, which together underlies increases in adolescent risk-taking behavior. While influential, recent suggestions have called for more expansive and integrative models of adolescent neurobehavioral development, calling for the incorporation of additional methodological approaches (Pfeifer and Allen, 2012), consideration of the changing importance of social contexts during development (Crone and Dahl, 2012), and more nuanced and complex roles for the amygdala and striatum in affective valuation and learning (Somerville et al., 2014). Imbalance models (Casey, 2015; Casey et al., 2010) further highlight the importance of non-linear changes during the transitions from childhood to adolescence and from adolescence to adulthood. Such models emphasize the importance of hormonal changes in conjunction with circuit-based structural and functional neural changes, which together create an imbalance underlying behavioral development that could have adaptive or maladaptive consequences (Casey, 2015; Casey et al., 2010). A recent example of such efforts suggests that adolescents may interpret threatening stimuli or situations as thrilling or exciting, leading to a tendency to reinterpret avoidance based signals as approachable (Spielberg et al., 2014). According to this hypothesis, the amygdala and striatum may in fact work together to promote risk-taking behavior in certain situations, driven in part by developmental changes in pubertal hormone levels (Spielberg et al., 2014) Such interactions may have implications for individual differences in temperament, as behaviorally inhibited individuals show reduced resting state functional connectivity between the amygdala and striatum (Roy et al., 2014), and for the development of internalizing illness as well. Given that the drastic developmental changes in the amygdala and striatum early in life, an intriguing further possibility is that early experiences may shape later ventral striatal function through the amygdala.

8. Effects of early life stress on amygdala and striatal development

While the amygdala and ventral striatum are active and functioning early in life, the evidence indicates that their functionality continues to develop throughout childhood and adolescence making them highly susceptible to environmental influence throughout development. Thus the association between ELS and behavioral outcomes related to internalizing illness may be mediated by changes effected by ELS on amygdala and ventral striatum function and their interaction.

8.1. Rodent models of early life stress

Rodent models instilling disruptions in the early caregiving environment demonstrate that stable caregiving regulates behavior often by providing a regulatory buffer against stressors. This phenomenon is accomplished by caregiver presence acting on the HPA axis in part by tempering the release of the stress hormone corticosterone, and subsequently dampening the amygdala response to stress/threat (Gunnar and Quevedo, 2007; reviewed in Lupien et al., 2000; Tottenham, 2012). During a sensitive period of development prior to PN10, rat pups will continue to approach a stimulus paired with an aversive outcome (i.e., shock), showing significantly lower levels of corticosterone when conditioned in the presence (vs. absence) of a maternal figure (Moriceau and Sullivan, 2006). After approximately PN10, rat pups exhibit a normative switch to appropriately avoid an aversively conditioned stimulus, which is dependent upon the interactions between dopaminergic systems and the release of corticosterone (Barr et al., 2009; Moriceau et al., 2010; Moriceau and Sullivan, 2004), highlighting the importance of stable caregiver presence early in life. Interestingly, the infusion of corticosterone in pups conditioned in the presence of a maternal figure, and conditioning in the absence of a maternal figure abolishes this effect, leading to intact fear conditioning and subsequent avoidance behavior (Moriceau and Sullivan, 2006). The absence of a caregiver during fear learning thus abolishes the stress hyporesponsivity typically characterizing early life.

The absence of a caregiver is a highly potent stressor for a developing organism. Experimental inductions of chronic stress have largely centered upon creating conditions of caregiver deprivation. For example, in contrast to typically reared rats, those reared in a resource deprived environment (i.e., lack of material to ensure nest building) exhibit intact fear learning as indexed by increased freezing behaviors, decreased approach towards an aversive conditioned stimulus, and increased levels of corticosterone (Moriceau et al., 2009). Repeated maternal separation, another form of chronic stress induces neuronal changes in mPFC––i.e., increased dendritic branching, length and spine density (Muhammad et al., 2012)––which, speculatively, could be driven by the accelerated adult-like amygdala function instantiated after chronic stress. Chronic ELS may thus accelerate the development of an adult-like stress response at an earlier stage of life, which may facilitate the development of phenotypes associated with internalizing illness (i.e., anxiety, depression) later in life (Heim and Nemeroff, 2001; Heim et al., 2004; reviewed in Rincón-Cortés, 2014)

Caregiver deprivation has pervasive effects extending past accelerated threat detection and fear learning to alterations in reward-related pathways and behaviors, which may also play a role in the development of anxious phenotypes. Isolation rearing of rats (at approximately postnatal day 20) in socially deprived conditions (i.e., near, but not with, the rest of their colony, whereby they can still see, hear and smell the rest of the group) is associated with significant decreases in reward-related behaviors later in life and anxious behaviors (Matthews and Robbins, 2003). Rats exposed to isolation rearing exhibit increased rates of hyperactivity in novel situations and increased susceptibility to dopaminergic agonists (reviewed in Robbins et al., 1996). These effects could be associated with alterations in presynaptic dopaminergic release, whereby increases in presynaptic DA transmission into the ventral striatum (nucleus accumbens) result in an inability to suppress reflexive actions during conditioning (Powell et al., 2003). Relatedly, during fear conditioning, isolation reared rats show increased levels of dopaminergic release into the nucleus accumbens as compared to control rats when placed in an aversively conditioned context (Fulford and Marsden, 1998). These findings might be considered in light of the fact that ELS induced corticosterone release, acts not just on the amygdala, but also on midbrain dopaminergic nuclei (Härfstrand et al., 1986; Overton et al., 1996), inducing dopaminergic firing. The inability to regulate dopaminergic release into the nucleus

accumbens after ELS may lead to over responding to an aversively conditioned stimulus, maladaptive coping responses (Fulford and Marsden, 1998) and the subsequent development of anxious phenotypes.

The timing and nature of ELS is a critical factor to consider with respect to the relationship between changes in amygdala and ventral striatal function, caregiver deprivation and subsequent development of behaviors associated with internalizing illness (Gee and Casey, 2015). Whereas isolation rearing in the preadolescent period appears to result in a more anxious phenotype, repeated maternal separation experienced between postnatal days 5 and 20 in rats (roughly early childhood) is associated with the emergence of a depressive phenotype later in life. Such phenotypes are characterized by lower levels of locomotor activity in novel environments, and a reduced preference for rewarding stimuli (Matthews et al., 1996). The relation here between ELS and decreased reward-related behaviors suggests abnormal dopaminergic function (Matthews and Robbins, 2003) and the instantiation of anhedonic symptoms, both hallmarks of depression (Pizzagalli et al., 2008). Chronic ELS is associated with glucocorticoid induced stimulation of DA release into the NAcc, leading to sensitization of DA neurons in the ventral striatum (reviewed in Meaney et al., 2002). Relatedly, repeated maternal separation from PN1 to PN14 is associated with increased survival of midbrain DA neurons and increased rates of reward seeking in male (but not female) rats later in life (Chocyk et al., 2015), which has implications for drug-seeking/risk-taking behaviors as a potential means to satisfy decreased responses to reward. The effects of caregiver deprivation on striatal and dopaminergic function thus create conditions that increase one's vulnerability to internalizing illness.

8.2. Human models of early life stress

Human work investigating the effects of ELS on socio-affective behavior is limited in that it must focus on naturally occurring instances of stress––i.e., individuals suffering from emotional neglect, maltreatment, or caregiver deprivation in the form of previous institutionalization. Individuals with a history of previous institutionalization (PI)––being reared in orphanage care early in life prior to being adopted into stable families––are of particular import because such individuals were placed into conditions of severe threat and a deprived environment without their biological caregivers, closely paralleling animal caregiver deprivation paradigms. Caregiver deprivation in humans significantly impacts the structural development of the amygdala. The length of time spent in institutionalized care positively correlates with amygdala size, and PI individuals further tend to have larger amygdalae in comparison to individuals reared with their biological parents from birth (Tottenham et al., 2010 though see also Hanson et al., 2014). Length of time spent in institutionalized care is also associated with diminished emotion regulation abilities when exposed to negative emotional stimuli: PI individuals make more errors in an emotional go/no-go task when attempting to inhibit responses to negatively valenced (i.e., fear) faces (Tottenham et al., 2010).

The association between the structural development of the amygdala and emotion regulation abilities in PI individuals implies a relationship between the function of this region in humans and the ability to appraise and respond to the value of affective stimuli. This association could in turn relate to the higher degrees of anxiety often exhibited by such samples (Ellis et al., 2004; Zeanah et al., 2009). Lab-based fMRI studies in humans indeed report that PI individuals exhibiting higher parental reports of anxiety also show stronger amygdala activation to threatening stimuli (i.e., fearful faces) than do comparison individuals (Gee et al., 2013a; Tottenham et al., 2011). Further, the degree of amygdala response to threatening stimuli negatively relates to measures of social competence and proportion of time making eye-contact with affective facial displays (Tottenham et al., 2011). Individual differences in anxiety in PI children and adolescents relates to individual differences in amygdala-mPFC functional connectivity. PI individuals demonstrating higher levels of separation anxiety, for example, tend to show positive amygdala-mPFC functional connectivity when viewing fear faces, whereas those PIs with lower levels of anxiety show a more regulatory relationship (i.e., negative connectivity) (Gee et al., 2013a). These findings suggest a strong link between neural changes as a function of ELS and the development of anxiety-related behaviors, as well as the potential for an adaptive response to ELS (i.e., developing a more mature neural phenotype earlier on). Further, consistent with a role for the amygdala in social and affiliative behaviors (Adolphs, 2009; Adolphs et al., 1998; Bickart et al., 2012), caregiver deprivation also impacts one's appraisal of valued social stimuli. PI individuals do not show discrimination in the amygdala between the face of one's own mother compared to that of a stranger (Olsavsky et al., 2013), whereas comparison individuals show a robustly stronger amygdala response to one's mother, possibly reflecting an enhanced social and motivational value of the stimulus. The amount of time spent in institutionalized care negatively correlates with the degree to which the amygdala discriminates between mother and stranger (Olsavsky et al., 2013), indicating that ELS significantly alters one's appraisal of valued social stimuli.

Caregiver deprivation in humans is associated with altered reward-related behaviors and ventral striatal function. PI individuals exhibit a diminished ability to differentiate reward predicting cues of varying magnitude (low, medium, high) in the ventral striatum or caudate nucleus, whereas comparison individuals showed greater striatal responses to medium and high reward cues compared to low (Mehta et al., 2010). Adolescent PIs also demonstrate increased levels of depressive symptoms and blunted responses to rewarding socio-affective cues (i.e., happy faces) in relation to comparison adolescents (Goff et al., 2013). Moreover, the degree of ventral striatum activation to happy faces negatively correlated with depression scores in control and ELS individuals, though this effect held when considering only participants with a history of ELS (Goff et al., 2013), supporting rodent studies revealing a decrease in responses to reward-related stimuli after repeated maternal separation early in life. These initial findings support an association in humans between ELS and reward-related behaviors, which in turn may relate to the expression/development of depressive symptoms as mediated by altered ventral striatal function.

Reward related behaviors also encompass the tendency to take risks, which are also associated with caregiver deprivation. Laboratory based measures of risk-taking such as the Balloon Analogue Risk Taking (BART; Lejuez et al., 2002) task, in which participants have the opportunity to pump a balloon with air to accumulate incentives (e.g., money, points) and can cash out (i.e., stop pumping) at any point, as balloons could burst at random. Burst balloons result in participants losing whatever has been accumulated on that trial. Performance on the BART has evidenced decreased levels of risk-taking in PI adolescents as compared to non-adopted adolescents, and a negative relationship between risk-taking behavior and depressive symptoms in PI individuals (Loman et al., 2014). A modified version of the BART aimed at assessing exploration (pumping more) versus exploitation (cashing out quickly) demonstrates that PI individuals show lower levels of risk-taking (i.e., cash out more) versus comparison individuals when exploitation is the advantageous strategy; this pattern of results is mediated by anxiety, such that PI individuals with higher levels of anxiety tended to show lower levels of risk-taking behavior (Humphreys et al., 2015). The interplay between exploration and exploitation as a function of

context suggests that interactions between the amygdala and ventral striatum (i.e., approach/avoid) are at play. While ELS is often associated with maladaptive consequences, in some situations it may confer adaptive strategies.

9. Discussion

9.1. Effects of ELS on amygdalostriatal interactions

The findings discussed in this review highlight the importance of the amygdala and ventral striatum to affective valuation and learning across development, and the impact of ELS on neurobehavioral development associated with the onset of internalizing illness. While a significant amount of evidence highlights the importance of the relationship between these two regions in maturity, there is a lack of evidence regarding role of ELS in modulating the development of amygdalostriatal functional interactions. Based on our review of the literature, we propose that ELS affects the ability of amygdala-based value related signals to reach the ventral striatum; we suggest that ELS induced accelerated amygdala development may diminish the opportunity to develop typical functional interactions with the ventral striatum (see Fig. 1). Amygdala appraisal of the value of positive stimuli may remain intact as a function of ELS (Gee et al., 2013a), but the communication of these signals to the ventral striatum may be disrupted, albeit in certain cases (e.g., when exploitation is the most adaptive strategy) may remain intact (see Humphreys et al., 2015). The oft observed decreased ventral striatal reward response in individuals with a history of ELS that emerges in adolescence and blunted subjective ratings of the value of reward predicting cues (Dillon et al., 2009; Goff et al., 2013; Mehta et al., 2010) suggest a potential impairment in either the relaying of stimulus and action-outcome value information between the amygdala and ventral striatum or the assessment of this information by the ventral striatum. We propose that the modulation of the interaction between the amygdala and ventral striatum mediates the relationship between ELS and the later onset of symptoms pertaining to internalizing illness.

The proposed effects of ELS on amygdalostriatal interactions likely involve additional neural mechanisms influenced by ELS, including altered mesolimbic dopaminergic function resulting from increased presence of stress hormones (Matthews and Robbins, 2003), which can affect DA transmission into the amygdala (Barr et al., 2009) and NAcc (Matthews and Robbins, 2003), and/or connectivity with mPFC (Callaghan and Richardson, 2012; Gee et al., 2013a). Interactions between corticosterone and dopamine may therefore play an important role in the modification of amygdalostriatal interactions after ELS. Rodent studies may continue to probe these interactions through assessments of dopaminergic transmission during such tasks in animals that experienced ELS in the form of repeated maternal separation during infancy. Characterizing the effects of ELS on amygdalostriatal interactions and the relation to internalizing symptoms can be tested empirically in human developmental samples by leveraging functional connectivity approaches (Friston, 2009; Friston et al., 1997) with physiological (e.g., skin conductance) and hormonal assays (Gee et al., 2013a), as well as computational modeling techniques (Daw et al., 2006; Niv, 2009; Schonberg et al., 2007) in ELS and comparison individuals during affective learning. Adoption of paradigms commonly employed in the animal literature (outcome devaluation, PIT), as has been done in adult studies (Lewis et al., 2013; Prévost et al., 2011; Tricomi and Lempert, 2015) are warranted as they may be more appropriately designed to tease apart developmental functional differences in amygdalostriatal interactions vis-à-vis ELS.

In light of this proposal, it is useful to briefly consider thoughts pertaining to potential intervention for those afflicted with internalizing illness associated with ELS. The findings that the amygdala and ventral striatum exhibit differential structural and functional developmental trajectories (Galván, 2010; Gee et al., 2013b; Giedd et al., 1996b; Payne et al., 2010; Raznahan et al., 2014) suggest differing periods of plasticity. Pubertal hormone changes are thought to be one significant driving agent of behavioral and neurodevelopmental change, particularly as a result of effects within dopaminergic reward-related neural pathways centering on corticostriatal circuits (Bramen et al., 2011; Fareri et al., 2015b; Herting et al., 2014; Koolschijn et al., 2014; Peper et al., 2011). Normative changes in pubertal hormone concentration during the transition to adolescence facilitate increases in reward-related behaviors in rodents, for example (reviewed in Blakemore et al., 2010), and may result in an overall shift in motivation towards social needs (Forbes and Dahl, 2010). Perhaps it is thus possible to leverage the timing of treatment for internalizing illness as a result of ELS against the timing of change and neural plasticity. In other words potential treatments––e.g., pharmacological, cognitive, behavioral––for internalizing illness associated with ELS may target processes and neurobiological mechanisms more associated with ventral striatum, given the relative later onset of developmental change in this structure and the relative earlier phase of plasticity in the amygdala (Payne et al., 2010).

9.2. Additional forms and moderators of ELS

While we believe the absence of species expected caregiving to be a unique stressor and threat to an organism's survival, ELS can occur in a variety of additional forms, particularly in humans. Maltreatment in various forms (e.g., physical/emotional/sexual abuse, emotional neglect) is another potent stressor that can represent a threat and a deprived environment. A history of childhood maltreatment and emotional neglect both tend to have similar effects on amygdala reactivity (Dannlowski et al., 2013), with the degree of experienced stress associated with heightened amygdala reactivity to subliminally presented negative (vs. positive) facial expressions and faster reaction time when detecting threatening affective stimuli than controls (Maheu et al., 2010). Adults with a history of childhood maltreatment exhibit blunted subjective ratings (i.e., less positive) and decreased ventral striatal responses to anticipation of reward predicting cues in comparison to those with no history of ELS (Dillon et al., 2009). Maltreated individuals do not show differential reaction time when choosing between risky and safe options for obtaining monetary reward, while control individuals take longer when making risky choices (Guyer et al., 2006), suggesting that maltreatment alters sensitivity to incentive value. However, Sujan and colleagues report that laboratory measures of risk-taking may not necessarily reflect real-world risk-taking, particularly when considering effects of ELS (Sujan et al., 2014); alternate methods of testing risk-taking in the laboratory may be more useful in relating to real-world behaviors (Congdon, 2013; Pleskac, 2008).

Additional moderating factors surrounding ELS should be considered when assessing the impact of ELS on neural and behavioral development, including SES and sex differences. Low SES both significantly impacts children's cognitive, social and affective development and subsequent mental health outcomes (Brooks-Gunn and Duncan, 1997), and also may create conditions facilitating poor parent-child interactions (i.e., abuse, neglect) vis-à-vis family stress (Brooks-Gunn and Duncan, 1997). Although a nascent direction of the field, emergent studies report a link between low SES and amygdala and hippocampal development similarly to ELS (Hackman and Farah, 2009; Hanson et al., 2014; Luby et al., 2013; Noble et al., 2012). Additionally, much of the

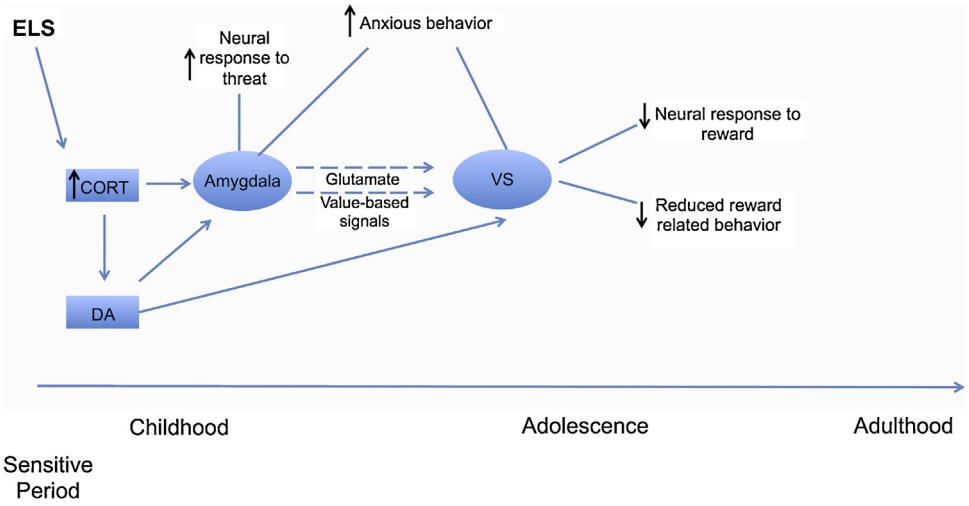

Fig. 1. A working conceptual model of effects of ELS on amygdalostriatal interactions. Based on a synthesis of human and non-human animal research we suggest that ELS acts on neural systems associated with affective valuation by modulating (i.e., decreasing) the ability of the amygdala to send value-based information to the ventral striatum via unidirectional excitatory glutamatergic projections (denoted by dashed lines). During sensitive periods of development, ELS causes increases in the release and circulation of stress hormones (i.e., corticosterone, cortisol), which act not just to accelerate amygdala development but to interact with midbrain dopaminergic systems, resulting in the increased release of dopamine into the amygdala and the ventral striatum. The increased levels of dopamine may be inappropriately regulated as a function of ELS, leading to subsequent neural and behavioral phenotypes associated with the emergence of behaviors during adolescence associated with internalizing illness such as anxiety and depression that may persist into adulthood.

extant literature concerning ELS, amygdala/ventral striatal development and internalizing illness do not report sex differences (Chocyk et al., 2015; Matthews et al., 1996, 2001; Pechtel and Pizzagalli, 2011). Considering that the prevalence of internalizing illnesses show sex specific differences in their prevalence after puberty (Paus et al., 2008) and normative subcortical structural development shows sex differences as well (Goddings et al., 2013; Raznahan et al., 2014; Wierenga et al., 2014), the lack of studies of ELS effects on neural and behavioral development reporting sex differences is striking. Future studies can take into account changes in pubertal hormone levels, for example, to better assess the consistency of sex-specific effects in the relationship between ELS, neural development and socio-affective development.

9.3. Limitations

Animal models are crucial to our understanding of the behavioral and neural consequences of chronic early psychosocial stressors in humans because they allow for precise experimental control and an ability to understand in a more mechanistic manner how ELS affects neural and behavioral development. However, an important gap in the literature concerns differences in the types of stressors administered, the experimental paradigms employed, and the response outcomes measured across species. The human literature would greatly benefit from future efforts to parallel paradigms employed in rodents, both in the reward and aversive domains and when trying to characterize the relationship between ELS, amygdala-striatal functional interactions and internalizing illness. One elegant study (Malter Cohen et al., 2013) mimicked both the conditions of human institutional rearing in mice (i.e., severely deprived nesting conditions) and a task typically used in studies of human affective development (i.e., a rodent analogue of an emotional go/no-go task (Gee et al., 2013b; Hare et al., 2008). A striking parallel to human findings (Tottenham et al., 2011) emerged, with increased amygdala reactivity in preadolescent ELS mice compared to preadolescent controls in response to threatening stimuli; ELS mice also demonstrated slower response latency and increased amygdala activity to a threatening stimulus (Malter Cohen et al., 2013).

Though we have focused this review on the role of the amygdala and striatum, these two regions work in concert with additional regions to support affective valuation and learning, including the hippocampus, medial and lateral PFC and midbrain dopaminergic nuclei (Baxter and Murray, 2002; Davis and Whalen, 2001; Haber et al., 2000; Haber and Knutson, 2010; Pennartz et al., 2011), many of which encode diverse value-based signals informing decision-making (Bartra et al., 2013; Fareri and Delgado, 2014) and are subject to developmental effects of stress(Chattarji et al., 2015; Hollon et al., 2015; Tottenham and Sheridan, 2009). One connection of interest involves the OFC––another site of integration between sensory information, affective processes and decision-making (Kringelbach, 2005)––and the BLA. Both regions are implicated in representing the value of expected outcomes during learning (Schoenbaum et al., 1998), though BLA discrimination of predictive stimuli tends to occur more quickly than that in OFC (Schoenbaum et al., 1999). OFC neurons increase firing rates during reversal learning (i.e., when stimulus-outcome contingencies reverse), but BLA neurons maintain representations of the original stimulus-value representations (Schoenbaum et al., 2000). The literature would benefit from investigations of how ELS impacts this relationship in service of potentially highlighting differences (or similarities) in comparison to BLA-ventral striatal interactions.

9.4. Future directions

Recent advances in cognitive neuroscience incorporating the use of multimodal and interdisciplinary techniques represent promising directions toward more comprehensive understanding of the mechanisms that ELS exerts on neurobehavioral development and the onset of internalizing illness. Neurogenetic approaches (Bogdan et al., 2012a) represent one such avenue, considering the fact that ELS can induce genetic alterations often observed through DNA methylation. Methylation can be a normative process: for example, methylation is necessary in the dopaminergic system for reward-learning processes in rats (Day

et al., 2013). Methylation can also exert negative effects, however, via the turning off of a gene (Szyf and Bick, 2013). In humans ELS is associated with increased methylation and decreased expression of stress-related gene receptors (McGowan et al., 2009) in the hippocampus. Within the context of the amygdala and striatum, future studies might examine neurogenetic effects of ELS on variability in the serotonin transporter gene (5HTTPLR), which is related to the ability to extinguish fear (Hartley et al., 2012) and dopaminergic genes (e.g., DAARP-32, DRD2) implicated in the ability to learn from rewards and punishments (Doll et al., 2011). Such approaches may also have implications for epigenetic studies of the effects of ELS (Bogdan et al., 2012b; Nikolova and Hariri, 2015).

Caregiver deprivation is clearly a severe psychosocial stressor, yet the question of how a history of caregiver deprivation influences the ability to represent and value different types of social stimuli later in life (e.g., parents vs. peers) has remained largely uninvestigated. As peer groups normatively become more important during the transitions into adolescence (Crone and Dahl, 2012; Steinberg, 2008), it remains to be seen whether individuals with a history of ELS differentially represent other types of socially valued others in comparison to their caregivers, and whether the function of neural social learning mechanisms involving the amygdala and striatum are altered when interacting with and learning about new peers (Baumgartner et al., 2008; Fareri et al., 2015a, 2012; Kishida and Montague, 2012; Todorov et al., 2008; Xiang et al., 2013). The ability to process social signals such as the reciprocation of trust is critical to the formation and maintenance of social relationships (Fareri et al., 2015a, 2012; King-Casas, 2005; Phan et al., 2010; Rilling and Sanfey, 2011). Characterizing how ELS may modify such social valuation mechanisms is a critical and promising avenue for the field, additionally lending itself to the incorporation of interdisciplinary methods (e.g., computational learning approaches, neurogenetics).

Finally, we have noted the importance of puberty as a potential driving agent of normative neural and behavioral developmental changes. There is evidence to suggest that adverse early life experiences may lead to an acceleration of developmental changes as a survival-based adaptation; these may include earlier onset of puberty (Belsky, 2012; Belsky et al., 2007). If this is indeed true, then the change in timing of puberty may subsequently impact the timing of neural development, which may then have significant downstream socio-emotional consequences. The field would greatly benefit from future investigations of the interaction between a history of ELS, timing of pubertal changes, and subsequent structural and functional changes in the amygdala and striatum.

9.5. General discussion

We have proposed that the link between ELS and behavioral phenotypes associated with internalizing illnesses are mediated by changes in amygdala and striatal function and their interaction. It is worth noting that even chronic stress experienced early in life can be adaptive under certain circumstances. ELS may act to accelerate functional amygdala development (Callaghan et al., 2013), particularly with respect to its relationship with the mPFC (Callaghan and Richardson, 2012; Gee et al., 2013a). In such situations, the brain may thus have adapted as a result of the early threats imposed by the lack of species expected caregiving to facilitate threat detection and the ability to respond. Additional recent evidence suggests that exhibiting more less exploitative behavior can be adaptive in circumstances where exploration is associated with a high certainty of potential loss (Humphreys et al., 2015). In line with studies of acute stress on decision-making in adult humans that indicate a reliance on habitual, reflexive actions under acute stress (Otto et al., 2013; Porcelli and Delgado, 2009), chronic stress may predispose individuals to rely on exploitative behavior when it in fact is a safer choice and associated with a higher expected return. Thus, while ELS indeed can have maladaptive mental health consequences, it is important to consider not only the timing and nature of the adverse early life experiences (Gee and Casey, 2015), but also that the environmental conditions experienced early in life may make afflicted individuals better predisposed to handle future adverse consequences.

Acknowledgements

This work was supported by the National Institute of Mental Health (R01MH091864 to N.T.) and the Dana Foundation (20122240). The authors would like to thank Dr. Dylan Gee for helpful comments.

References

Adolphs, R., Tranel, D., Damasio, A., 1998. The human amygdala in social judgment. Nature 393, 470–474, http://dx.doi.org/10.1038/30982.
Adolphs, R., 2009. The social brain: neural basis of social knowledge. Annu. Rev. Psychol. 60, 693–716, http://dx.doi.org/10.1146/annurev.psych.60.110707.163514.
Alexander, G.E., DeLong, M.R., Strick, P.L., 1986. Parallel organization of functionally segregated circuits linking basal ganglia and cortex. Annu. Rev. Neurosci. 9, 357–381, http://dx.doi.org/10.1146/annurev.ne.09.030186.002041.
Ambroggi, F., Ishikawa, A., Fields, H.L., Nicola, S.M., 2008. Basolateral amygdala neurons facilitate reward-seeking behavior by exciting nucleus accumbens neurons. Neuron 59, 648–661, http://dx.doi.org/10.1016/j.neuron.2008.07.004.
Andersen, S.L., Dumont, N.L., Teicher, M.H., 1997. Developmental differences in dopamine synthesis inhibition by (±)-7-OH-DPAT. Naunyn-Schmiedeberg's Arch. Pharmacol., 173–181.
Balleine, B.W., Dickinson, A., 1998. Goal-directed instrumental action: contingency and incentive learning and their cortical substrates. Neuropsychopharmacology, 407–419.
Balleine, B.W., Delgado, M.R., Hikosaka, O., 2007. The role of the dorsal striatum in reward and decision-making. J. Neurosci. 27, 8161–8165, http://dx.doi.org/10.1523/JNEUROSCI.1554-07.2007.
Barkley-Levenson, E., Galvan, A., 2014. Neural representation of expected value in the adolescent brain. Proc. Natl. Acad. Sci. U. S. A. 111, 1646–1651, http://dx.doi.org/10.1073/pnas.1319762111.
Barr, G.A., Moriceau, S., Shionoya, K., Muzny, K., Gao, P., Wang, S., Sullivan, R.M., 2009. Transitions in infant learning are modulated by dopamine in the amygdala. Nat. Neurosci. 12, 1367–1369, http://dx.doi.org/10.1038/nn.2403.
Bartra, O., McGuire, J.T., Kable, J.W., 2013. The valuation system: a coordinate-based meta-analysis of BOLD fMRI experiments examining neural correlates of subjective value. Neuroimage 76, 412–427, http://dx.doi.org/10.1016/j.neuroimage.2013.02.063.
Baumgartner, T., Heinrichs, M., Vonlanthen, A., Fischbacher, U., Fehr, E., 2008. Oxytocin shapes the neural circuitry of trust and trust adaptation in humans. Neuron 58, 639–650, http://dx.doi.org/10.1016/j.neuron.2008.04.009.
Baxter, M.G., Murray, E.A., 2002. The amygdala and reward. Nat. Rev. Neurosci. 3, 563–573, http://dx.doi.org/10.1038/nrn875.
Belova, M.A., Paton, J.J., Morrison, S.E., Salzman, C.D., 2007. Expectation modulates neural responses to pleasant and aversive stimuli in primate amygdala. Neuron 55, 970–984, http://dx.doi.org/10.1016/j.neuron.2007.08.004.
Belova, M.A., Paton, J.J., Salzman, C.D., 2008. Moment-to-moment tracking of state value in the amygdala. J. Neurosci. 28, 10023–10030, http://dx.doi.org/10.1523/JNEUROSCI.1400-08.2008.
Belsky, J., Steinberg, L.D., Houts, R.M., Friedman, S.L., DeHart, G., Cauffman, E., Roisman, G.I., Halpern Felsher, B.L., Susman, E., 2007. Family rearing antecedents of pubertal timing. Child Dev. 78, 1302–1321, http://dx.doi.org/10.1111/j.1467-8624.2007.01067.x.
Belsky, J., 2012. The development of human reproductive strategies: progress and prospects. Curr. Directions Psychol. Sci. 21, 310–316, http://dx.doi.org/10.1177/0963721412453588.
Bickart, K.C., Hollenbeck, M.C., Barrett, L.F., Dickerson, B.C., 2012. Intrinsic amygdala-cortical functional connectivity predicts social network size in humans. J. Neurosci. 32, 14729–14741, http://dx.doi.org/10.1523/JNEUROSCI.1599-12.2012.
Bjork, J.M., Knutson, B., Fong, G.W., Caggiano, D.M., Bennett, S.M., Hommer, D.W., 2004. Incentive-elicited brain activation in adolescents: similarities and differences from young adults. J. Neurosci. 24, 1793–1802, http://dx.doi.org/10.1523/JNEUROSCI.4862-03.2004.
Bjork, J.M., Smith, A.R., Chen, G., Hommer, D.W., 2010. Adolescents, adults and rewards: comparing motivational neurocircuitry recruitment using fMRI. PLoS One 5, e11440, http://dx.doi.org/10.1371/journal.pone.0011440.
Blakemore, S.-J., Burnett, S., Dahl, R.E., 2010. The role of puberty in the developing adolescent brain. Hum. Brain Mapp. 31, 926–933, http://dx.doi.org/10.1002/hbm.21052.
Bogdan, R., Hyde, L.W., Hariri, A.R., 2012a. A neurogenetics approach to understanding individual differences in brain, behavior, and risk for

psychopathology. Mol. Psychiatry 18, 288–299, http://dx.doi.org/10.1038/mp.2012.35.
Bogdan, R., Williamson, D.E., Hariri, A.R., 2012b. Mineralocorticoid receptor Iso/Val (rs5522) genotype moderates the association between previous childhood emotional neglect and amygdala reactivity. Am. J. Psychiatry 169, 515–522, http://dx.doi.org/10.1176/appi.ajp.2011.11060855.
Bouwmeester, H., Wolterink, G., van Ree, J.M., 2002. Neonatal development of projections from the basolateral amygdala to prefrontal, striatal, and thalamic structures in the rat. J. Comp. Neurol. 442, 239–249.
Bramen, J.E., Hranilovich, J.A., Dahl, R.E., Forbes, E.E., Chen, J., Toga, A.W., Dinov, I.D., Worthman, C.M., Sowell, E.R., 2011. Puberty influences medial temporal lobe and cortical gray matter maturation differently in boys than girls matched for sexual maturity. Cereb. Cortex 21, 636–646, http://dx.doi.org/10.1093/cercor/bhq137.
Britt, J.P., Benaliouad, F., McDevitt, R.A., Stuber, G.D., Wise, R.A., Bonci, A., 2012. Synaptic and behavioral profile of multiple glutamatergic inputs to the nucleus accumbens. Neuron 76, 790–803, http://dx.doi.org/10.1016/j.neuron.2012.09.040.
Brooks-Gunn, J., Duncan, G.J., 1997. The effects of poverty on children. Future Children 7, 55–71.
Callaghan, B.L., Richardson, R., 2012. Early-life stress affects extinction during critical periods of development: an analysis of the effects of maternal separation on extinction in adolescent rats. Stress 15, 671–679, http://dx.doi.org/10.3109/10253890.2012.667463.
Callaghan, B.L., Richardson, R., 2013. Early experiences and the development of emotional learning systems in rats. Biol. Mood Anxiety Disord. 3, 8, http://dx.doi.org/10.1186/2045-5380-3-8.
Callaghan, B.L., Graham, B.M., Li, S., Richardson, R., 2013. From resilience to vulnerability: mechanistic insights into the effects of stress on transitions in critical period plasticity. Front Psychiatry 4, 90, http://dx.doi.org/10.3389/fpsyt.2013.00090.
Cardinal, R.N., Everitt, B.J., 2004. Neural and psychological mechanisms underlying appetitive learning: links to drug addiction. Curr. Opin. Neurobiol. 14, 156–162, http://dx.doi.org/10.1016/j.conb.2004.03.004.
Casey, B.J., Duhoux, S., Malter Cohen, M., 2010. Adolescence: what do transmission, transition, and translation have to do with it? Neuron 67, 749–760, http://dx.doi.org/10.1016/j.neuron.2010.08.033.
Casey, B.J., 2015. Beyond simple models of self-Control to circuit-based accounts of adolescent behavior. Annu. Rev. Psychol. 66, 295–319, http://dx.doi.org/10.1146/annurev-psych-010814-015156.
Chareyron, L.J., Lavenex, P.B., Lavenex, P., 2012. Postnatal development of the amygdala: a stereological study in rats. J. Comp. Neurol. 520, 3745–3763, http://dx.doi.org/10.1002/cne.23132.
Chattarji, S., Tomar, A., Suvrathan, A., Ghosh, S., Rahman, M.M., 2015. Neighborhood matters: divergent patterns of stress-induced plasticity across the brain. Nat. Neurosci. 18, 1364–1375, http://dx.doi.org/10.1038/nn.4115.
Cho, Y.T., Ernst, M., Fudge, J.L., 2013. Cortico-Amygdala-Striatal circuits are organized as hierarchical subsystems through the primate amygdala. J. Neurosci. 33, 14017–14030, http://dx.doi.org/10.1523/JNEUROSCI.0170-13.2013.
Chocyk, A., Majcher-Maślanka, I., Przyborowska, A., Maćkowiak, M., Wędzony, K., 2015. Early-life stress increases the survival of midbrain neurons during postnatal development and enhances reward-related and anxiolytic behaviors in a sex-dependent fashion. Int. J. Dev. Neurosci. 44, 33–47, http://dx.doi.org/10.1016/j.ijdevneu.2015.05.002.
Cohen, J.R., Asarnow, R.F., Sabb, F.W., Bilder, R.M., Bookheimer, S.Y., Knowlton, B.J., Poldrack, R.A., 2010. A unique adolescent response to reward prediction errors. Nat. Neurosci. 13, 669–671, http://dx.doi.org/10.1038/nn.2558.
Congdon, E., 2013. Differences in neural activation as a function of risk-taking task parameters. 1–14. 10.3389/fnins.2013.00173/abstract.
Conti, G., Hansman, C., Heckman, J.J., Novak, M.F.X., Ruggiero, A., Suomi, S.J., 2012. Primate evidence on the late health effects of early-life adversity. Proc. Natl. Acad. Sci. U. S. A. 109, 8866–8871, http://dx.doi.org/10.1073/pnas.1205340109.
Corbit, L.H., Balleine, B.W., 2005. Double dissociation of basolateral and central amygdala lesions on the general and outcome-specific forms of pavlovian-instrumental transfer. J. Neurosci. 25, 962–970, http://dx.doi.org/10.1523/JNEUROSCI.4507-04.2005.
Corbit, L.H., Balleine, B.W., 2011. The general and outcome-specific forms of Pavlovian-instrumental transfer are differentially mediated by the nucleus accumbens core and shell. J. Neurosci. 31, 11786–11794, http://dx.doi.org/10.1523/JNEUROSCI.2711-11.2011.
Corcoran, C.A., Pierre, P.J., Haddad, T., Bice, C., Suomi, S.J., Grant, K.A., Friedman, D.P., Bennett, A.J., 2012. Long-term effects of differential early rearing in rhesus macaques: behavioral reactivity in adulthood. Dev. Psychobiol. 54, 546–555, http://dx.doi.org/10.1002/dev.20613.
Cressman, V.L., Balaban, J., Steinfeld, S., Shemyakin, A., Graham, P., Parisot, N., Moore, H., 2010. Prefrontal cortical inputs to the basal amygdala undergo pruning during late adolescence in the rat. J. Comp. Neurol. 518, 2693–2709, http://dx.doi.org/10.1002/cne.22359.
Crone, E.A., Dahl, R.E., 2012. Understanding adolescence as a period of social–affective engagement and goal flexibility. Nat. Rev. Neurosci. 13, 636–650, http://dx.doi.org/10.1038/nrn3313.
Dannlowski, U., Kugel, H., Huber, F., Stuhrmann, A., Redlich, R., Grotegerd, D., Dohm, K., Sehlmeyer, C., Konrad, C., Baune, B.T., Arolt, V., Heindel, W., Zwitserlood, P., Suslow, T., 2013. Childhood maltreatment is associated with an automatic negative emotion processing bias in the amygdala. Hum. Brain Mapp. 34, 2899–2909, http://dx.doi.org/10.1002/hbm.22112.
Davis, M., Whalen, P.J., 2001. The amygdala: vigilance and emotion. Mol. Psychiatry 6, 13–34.
Davis, M., 1992. The role of the amygdala in fear and anxiety. Annu. Rev. Neurosci. 15, 353–375, http://dx.doi.org/10.1146/annurev.ne.15.030192.002033.
Daw, N.D., O'Doherty, J.P., Dayan, P., Seymour, B., Dolan, R.J., 2006. Cortical substrates for exploratory decisions in humans. Nature 441, 876–879, http://dx.doi.org/10.1038/nature04766.
Daw, N.D., Gershman, S.J., Seymour, B., Dayan, P., Dolan, R.J., 2011. Model-based influences on humans' choices and striatal prediction errors. Neuron 69, 1204–1215, http://dx.doi.org/10.1016/j.neuron.2011.02.027.
Day, J.J., Childs, D., Guzman-Karlsson, M.C., Kibe, M., Moulden, J., Song, E., Tahir, A., Sweatt, J.D., 2013. DNA methylation regulates associative reward learning. Nat. Neurosci. 16, http://dx.doi.org/10.1038/nn.3504.
Decety, J., Michalska, K.J., 2009. Neurodevelopmental changes in the circuits underlying empathy and sympathy from childhood to adulthood. Dev. Sci. 13, 886–899, http://dx.doi.org/10.1111/j.1467-7687.2009.00940.x.
Decety, J., Michalska, K.J., Kinzler, K.D., 2011. The contribution of emotion and cognition to moral sensitivity: a neurodevelopmental study. Cereb. Cortex 22, 209–220, http://dx.doi.org/10.1093/cercor/bhr111.
Defoe, I.N., Dubas, J.S., Figner, B., van Aken, M.A.G., 2015. A meta-analysis on age differences in risky decision making: adolescents versus children and adults. Psychol. Bull. 141, 48–84, http://dx.doi.org/10.1037/a0038088.
Delgado, M.R., Li, J., Schiller, D., Phelps, E.A., 2008. The role of the striatum in aversive learning and aversive prediction errors. Philos. Trans. R. Soc. Lond. B: Biol. Sci. 363, 3787–3800, http://dx.doi.org/10.1098/rstb.2008.0161.
Delgado, M.R., 2007. Reward-related responses in the human striatum. Ann. N. Y. Acad. Sci. 1104, 70–88, http://dx.doi.org/10.1196/annals.1390.002.
Dillon, D.G., Holmes, A.J., Birk, J.L., Brooks, N., Lyons-Ruth, K., Pizzagalli, D.A., 2009. Childhood adversity is associated with left basal ganglia dysfunction during reward anticipation in adulthood. Biol. Psychiatry 66, 206–213, http://dx.doi.org/10.1016/j.biopsych.2009.02.019.
Doll, B.B., Hutchison, K.E., Frank, M.J., 2011. Dopaminergic genes predict individual differences in susceptibility to confirmation bias. J. Neurosci. 31, 6188–6198, http://dx.doi.org/10.1523/JNEUROSCI.6486-10.2011.
Ellis, B.H., Fisher, P.A., Zaharie, S., 2004. Predictors of disruptive behavior, developmental delays anxiety, and affective symptomatology among institutionally reared romanian children. J. Am. Acad. Child Adolesc. Psychiatry 43, 1283–1292, http://dx.doi.org/10.1097/01.chi.0000136562.24085.160.
Ernst, M., Nelson, E.E., Jazbec, S., McClure, E.B., Monk, C.S., Leibenluft, E., Blair, J., Pine, D.S., 2005. Amygdala and nucleus accumbens in responses to receipt and omission of gains in adults and adolescents. Neuroimage 25, 1279–1291, http://dx.doi.org/10.1016/j.neuroimage.2004.12.038.
Ernst, M., Pine, D.S., Hardin, M., 2006. Triadic model of the neurobiology of motivated behavior in adolescence. Psychol. Med. 36, 299–312, http://dx.doi.org/10.1017/S0033291705005891.
Everitt, B.J., Morris, K.A., O'Brien, A., Robbins, T.W., 1991. The basolateral amygdala-ventral striatal system and conditioned place preference: further evidence of limbic-striatal interactions underlying reward-related processes. Neuroscience 42, 1–18.
Fareri, D.S., Delgado, M.R., 2014. The Imortance of Social Rewards and Social Networks in the Human Brain. Neuroscientist, http://dx.doi.org/10.1177/1073858414521869.
Fareri, D.S., Martin, L.N., Delgado, M.R., 2008. Reward-related processing in the human brain: developmental considerations. Dev. Psychopathol. 20, 1191–1211, http://dx.doi.org/10.1017/S0954579408000576.
Fareri, D.S., Chang, L.J., Delgado, M.R., 2012. Effects of direct social experience on trust decisions and neural reward circuitry. Front. Neurosci. 6, http://dx.doi.org/10.3389/fnins.2012.00148, 148–17.
Fareri, D.S., Chang, L.J., Delgado, M.R., 2015a. Computational substrates of social value in interpersonal collaboration. J. Neurosci. 35, 8170–8180, http://dx.doi.org/10.1523/JNEUROSCI.4775-14.2015.
Fareri, D.S., Gabard-Durnam, L., Goff, B., Flannery, J., Gee, D.G., Lumian, D.S., Caldera, C., Tottenham, N., 2015b. Normative development of ventral striatal resting state connectivity in humans. Neuroimage 118, 422–437, http://dx.doi.org/10.1016/j.neuroimage.2015.06.022.
Fiorillo, C.D., 2013. Two dimensions of value: dopamine neurons represent reward but not aversiveness. Science 341, 546–549, http://dx.doi.org/10.1126/science.1238699.
Forbes, E.E., Dahl, R.E., 2010. Pubertal development and behavior: hormonal activation of social and motivational tendencies. Brain Cogn. 72, 66–72, http://dx.doi.org/10.1016/j.bandc.2009.10.007.
Friston, K.J., Buechel, C., Fink, G.R., Morris, J., Rolls, E., Dolan, R.J., 1997. Psychophysiological and modulatory interactions in neuroimaging. Neuroimage 6, 218–229, http://dx.doi.org/10.1006/nimg.1997.0291.
Friston, K., 2009. Causal modelling and brain connectivity in functional magnetic resonance imaging. PLoS Biol.
Fulford, A.J., Marsden, C.A., 1998. Isolation-rearing on conditioned dopamine release. J. Neurochem. 70, 384–390.
Gabard-Durnam, L.J., Flannery, J., Goff, B., Gee, D.G., Humphreys, K.L., Telzer, E., Hare, T., Tottenham, N., 2014. The development of human amygdala functional connectivity at rest from 4 to 23 years: a cross-sectional study. Neuroimage 95, 193–207, http://dx.doi.org/10.1016/j.neuroimage.2014.03.038.

Galván, A., McGlennen, K.M., 2012. Enhanced striatal sensitivity to aversive reinforcement in adolescents versus adults. J. Cogn. Neurosci. 25, 284–296, http://dx.doi.org/10.1162/jocn_a_00326.
Galván, A., Hare, T.A., Parra, C.E., Penn, J., Voss, H., Glover, G., Casey, B.J., 2006. Earlier development of the accumbens relative to orbitofrontal cortex might underlie risk-taking behavior in adolescents. J. Neurosci. 26, 6885–6892, http://dx.doi.org/10.1523/JNEUROSCI.1062-06.2006.
Galván, A., 2010. Adolescent development of the reward system. Front. Hum. Neurosci. 4, 6, http://dx.doi.org/10.3389/neuro.09.006.2010.
Galván, A., 2013. Neural Systems Underlying Reward and Approach Behaviors in Childhood and Adolescence. Curr. Top. Behav. Neurosci., http://dx.doi.org/10.1007/7854_2013_240.
Gee, D.G., Casey, B.J., 2015. The impact of developmental timing for stress and recovery. Neurobiol. Stress 1, 184–194, http://dx.doi.org/10.1016/j.ynstr.2015.02.001.
Gee, D.G., Gabard-Durnam, L.J., Flannery, J., Goff, B., Humphreys, K.L., Telzer, E.H., Hare, T.A., Bookheimer, S.Y., Tottenham, N., 2013a. Early developmental emergence of human amygdala-prefrontal connectivity after maternal deprivation. Proc. Natl. Acad. Sci. U. S. A., http://dx.doi.org/10.1073/pnas.1307893110.
Gee, D.G., Humphreys, K.L., Flannery, J., Goff, B., Telzer, E.H., Shapiro, M., Hare, T.A., Bookheimer, S.Y., Tottenham, N., 2013b. A developmental shift from positive to negative connectivity in human amygdala-prefrontal circuitry. J. Neurosci. 33, 4584–4593, http://dx.doi.org/10.1523/JNEUROSCI.3446-12.2013.
Geier, C.F., Terwilliger, R., Teslovich, T., Velanova, K., Luna, B., 2010. Immaturities in reward processing and its influence on inhibitory control in adolescence. Cereb. Cortex 20, 1613–1629, http://dx.doi.org/10.1093/cercor/bhp225.
Giedd, J.N., Snell, J.W., Lange, N., Rajapakse, J.C., Casey, B.J., Kozuch, P.L., Vaituzis, A.C., Vauss, Y.C., Hamburger, S.D., Kaysen, D., Rapoport, J.L., 1996a. Quantitative magnetic resonance imaging of human brain development: ages 4–18. Cereb. Cortex 6, 551–560.
Giedd, J.N., Vaituzis, C., Hamburger, S.D., Lange, N., Rajapakse, J.C., Kaysen, D., Vauss, Y.C., Rapoport, J.L., 1996b. Quantitative MRI of the temporal lobe, amygdala, and hippocampus in normal human development: ages 4–18 years. J. Comp. Neurol. 366, 223–230.
Giedd, J.N., 2004. Structural magnetic resonance imaging of the adolescent brain. Ann. N. Y. Acad. Sci. 1021, 77–85, http://dx.doi.org/10.1196/annals.1308.009.
Gilmore, J.H., Shi, F., Woolson, S.L., Knickmeyer, R.C., Short, S.J., Lin, W., Zhu, H., Hamer, R.M., Styner, M., Shen, D., 2012. Longitudinal development of cortical and subcortical gray matter from birth to 2 years. Cereb. Cortex 22, 2478–2485, http://dx.doi.org/10.1093/cercor/bhr327.
Goddings, A.-L., Mills, K.L., Clasen, L.S., Giedd, J.N., Viner, R.M., Blakemore, S.-J., 2013. The influence of puberty on subcortical brain development. Neuroimage, http://dx.doi.org/10.1016/j.neuroimage.2013.09.073.
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. Neuroscience 249, 129–138, http://dx.doi.org/10.1016/j.neuroscience.2012.12.010.
Gottfried, J.A., O'Doherty, J., Dolan, R.J., 2003. Encoding predictive reward value in human amygdala and orbitofrontal cortex. Science 301, 1104–1107, http://dx.doi.org/10.1126/science.1087919.
Green, J.G., McLaughlin, K.A., Berglund, P.A., Gruber, M.J., Sampson, N.A., Zaslavsky, A.M., Kessler, R.C., 2010. Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication I: associations with first onset of DSM-IV disorders. Arch. Gen. Psychiatry 67, 113–123, http://dx.doi.org/10.1001/archgenpsychiatry.2009.186.
Groenewegen, H.J., Wright, C.I., Beijer, A.V.J., Voorn, P., 1999. Convergence and segregation of ventral striatal inputs and outputs. Ann. N. Y. Acad. Sci. 877, 49–63, http://dx.doi.org/10.1111/j.1749-6632.1999.tb09260.x.
Gunnar, M., Quevedo, K., 2007. The neurobiology of stress and development. Annu. Rev. Psychol. 58, 145–173, http://dx.doi.org/10.1146/annurev.psych.58.110405.085605.
Guyer, A.E., Kaufman, J., Hodgdon, H.B., Masten, C.L., Jazbec, S., Pine, D.S., Ernst, M., 2006. Behavioral alterations in reward system function. J. Am. Acad. Child Adolesc. Psychiatry 45, 1059–1067, http://dx.doi.org/10.1097/01.chi.0000227882.50404.11.
Guyer, A.E., Monk, C.S., McClure-Tone, E.B., Nelson, E.E., Roberson-Nay, R., Adler, A.D., Fromm, S.J., Leibenluft, E., Pine, D.S., Ernst, M., 2008. A developmental examination of amygdala response to facial expressions. J. Cogn. Neurosci. 20, 1565–1582, http://dx.doi.org/10.1162/jocn.2008.20114.
Härfstrand, A., Fuxe, K., Cintra, A., Agnati, L.F., Zini, I., Wikström, A.C., Okret, S., Yu, Z.Y., Goldstein, M., Steinbusch, H., 1986. Glucocorticoid receptor immunoreactivity in monoaminergic neurons of rat brain. Proc. Natl. Acad. Sci. U. S. A. 83, 9779–9783.
Haber, S.N., Behrens, T.E.J., 2014. The neural network underlying incentive-Based learning: implications for interpreting circuit disruptions in psychiatric disorders. Neuron 83, 1019–1039, http://dx.doi.org/10.1016/j.neuron.2014.08.031.
Haber, S.N., Knutson, B., 2010. The reward circuit: linking primate anatomy and human imaging. Neuropsychopharmacology 35, 4–26, http://dx.doi.org/10.1038/npp.2009.129.
Haber, S.N., Fudge, J.L., McFarland, N.R., 2000. Striatonigrostriatal pathways in primates form an ascending spiral from the shell to the dorsolateral striatum. J. Neurosci. 20, 2369–2382.
Haber, S.N., Kim, K.-S., Mailly, P., Calzavara, R., 2006. Reward-related cortical inputs define a large striatal region in primates that interface with associative cortical connections, providing a substrate for incentive-based learning. J. Neurosci. 26, 8368–8376, http://dx.doi.org/10.1523/JNEUROSCI.0271-06.2006.
Hackman, D.A., Farah, M.J., 2009. Socioeconomic status and the developing brain. Trends Cogn. Sci. 13, 65–73, http://dx.doi.org/10.1016/j.tics.2008.11.003.
Hanson, J.L., Nacewicz, B.M., Sutterer, M.J., Cayo, A.A., Schaefer, S.M., Rudolph, K.D., Shirtcliff, E.A., Pollak, S.D., Davidson, R.J., 2014. Behavioral problems after early life stress: contributions of the hippocampus and amygdala. Biol. Psychiatry, http://dx.doi.org/10.1016/j.biopsych.2014.04.020.
Hare, T.A., Tottenham, N., Galván, A., Voss, H.U., Glover, G.H., Casey, B.J., 2008. Biological substrates of emotional reactivity and regulation in adolescence during an emotional go-nogo task. Biol. Psychiatry 63, 927–934, http://dx.doi.org/10.1016/j.biopsych.2008.03.015.
Hart, G., Leung, B.K., Balleine, B.W., 2013. Neurobiology of learning and memory. Neurobiol. Learn. Mem., 1–15, http://dx.doi.org/10.1016/j.nlm.2013.11.003.
Hartley, C.A., Phelps, E.A., 2010. Changing fear: the neurocircuitry of emotion regulation. Neuropsychopharmacology 35, 136–146, http://dx.doi.org/10.1038/npp.2009.121.
Hartley, C.A., Phelps, E.A., 2012. Anxiety and decision-making. Biol. Psychiatry 72, 113–118, http://dx.doi.org/10.1016/j.biopsych.2011.12.027.
Hartley, C.A., McKenna, M.C., Salman, R., Holmes, A., Casey, B.J., Phelps, E.A., Glatt, C.E., 2012. Serotonin transporter polyadenylation polymorphism modulates the retention of fear extinction memory. Proc. Natl. Acad. Sci. U. S. A. 109, 5493–5498, http://dx.doi.org/10.1073/pnas.1202044109/-/DCSupplemental/sapp.pdf.
Heim, C., Nemeroff, C.B., 2001. The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. BPS 49, 1023–1039.
Heim, C., Plotsky, P.M., Nemeroff, C.B., 2004. Importance of studying the contributions of early adverse experience to neurobiological findings in depression. Neuropsychopharmacology 29, 641–648, http://dx.doi.org/10.1038/sj.npp.1300397.
Heller, A.S., Johnstone, T., Light, S.N., Peterson, M.J., Kolden, G.G., Kalin, N.H., Davidson, R.J., 2013. Relationships between changes in sustained fronto-striatal connectivity and positive affect in major depression resulting from antidepressant treatment. Am. J. Psychiatry 170, 197–206, http://dx.doi.org/10.1176/appi.ajp.2012.12010014.
Herting, M.M., Gautam, P., Spielberg, J.M., Kan, E., Dahl, R.E., Sowell, E.R., 2014. The role of testosterone and estradiol in brain volume changes across adolescence: a longitudinal structural MRI study. Hum. Brain Mapp. 35, 5633–5645, http://dx.doi.org/10.1002/hbm.22575.
Hofer, M.A., 2006. Psychobiological roots of early attachment. Curr. Directions Psychol. Sci. 15, 84–88.
Hollerman, J., Schultz, W., 1998. Dopamine neurons report an error in the temporal prediction of reward during learning. Nat. Neurosci. 1, 304–309.
Hollon, N.G., Burgeno, L.M., Phillips, P.E.M., 2015. Stress effects on the neural substrates of motivated behavior. Nat. Neurosci. 18, 1405–1412, http://dx.doi.org/10.1038/nn.4114.
Hu, S., Pruessner, J.C., Coupé, P., Collins, D.L., 2013. Volumetric analysis of medial temporal lobe structures in brain development from childhood to adolescence. Neuroimage 74, 276–287, http://dx.doi.org/10.1016/j.neuroimage.2013.02.032.
Humphreys, K.L., Lee, S.S., Telzer, E.H., Gabard-Durnam, L.J., Goff, B., Flannery, J., Tottenham, N., 2015. Exploration-exploitation strategy is dependent on early experience. Dev. Psychobiol. 57, 313–321, http://dx.doi.org/10.1002/dev.21293.
Jones, R.M., Somerville, L.H., Li, J., Ruberry, E.J., Powers, A., Mehta, N., Dyke, J., Casey, B.J., 2014. Adolescent-specific patterns of behavior and neural activity during social reinforcement learning. Cogn. Affective Behav. Neurosci., http://dx.doi.org/10.3758/s13415-014-0257-z.
Kable, J.W., Glimcher, P.W., 2007. The neural correlates of subjective value during intertemporal choice. Nat. Neurosci. 10, 1625–1633, http://dx.doi.org/10.1038/nn2007.
King-Casas, B., 2005. Getting to know you: reputation and trust in a two-Person economic exchange. Science 308, 78–83, http://dx.doi.org/10.1126/science.1108062.
Kishida, K.T., Montague, P.R., 2012. Imaging models of valuation during social interaction in humans. Biol. Psychiatry 72, 93–100, http://dx.doi.org/10.1016/j.biopsych.2012.02.037.
Knutson, B., Adams, C., Fong, G., Hommer, D., 2001. Anticipation of increasing monetary reward selectively recruits nucleus accumbens. J. Neurosci. 21, RC159, 20015472[pii].
Knutson, B., Taylor, J., Kaufman, M., Peterson, R., Glover, G., 2005. Distributed neural representation of expected value. J. Neurosci. 25, 4806–4812, http://dx.doi.org/10.1523/JNEUROSCI.0642-05.2005.
Koolschijn, P.C.M.P., Peper, J.S., Crone, E.A., 2014. The influence of sex steroids on structural brain maturation in adolescence. PLoS One 9, e83929, http://dx.doi.org/10.1371/journal.pone.0083929.t002.
Kringelbach, M.L., 2005. The human orbitofrontal cortex: linking reward to hedonic experience. Nat. Rev. Neurosci. 6, 691–702, http://dx.doi.org/10.1038/nrn1747.
LaBar, K.S., Gatenby, J.C., Gore, J.C., Ledoux, J.E., Phelps, E.A., 1998. Human amygdala activation during conditioned fear acquisition and extinction: a mixed-trial fMRI study. Neuron 20, 937–945.
LeDoux, J.E., 2000. Emotion circuits in the brain. Annu. Rev. Neurosci. 23, 155–184, http://dx.doi.org/10.1146/annurev.neuro.23.1.155.
Lejuez, C.W., Read, J.P., Kahler, C.W., Richards, J.B., Ramsey, S.E., Stuart, G.L., Strong, D.R., Brown, R.A., 2002. Evaluation of a behavioral measure of risk taking: the

balloon analogue risk task (BART). J. Exp. Psychol. Appl. 8, 75–84, http://dx.doi.org/10.1037//1076-898X.8.2.75.
Levita, L., Hare, T.A., Voss, H.U., Glover, G., Ballon, D.J., Casey, B.J., 2009. The bivalent side of the nucleus accumbens. Neuroimage 44, 1178–1187, http://dx.doi.org/10.1016/j.neuroimage.2008.09.039.
Lewis, A.H., Niznikiewicz, M.A., Delamater, A.R., Delgado, M.R., 2013. Avoidance-based human pavlovian-to-instrumental transfer. Eur. J. Neurosci. 38, 3740–3748, http://dx.doi.org/10.1111/ejn.12377.
Li, J., Schiller, D., Schoenbaum, G., Phelps, E.A., Daw, N.D., 2011. Differential roles of human striatum and amygdala in associative learning. Nat. Neurosci. 14, 1250–1252, http://dx.doi.org/10.1038/nn.2904.
Loman, M.M., Johnson, A.E., Quevedo, K., Lafavor, T.L., Gunnar, M.R., 2014. Risk-taking and sensation-seeking propensity in postinstitutionalized early adolescents. J. Child Psychol. Psychiatry Allied Disciplines 55, 1145–1152, http://dx.doi.org/10.1111/jcpp.12208.
Luby, J., Belden, A., Botteron, K., Marrus, N., Harms, M.P., Babb, C., Nishino, T., Barch, D., 2013. The effects of poverty on childhood brain development: the mediating effect of caregiving and stressful life events. JAMA Pediatr. 167, 1135–1142, http://dx.doi.org/10.1001/jamapediatrics.2013.3139.
Lupien, S.J., King, S., Meaney, M.J., McEwen, B.S., 2000. Child's stress hormone levels correlate with mother's socioeconomic status and depressive state. Biol. Psychiatry, 976–980.
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, http://dx.doi.org/10.1038/nrn2639.
Maheu, F.S., Dozier, M., Guyer, A.E., Mandell, D., Peloso, E., Poeth, K., Jenness, J., Lau, J.Y.F., Ackerman, J.P., Pine, D.S., Ernst, M., 2010. A preliminary study of medial temporal lobe function in youths with a history of caregiver deprivation and emotional neglect. Cogn. Affective Behav. Neurosci. 10, 34–49, http://dx.doi.org/10.3758/CABN.10.1.34.
Malter Cohen, M., Jing, D., Yang, R.R., Tottenham, N., Lee, F.S., Casey, B.J., 2013. Early-life stress has persistent effects on amygdala function and development in mice and humans. Proc. Natl. Acad. Sci. U. S. A. 110, 18274–18278, http://dx.doi.org/10.1073/pnas.1310163110.
Masten, A.S., Cicchetti, D., 2010. Developmental cascades. Dev. Psychopathol. 22, 491–495, http://dx.doi.org/10.1017/S0954579410000222.
Matsumoto, M., Hikosaka, O., 2009. Two types of dopamine neuron distinctly convey positive and negative motivational signals. Nature 459, 837–841, http://dx.doi.org/10.1038/nature08028.
Matthews, K., Robbins, T.W., 2003. Early experience as a determinant of adult behavioural responses to reward: the effects of repeated maternal separation in the rat. Neurosci. Biobehav. Rev. 27, 45–55, http://dx.doi.org/10.1016/S0149-7634(03)00008-3.
Matthews, K., Wilkinson, L.S., Robbins, T.W., 1996. Repeated maternal separation of preweanling rats attenuates behavioral responses to primary and conditioned incentives in adulthood. Physiol. Behav. 59, 99–107.
Matthews, K., Dalley, J.W., Matthews, C., Tsai, T.H., Robbins, T.W., 2001. Periodic Maternal Separation of Neonatal Rats Produces Region- and Gender- Specific Effects on Biogenic Amine Content in Postmortem Adult Brain, 1–10.
McCutcheon, J.E., Conrad, K.L., Carr, S.B., Ford, K.A., McGehee, D.S., Marinelli, M., 2012. Dopamine neurons in the ventral tegmental area fire faster in adolescent rats than in adults. J. Neurophysiol. 108, 1620–1630, http://dx.doi.org/10.1152/jn.00077.2012.
McGowan, P.O., Sasaki, A., D'Alessio, A.C., Dymov, S., Labonté, B., Szyf, M., Turecki, G., Meaney, M.J., 2009. Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. Nat. Neurosci. 12, 342–348, http://dx.doi.org/10.1038/nn.2270.
McLaughlin, K.A., Sheridan, M.A., Lambert, H.K., 2014. Childhood adversity and neural development: deprivation and threat as distinct dimensions of early experience. Neurosci. Biobehav. Rev. 47, 578–591, http://dx.doi.org/10.1016/j.neubiorev.2014.10.012.
Meaney, M.J., Brake, W., Gratton, A., 2002. Environmental regulation of the development of mesolimbic dopamine systems: a neurobiological mechanism for vulnerability to drug abuse? Psychoneuroendocrinology 27, 127–138.
Mehta, M.A., Gore-Langton, E., Golembo, N., Colvert, E., Williams, S.C.R., Sonuga-Barke, E., 2010. Hyporesponsive reward anticipation in the basal ganglia following severe institutional deprivation early in life. J. Cogn. Neurosci. 22, 2316–2325, http://dx.doi.org/10.1162/jocn.2009.21394.
Meredith, G.E., Pattiselanno, A., 1996. Shell and core in monkey and human nucleus accumbens identified with antibodies to calbindin-D28k. Journal of . . ..
Merker, B., 2013. Cortical gamma oscillations: the functional key is activation, not cognition. Neurosci. Biobehav. Rev. 37, 401–417, http://dx.doi.org/10.1016/j.neubiorev.2013.01.013.
Middleton, F., Strick, P., 2000. Basal ganglia and cerebellar loops: motor and cognitive circuits. Brain Res. Brain Res. Rev. 31, 236–250, S0165017399000405[pii].
Monk, C.S., McClure, E.B., Nelson, E.E., Zarahn, E., Bilder, R.M., Leibenluft, E., Charney, D.S., Ernst, M., Pine, D.S., 2003. Adolescent immaturity in attention-related brain engagement to emotional facial expressions. Neuroimage 20, 420–428, http://dx.doi.org/10.1016/S1053-8119(03)00355-0.
Moore, W.E., Pfeifer, J.H., Masten, C.L., Mazziotta, J.C., Iacoboni, M., Dapretto, M., 2012. Facing puberty: associations between pubertal development and neural responses to affective facial displays. Soc. Cogn. Affective Neurosci. 7, 35–43, http://dx.doi.org/10.1093/scan/nsr066.
Moriceau, S., Sullivan, R.M., 2004. Corticosterone influences on Mammalian neonatal sensitive-period learning. Behav. Neurosci. 118, 274–281, http://dx.doi.org/10.1037/0735-7044.118.2.274.
Moriceau, S., Sullivan, R.M., 2006. Maternal presence serves as a switch between learning fear and attraction in infancy. Nat. Neurosci. 9, 1004–1006, http://dx.doi.org/10.1038/nn1733.
Moriceau, S., Shionoya, K., Jakubs, K., Sullivan, R.M., 2009. Early-life stress disrupts attachment learning: the role of amygdala corticosterone, locus ceruleus corticotropin releasing hormone, and olfactory bulb norepinephrine. J. Neurosci. 29, 15745–15755, http://dx.doi.org/10.1523/JNEUROSCI.4106-09.2009.
Moriceau, S., Roth, T.L., Sullivan, R.M., 2010. Rodent model of infant attachment learning and stress. Dev. Psychobiol. 52, 651–660, http://dx.doi.org/10.1002/dev.20482.
Motzkin, J.C., Philippi, C.L., Wolf, R.C., Baskaya, M.K., Koenigs, M., 2014. Ventromedial prefrontal cortex is critical for the regulation of amygdala activity in humans. BPS 1–9, http://dx.doi.org/10.1016/j.biopsych.2014.02.014.
Muhammad, A., Carroll, C., Kolb, B., 2012. Stress during development alters dendritic morphology in the nucleus accumbens and prefrontal cortex. Neuroscience 216, 103–109, http://dx.doi.org/10.1016/j.neuroscience.2012.04.041.
Nikolova, Y.S., Hariri, A.R., 2015. Can we observe epigenetic effects on human brain function? Trends Cogn. Sci. 19, 366–373, http://dx.doi.org/10.1016/j.tics.2015.05.003.
Niv, Y., Schoenbaum, G., 2008. Dialogues on prediction errors. Trends Cogn. Sci. 12, 265–272, http://dx.doi.org/10.1016/j.tics.2008.03.006, S1364-6613(08)00137-X[pii].
Niv, Y., 2009. Reinforcement learning in the brain. J. Math. Psychol. 53, 139–154.
Noble, K.G., Houston, S.M., Kan, E., Sowell, E.R., 2012. Neural correlates of socioeconomic status in the developing human brain. Dev. Sci. 15, 516–527, http://dx.doi.org/10.1111/j.1467-7687.2012.01147.x.
O'Doherty, J., Rolls, E.T., Francis, S., Bowtell, R., McGlone, F., 2001. Representation of pleasant and aversive taste in the human brain. J. Neurophysiol. 85, 1315–1321.
O'Doherty, J.P., Deichmann, R., Critchley, H.D., Dolan, R.J., 2002. Neural responses during anticipation of a primary taste reward. Neuron 33, 815–826.
O'Doherty, J., Dayan, P., Schultz, J., Deichmann, R., Friston, K., Dolan, R., 2004. Dissociable roles of ventral and dorsal striatum in instrumental conditioning. Science 304, 452–454, http://dx.doi.org/10.1126/science.1094285, 304/5669/452 [pii].
Olsavsky, A.K., Telzer, E.H., Shapiro, M., Humphreys, K.L., Flannery, J., Goff, B., Tottenham, N., 2013. Indiscriminate amygdala response to mothers and strangers after early maternal deprivation. Biol. Psychiatry 74, 853–860, http://dx.doi.org/10.1016/j.biopsych.2013.05.025.
Olsson, A., Phelps, E.A., 2004. Learned fear of unseen faces after Pavlovian, observational, and instructed fear. Psychol. Sci. 15, 822–828, http://dx.doi.org/10.1111/j.0956-7976.2004.00762.x.
Ostby, Y., Tamnes, C.K., Fjell, A.M., Westlye, L.T., Due-Tonnessen, P., Walhovd, K.B., 2009. Heterogeneity in subcortical brain development: a structural magnetic resonance imaging study of brain maturation from 8 to 30 years. J. Neurosci. 29, 11772–11782, http://dx.doi.org/10.1523/JNEUROSCI.1242-09.2009.
Otto, A.R., Raio, C.M., Chiang, A., Phelps, E.A., Daw, N.D., 2013. Working-memory capacity protects model-based learning from stress. Proc. Natl. Acad. Sci. U. S. A. 110, 20941–20946, http://dx.doi.org/10.1073/pnas.1312011110.
Overton, P.G., Tong, Z.Y., Brain, P.F., Clark, D., 1996. Preferential occupation of mineralocorticoid receptors by corticosterone enhances glutamate-induced burst firing in rat midbrain dopaminergic neurons. Brain Res. 737, 146–154.
Pagliaccio, D., Luby, J.L., Gaffrey, M.S., Belden, A.C., Botteron, K.N., Harms, M.P., Barch, D.M., 2013. Functional brain activation to emotional and nonemotional faces in healthy children: evidence for developmentally undifferentiated amygdala function during the school-age period. Cogn. Affective Behav. Neurosci. 13, 771–789, http://dx.doi.org/10.3758/s13415-013-0167-5.
Paton, J., Belova, M., Morrison, S., Salzman, C., 2006. The primate amygdala represents the positive and negative value of visual stimuli during learning. Nature 439, 865–870, http://dx.doi.org/10.1038/nature04490, nature04490[pii].
Paus, T., Keshavan, M., Giedd, J.N., 2008. Why do many psychiatric disorders emerge during adolescence? Nat. Rev. Neurosci. 9, 947–957, http://dx.doi.org/10.1038/nrn2513.
Payne, C., Machado, C.J., Bliwise, N.G., Bachevalier, J., 2010. Maturation of the hippocampal formation and amygdala in Macaca mulatta: a volumetric magnetic resonance imaging study. Hippocampus 20, 922–935, http://dx.doi.org/10.1002/hipo.20688.
Pechtel, P., Pizzagalli, D.A., 2011. Effects of early life stress on cognitive and affective function: an integrated review of human literature. Psychopharmacology 214, 55–70, http://dx.doi.org/10.1007/s00213-010-2009-2.
Pennartz, C.M.A., Ito, R., Verschure, P.F.M.J., Battaglia, F.P., Robbins, T.W., 2011. The hippocampal striatal axis in learning, prediction and goal-directed behavior. Trends Neurosci. 34, 548–559, http://dx.doi.org/10.1016/j.tins.2011.08.001.
Peper, J.S., van den Heuvel, M.P., Mandl, R.C.W., Pol, H.E.H., van Honk, J., 2011. Sex steroids and connectivity in the human brain: a review of neuroimaging studies. Psychoneuroendocrinology 36, 1101–1113, http://dx.doi.org/10.1016/j.psyneuen.2011.05.004.
Perlman, S.B., Pelphrey, K.A., 2011. Developing connections for affective regulation: age-related changes in emotional brain connectivity. J. Exp. Child Psychol. 108, 607–620, http://dx.doi.org/10.1016/j.jecp.2010.08.006.

Pfeifer, J.H., Allen, N.B., 2012. Arrested development? Reconsidering dual-systems models of brain function in adolescence and disorders. Trends Cogn. Sci. 16, 322–329, http://dx.doi.org/10.1016/j.tics.2012.04.011.
Phan, K.L., Sripada, C.S., Angstadt, M., McCabe, K., 2010. Reputation for reciprocity engages the brain reward center. Proc. Natl. Acad. Sci. U. S. A. 1-6, http://dx.doi.org/10.1073/pnas.1008137107.
Phelps, E.A., LeDoux, J.E., 2005. Contributions of the amygdala to emotion processing: from animal models to human behavior. Neuron 48, 175–187, http://dx.doi.org/10.1016/j.neuron.2005.09.025.
Phelps, E.A., Delgado, M.R., Nearing, K.I., LeDoux, J.E., 2004. Extinction learning in humans: role of the amygdala and vmPFC. Neuron 43, 897–905, http://dx.doi.org/10.1016/j.neuron.2004.08.042.
Pitkänen, A., Amaral, D.G., 1998. Organization of the intrinsic connections of the monkey amygdaloid complex: projections originating in the lateral nucleus. J. Comp. Neurol. 398, 431–458.
Pitkänen, A., Savander, V., LeDoux, J.E., 1997. Organization of intra-amygdaloid circuitries in the rat: an emerging framework for understanding functions of the amygdala. Trends Neurosci. 20, 517–523.
Pizzagalli, D.A., Iosifescu, D., Hallett, L.A., Ratner, K.G., Fava, M., 2008. Reduced hedonic capacity in major depressive disorder: evidence from a probabilistic reward task. J. Psychiatr. Res. 43, 76–87, http://dx.doi.org/10.1016/j.jpsychires.2008.03.001.
Pizzagalli, D.A., Holmes, A.J., Dillon, D.G., Goetz, E.L., Birk, J.L., Bogdan, R., Dougherty, D.D., Iosifescu, D.V., Rauch, S.L., Fava, M., 2009. Reduced caudate and nucleus accumbens response to rewards in unmedicated individuals with major depressive disorder. Am. J. Psychiatry 166, 702–710, http://dx.doi.org/10.1176/appi.ajp.2008.08081201.
Pleskac, T.J., 2008. Decision making and learning while taking sequential risks. J. Exp. Psychol. Learn. Mem. Cogn. 34, 167–185, http://dx.doi.org/10.1037/0278-7393.34.1.167.
Pohlack, S.T., Nees, F., Ruttorf, M., Schad, L.R., Flor, H., 2012. Activation of the ventral striatum during aversive contextual conditioning in humans. Biol. Psychol. 91, 74–80, http://dx.doi.org/10.1016/j.biopsycho.2012.04.004.
Popescu, A.T., Popa, D., Paré, D., 2009. Coherent gamma oscillations couple the amygdala and striatum during learning. Nat. Neurosci. 12, 801–807, http://dx.doi.org/10.1038/nn.2305.
Porcelli, A.J., Delgado, M.R., 2009. Acute stress modulates risk taking in financial decision making. Psychol. Sci. 20, 278–283, http://dx.doi.org/10.1111/j.1467-9280.2009.02288.x.
Powell, S.B., Geyer, M.A., Preece, M.A., Pitcher, L.K., Reynolds, G.P., Swerdlow, N.R., 2003. Dopamine depletion of the nucleus accumbens reverses isolation-induced deficits in prepulse inhibition in rats. Neuroscience 119, 233–240, http://dx.doi.org/10.1016/S0306-4522(03)00122-2.
Prévost, C., McCabe, J.A., Jessup, R.K., Bossaerts, P., O'Doherty, J.P., 2011. Differentiable contributions of human amygdalar subregions in the computations underlying reward and avoidance learning. Eur. J. Neurosci. 34, 134–145, http://dx.doi.org/10.1111/j.1460-9568.2011.07686.x.
Raznahan, A., Shaw, P.W., Lerch, J.P., Clasen, L.S., Greenstein, D., Berman, R., Pipitone, J., Chakravarty, M.M., Giedd, J.N., 2014. Longitudinal four-dimensional mapping of subcortical anatomy in human development. Proc. Natl. Acad. Sci. U. S. A. 111, 1592–1597, http://dx.doi.org/10.1073/pnas.1316911111.
Rescorla, R., Wagner, A., 1972. A Theory of Pavlovian Conditioning: Variations in the Effectiveness of Reinforcment and Non Reinforcement, Classical Conditioning Ii. Appleton-Century-Crofts.
Richards, J.M., Plate, R.C., Ernst, M., 2013. A systematic review of fMRI reward paradigms used in studies of adolescents vs. adults: the impact of task design and implications for understanding neurodevelopment. Neurosci. Biobehav. Rev. 37, 976–991, http://dx.doi.org/10.1016/j.neubiorev.2013.03.004.
Rilling, J.K., Sanfey, A.G., 2011. The neuroscience of social decision-Making. Annu. Rev. Psychol., http://dx.doi.org/10.1146/annurev.psych.121208.131647.
Rincón-Cortés, M., 2014. Early life trauma and attachment: immediate and enduring effects on neurobehavioral and stress axis development, 1–15, 10.3389/fendo.2014.00033/abstract.
Robbins, T., Everitt, B., 1996. Neurobehavioural mechanisms of reward and motivation. Curr. Opin. Neurobiol. 6, 228–236, S0959-4388(96)80077-8[pii].
Robbins, T.W., Cador, M., Taylor, J.R., Everitt, B.J., 1989. Limbic-striatal interactions in reward-related processes. Neurosci. Biobehav. Rev. 13, 155–162.
Robbins, T.W., Jones, G.H., Wilkinson, L.S., 1996. Behavioural and neurochemical effects of early social deprivation in the rat. J. Psychopharmacol. 10, 39–47, http://dx.doi.org/10.1177/026988119601000107.
Robinson, O.J., Overstreet, C., Charney, D.R., Vytal, K., Grillon, C., 2013. Stress increases aversive prediction error signal in the ventral striatum. Proc. Natl. Acad. Sci. U. S. A. 110, 4129–4133, http://dx.doi.org/10.1073/pnas.1213923110.
Rolls, E.T., 2000. The orbitofrontal cortex and reward. Cereb. Cortex 10, 284–294.
Romeo, R.D., Mueller, A., Sisti, H.M., Ogawa, S., McEwen, B.S., Brake, W.G., 2003. Anxiety and fear behaviors in adult male and female C57BL/6 mice are modulated by maternal separation. Horm. Behav. 43, 561–567.
Roy, A.K., Benson, B.E., Degnan, K.A., Perez-Edgar, K., Pine, D.S., Fox, N.A., Ernst, M., 2014. Alterations in amygdala functional connectivity reflect early temperament. Biol. Psychol. 103, 248–254, http://dx.doi.org/10.1016/j.biopsycho.2014.09.007.
Rutledge, R.B., Dean, M., Caplin, A., Glimcher, P.W., 2010. Testing the reward prediction error hypothesis with an axiomatic model. J. Neurosci. 30, 13525–13536, http://dx.doi.org/10.1523/JNEUROSCI.1747–10.2010.
Sánchez, M.M., Ladd, C.O., Plotsky, P.M., 2001. Early adverse experience as a developmental risk factor for later psychopathology: evidence from rodent and primate models. Dev. Psychopathol. 13, 419–449, http://dx.doi.org/10.1017/S0954579401003029.
Salzman, C.D., Paton, J.J., Belova, M.A., Morrison, S.E., 2007. Flexible neural representations of value in the primate brain. Ann. N. Y. Acad. Sci. 1121, 336–354, http://dx.doi.org/10.1196/annals.1401.034.
Schiller, D., Delgado, M.R., 2010. Overlapping neural systems mediating extinction, reversal and regulation of fear. Trends Cogn. Sci., http://dx.doi.org/10.1016/j.tics.2010.04.002.
Schoenbaum, G., Chiba, A.A., Gallagher, M., 1998. Orbitofrontal cortex and basolateral amygdala encode expected outcomes during learning. Nat. Neurosci. 1, 155–159, http://dx.doi.org/10.1038/407.
Schoenbaum, G., Chiba, A.A., Gallagher, M., 1999. Neural encoding in orbitofrontal cortex and basolateral amygdala during olfactory discrimination learning. J. Neurosci. 19, 1876–1884.
Schoenbaum, G., Chiba, A.A., Gallagher, M., 2000. Changes in functional connectivity in orbitofrontal cortex and basolateral amygdala during learning and reversal training. J. Neurosci. 20, 5179–5189.
Schonberg, T., Daw, N., Joel, D., O'Doherty, J., 2007. Reinforcement learning signals in the human striatum distinguish learners from nonlearners during reward-based decision making. J. Neurosci. 27, 12860–12867, http://dx.doi.org/10.1523/JNEUROSCI.2496-07.2007, 27/47/12860[pii].
Schultz, W., Dayan, P., Montague, P., 1997. A neural substrate of prediction and reward. Science 275, 1593–1599.
Sesack, S.R., Grace, A.A., 2010. Cortico-Basal Ganglia reward network: microcircuitry. Neuropsychopharmacology 35, 27–47, http://dx.doi.org/10.1038/npp.2009.93.
Sheridan, M.A., McLaughlin, K.A., 2014. Dimensions of early experience and neural development: deprivation and threat. Trends Cogn. Sci. 18, 580–585, http://dx.doi.org/10.1016/j.tics.2014.09.001.
Shiflett, M.W., Balleine, B.W., 2010. At the limbic-motor interface: disconnection of basolateral amygdala from nucleus accumbens core and shell reveals dissociable components of incentive motivation. Eur. J. Neurosci. 32, 1735–1743, http://dx.doi.org/10.1111/j.1460-9568.2010.07439.x.
Silvers, J.A., Insel, C., Powers, A., Franz, P., Weber, J., Mischel, W., Casey, B.J., Ochsner, K.N., 2014. Curbing craving: behavioral and brain evidence that children regulate craving when instructed to do so but have higher baseline craving than adults. Psychol. Sci. 25, 1932–1942, http://dx.doi.org/10.1177/0956797614546001.
Somerville, L.H., Casey, B.J., 2010. Developmental neurobiology of cognitive control and motivational systems. Curr. Opin. Neurobiol. 20, 236–241, http://dx.doi.org/10.1016/j.conb.2010.01.006.
Somerville, L.H., Jones, R.M., Casey, B.J., 2010. A time of change: behavioral and neural correlates of adolescent sensitivity to appetitive and aversive environmental cues. Brain Cogn. 72, 124–133, http://dx.doi.org/10.1016/j.bandc.2009.07.003.
Somerville, L.H., Hare, T., Casey, B.J., 2011. Frontostriatal maturation predicts cognitive control failure to appetitive cues in adolescents. J. Cogn. Neurosci. 23, 2123–2134, http://dx.doi.org/10.1162/jocn.2010.21572.
Somerville, L.H., van den Bulk, B.G., Skwara, A.C., 2014. Response to: the triadic model perspective for the study of adolescent motivated behavior. Brain Cogn., http://dx.doi.org/10.1016/j.bandc.2014.01.003.
Sowell, E.R., Thompson, P.M., Holmes, C.J., Jernigan, T.L., Toga, A.W., 1999. In vivo evidence for post-adolescent brain maturation in frontal and striatal regions. Nat. Neurosci. 2, 859–861, http://dx.doi.org/10.1038/13154.
Spear, L.P., 2000. The adolescent brain and age-related behavioral manifestations. Neurosci. Biobehav. Rev. 24, 417–463.
Spielberg, J.M., Olino, T.M., Forbes, E.E., Dahl, R.E., 2014. Exciting fear in adolescence: does pubertal development alter threat processing? Dev. Brain Res. 8, 86–95, http://dx.doi.org/10.1016/j.dcn.2014.01.004.
Steinberg, L., 2008. A social neuroscience perspective on adolescent risk-taking. Dev. Rev. 28, 78–106, http://dx.doi.org/10.1016/j.dr.2007.08.002.
Stuber, G.D., Sparta, D.R., Stamatakis, A.M., van Leeuwen, W.A., Hardjoprajitno, J.E., Cho, S., Tye, K.M., Kempadoo, K.A., Zhang, F., Deisseroth, K., Bonci, A., 2011. Excitatory transmission from the amygdala to nucleus accumbens facilitates reward seeking. Nature, 1–6, http://dx.doi.org/10.1038/nature10194.
Sujan, A.C., Humphreys, K.L., Ray, L.A., Lee, S.S., 2014. Differential association of child abuse with self-reported versus laboratory-based impulsivity and risk-taking in young adulthood. Child Maltreat. 19, 145–155, http://dx.doi.org/10.1177/1077559514543827.
Swartz, J.R., Carrasco, M., Wiggins, J.L., Thomason, M.E., Monk, C.S., 2014. Age-related changes in the structure and function of prefrontal cortex-amygdala circuitry in children and adolescents: a multi-modal imaging approach. Neuroimage 86, 212–220, http://dx.doi.org/10.1016/j.neuroimage.2013.08.018.
Szyf, M., Bick, J., 2013. DNA methylation: a mechanism for embedding early life experiences in the genome. Child Dev. 84, 49–57, http://dx.doi.org/10.1111/j.1467-8624.2012.01793.x.
Teicher, M.H., Andersen, S.L., Hostetter, J.C., 1995. Evidence for dopamine receptor pruning between adolescence and adulthood in striatum but not nucleus accumbens. Dev. Brain Res., 167–172.
Thomas, K.M., Drevets, W.C., Whalen, P.J., Eccard, C.H., Dahl, R.E., Ryan, N.D., Casey, B.J., 2001. Amygdala response to facial expressions in children and adults. BPS 49, 309–316.
Todorov, A., Baron, S.G., Oosterhof, N.N., 2008. Evaluating face trustworthiness: a model based approach. Soc. Cogn. Affective Neurosci. 3, 119–127, http://dx.doi.org/10.1093/scan/nsn009.

Tottenham, N., Sheridan, M.A., 2009. A review of adversity, the amygdala and the hippocampus: a consideration of developmental timing. Front. Hum. Neurosci. 3, 68, http://dx.doi.org/10.3389/neuro.09.068.2009.
Tottenham, N., Hare, T.A., Quinn, B.T., McCarry, T.W., Nurse, M., Gilhooly, T., Millner, A., Galván, A., Davidson, M.C., Eigsti, I.-M., Thomas, K.M., Freed, P.J., Booma, E.S., Gunnar, M.R., Altemus, M., Aronson, J., Casey, B.J., 2010. Prolonged institutional rearing is associated with atypically large amygdala volume and difficulties in emotion regulation. Dev. Sci. 13, 46–61, http://dx.doi.org/10.1111/j.1467-7687.2009.00852.x.
Tottenham, N., Hare, T.A., Millner, A., Gilhooly, T., Zevin, J.D., Casey, B.J., 2011. Elevated amygdala response to faces following early deprivation. Dev. Sci. 14, 190–204, http://dx.doi.org/10.1111/j.1467-7687.2010.00971.x.
Tottenham, N., Shapiro, M., Telzer, E.H., Humphreys, K.L., 2012. Amygdala response to mother. Dev. Sci. 15, 307–319, http://dx.doi.org/10.1111/j.1467-7687.2011.01128.x.
Tottenham, N., 2012. Human amygdala development in the absence of species-expected caregiving. Dev. Psychobiol. 54, 598–611, http://dx.doi.org/10.1002/dev.20531.
Tovote, P., Fadok, J.P., Lüthi, A., 2015. Neuronal circuits for fear and anxiety. Nat. Rev. Neurosci. 16, 317–331, http://dx.doi.org/10.1038/nrn3945.
Tricomi, E., Lempert, K.M., 2015. Value and probability coding in a feedback-based learning task utilizing food rewards. J. Neurophysiol. 113, 4–13, http://dx.doi.org/10.1152/jn.00086.2014.
Tricomi, E., Delgado, M.R., Fiez, J.A., 2004. Modulation of caudate activity by action contingency. Neuron 41, 281–292, S0896627303008481[pii].
Ulfig, N., Setzer, M., Bohl, J., 2003. Ontogeny of the human amygdala. Ann. N. Y. Acad. Sci. 985, 22–33.
van den Bos, W., Cohen, M.X., Kahnt, T., Crone, E.A., 2012. Striatum-medial prefrontal cortex connectivity predicts developmental changes in reinforcement learning. Cereb. Cortex 22, 1247–1255, http://dx.doi.org/10.1093/cercor/bhr198.
van der Meer, M., 2010. Integrating early results on ventral striatal gamma oscillations in the rat. Front. Neurosci., http://dx.doi.org/10.3389/fnins.2010.00300.
Van Leijenhorst, L., Gunther Moor, B., Op de Macks, Z.A., Rombouts, S.A.R.B., Westenberg, P.M., Crone, E.A., 2010a. Adolescent risky decision-making: neurocognitive development of reward and control regions. Neuroimage 51, 345–355, http://dx.doi.org/10.1016/j.neuroimage.2010.02.038.
Van Leijenhorst, L., Zanolie, K., Van Meel, C.S., Westenberg, P.M., Rombouts, S.A.R.B., Crone, E.A., 2010b. What motivates the adolescent? Brain regions mediating reward sensitivity across adolescence. Cereb. Cortex 20, 61–69, http://dx.doi.org/10.1093/cercor/bhp078.
Vink, M., Derks, J.M., Hoogendam, J.M., Hillegers, M., Kahn, R.S., 2014. Functional differences in emotion processing during adolescence and early adulthood. Neuroimage 91, 70–76, http://dx.doi.org/10.1016/j.neuroimage.2014.01.035.
Voorn, P., Vanderschuren, L.J.M.J., Groenewegen, H.J., Robbins, T.W., Pennartz, C.M.A., 2004. Putting a spin on the dorsal-ventral divide of the striatum. Trends Neurosci. 27, 468–474, http://dx.doi.org/10.1016/j.tins.2004.06.006.
Watanabe, N., Sakagami, M., Haruno, M., 2013. Reward prediction error signal enhanced by striatum-amygdala interaction explains the acceleration of probabilistic reward learning by emotion. J. Neurosci. 33, 4487–4493, http://dx.doi.org/10.1523/JNEUROSCI.3400-12.2013.
Whalen, P.J., Rauch, S.L., Etcoff, N.L., McInerney, S.C., Lee, M.B., Jenike, M.A., 1998. Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. J. Neurosci. 18, 411–418.
Whalen, P.J., Shin, L.M., McInerney, S.C., Fischer, H., Wright, C.I., Rauch, S.L., 2001. A functional MRI study of human amygdala responses to facial expressions of fear versus anger. Emotion 1, 70–83, http://dx.doi.org/10.1037/1528-3542.1.1.70.
Whalen, P.J., Kagan, J., Cook, R.G., Davis, F.C., Kim, H., Polis, S., McLaren, D.G., Somerville, L.H., McLean, A.A., Maxwell, J.S., Johnstone, T., 2004. Human amygdala responsivity to masked fearful eye whites. Science 306, 2061, http://dx.doi.org/10.1126/science.1103617.
Wierenga, L., Langen, M., Ambrosino, S., van Dijk, S., Oranje, B., Durston, S., 2014. Typical development of basal ganglia, hippocampus, amygdala and cerebellum from age 7–24. Neuroimage 96, 67–72, http://dx.doi.org/10.1016/j.neuroimage.2014.03.072.
Wittmann, B.C., 2014. Prior fear conditioning and reward learning interact in fear and reward networks, 1–11. 10.3389/fnbeh.2014.00067/abstract.
Xiang, T., Lohrenz, T., Montague, P.R., 2013. Computational substrates of norms and their violations during social exchange. J. Neurosci. 33, 1099–1108, http://dx.doi.org/10.1523/JNEUROSCI.1642–12.2013.
Yetnikoff, L., Reichard, R.A., Schwartz, Z.M., Parsely, K.P., Zahm, D.S., 2014. Protracted maturation of forebrain afferent connections of the ventral tegmental area in the rat. J. Comp. Neurol. 522, 1031–1047, http://dx.doi.org/10.1002/cne.23459.
Yin, H.H., Knowlton, B.J., Balleine, B.W., 2004. Lesions of dorsolateral striatum preserve outcome expectancy but disrupt habit formation in instrumental learning. Eur. J. Neurosci. 19, 181–189.
Zaborszky, L., Alheid, G.F., Beinfeld, M.C., Eiden, L.E., Heimer, L., Palkovits, M., 1985. Cholecystokinin innervation of the ventral striatum: a morphological and radioimmunological study. Neuroscience 14, 427–453.
Zeanah, C.H., Egger, H.L., Smyke, A.T., Nelson, C.A., Fox, N.A., Marshall, P.J., 2009. Institutional rearing and psychiatric disorders in romanian preschool children. Am. J. Psychiatry 166, 777–785.