A review of childhood maltreatment, latent vulnerability and the brain:

Implications for clinical practice and prevention

Mattia I Gerin[1,2], Elly Hanson, Essi Viding [1] and Eamon J McCrory[1,2]

[1] Division of Psychology and Language Sciences, University College London, London

[2] Anna Freud National Centre for Children and Families, London

Corresponding Author: Eamon J. McCrory, Division of Psychology and Language Sciences, University College London, Gower Street, London WC1 6BT, UK; Email: e.mccrory@ucl.ac.uk

Abstract

There is a well-established association between childhood maltreatment and later poor mental health and increasing recognition that we need to find ways to support children following such experiences to improve long-term outcomes. We suggest that the rationale for such a preventative approach is directly informed by the emerging findings from the field of functional neuroimaging. Here, we review the evidence from four neurocognitive systems: threat processing, reward processing, emotion regulation and executive control. We briefly summarise what is known about each system, review the evidence that altered functioning is implicated in common mental health problems, and describe how the functioning of each system is altered following maltreatment. Across domains, these neurocognitive alterations following child maltreatment are in line with those seen in adults presenting with mental health problems, yet most maltreated children studied do not have a presenting 'disorder'. This suggests that these neurocognitive alterations may potentiate the risk of future psychopathology. We discuss this possibility in the context of the theory of Latent Vulnerability (McCrory & Viding 2015). According to this model, children may respond to early adverse environments in ways that are potentially adaptive in the short term but which create vulnerability to future mental health problems in the long term. We also consider the clinical implications of the neuroimaging evidence - in particular, the growing need for a more preventative clinical approach.

Keywords: Child abuse; maltreatment; mental health; functional magnetic resonance imaging; resilience

Introduction

Childhood maltreatment, including physical, emotional, sexual abuse and neglect, are relatively common forms of adversity. Each year, in high income countries about 1% of children are referred to child protection services (Radford et al., 2011). However, the official rates of substantiated maltreatment seem to be just the tip of the iceberg. Self-reported measures suggest a much larger proportion of individuals experience abuse, neglect or are exposed to domestic violence during childhood (Gilbert et al., 2009; Radford et al., 2011). These negative early life experiences are associated with a wide range of negative outcomes, including reduced economical productivity, educational attainment and physical health (Gilbert et al., 2009). Moreover, recent longitudinal work suggests that childhood maltreatment is one of the most potent predictors of poor mental-health across the lifespan (Vachon et al., 2015; Widom et al., 2007). Population-attributable risk assessments from large cross-cultural studies, which assume the existence of a direct causal link between childhood maltreatment and future psychopathology, estimate that abuse and neglect account for a large proportion of psychological disorders onset during childhood and also adulthood (Green et al., 2010).

Despite the well-established association between childhood maltreatment and increased risk for psychopathology (Gilbert et al., 2009; Vachon et al., 2015), we do not know enough about the neurocognitive mechanisms by which increased vulnerability becomes embedded. Nor do we have a detailed understanding about what factors may promote resilience (Rutter, 2012). We need to better understand how maltreatment alters psychological and neurobiological functioning in ways that increase risk of mental health problems. Equally, we need to understand the intrinsic and extrinsic individual characteristics that can promote a positive outcome despite early adversity. These gaps in our understanding leaves clinicians and professionals that work within child protection services without adequate resources and knowledge that would allow them to identify and provide support for those individuals most likely to develop mental health difficulties in the future (McCrory

et al., 2017). Service provision in the U.K. has been primarily organised around a medical diagnostic model which assumes that individuals with similar clinical presentation are comparable. The evidence suggests that this is not the case (e.g. Nanni et al., 2012). Moreover, the systemic, attachment, social and educational needs of children are often not dealt with holistically alongside symptom presentation. Such an approach has limited the scope for clinicians to develop an understanding of how disorders emerge and unfold across development within complex systems. Although we know a lot about the risk and resilience factors associated with mental health problems, we still have a limited understanding of the *mechanisms* that shape how they develop following childhood maltreatment. In addition, the differences across disciplines have led to the compartmentalization of knowledge. We argue that there is a growing need for researchers, clinicians, parents, foster-carers, children and social workers to work more collaboratively if progress is to be made.

The Theory of Latent Vulnerability

In an effort to shift the focus on prevention and the developmental mechanisms associated with the emergence of mental health problems following childhood maltreatment, McCrory and Viding have proposed the theory of Latent Vulnerability (McCrory et al., 2017; McCrory and Viding, 2015). This theory offers a system-level approach that places emphasis on the neurocognitive mechanisms that link childhood maltreatment to subsequent mental health problems (see Figure 1 for a graphical illustration of the Latent Vulnerability model). According to this account, childhood maltreatment leads to measurable alterations that can be characterised at neurobiological and cognitive levels. These changes can be understood as developmental recalibrations to negative early experiences; in other words, they are not necessarily seen as signs of 'damage'. Rather, such changes may, in many instances, be adaptive within the context of maltreatment and confer short-term functional advantages (for example, faster detection of threat or reduced expectation of reward). However, such alterations are also thought to incur long-term costs (e.g. increased risk of

psychological problem or revictimization) as an individual may not be optimised to cope with the demands of more normative environments, such as school or a stable foster placement. Importantly, maltreatment related patterns of adaptation are understood to be 'latent' as they may appear *before* the emergence of a mental health problems and are not necessarily manifest symptoms or precursors of any future condition.

The theory of Latent Vulnerability focuses on maltreatment-related neurocognitive processes that increase, non-deterministically, the risk of future difficulties. In doing so, it complements a wider research literature demonstrating that a variety of maltreatment-related emotional states (such as shame), self and other representations (such as abuse-related self-blame), and psychological states (such as dissociation) also confer risk for future difficulties (Feiring and Cleland, 2007; Hanson, 2016; Yates et al., 2008). By focussing attention on the maltreatment-related processes and alterations that precede the emergence of more overt difficulties, this framework has the potential to increase the application of research to practice. First, a systematic investigation of the neurocognitive processes associated with increased vulnerability may help inform the development of a screening tool that could be used by frontline practitioners to identify those individuals at most risk of developing later mental health problems. Second, understanding the processes that instantiate increased vulnerability may inform the development of interventions that most effectively help to prevent maltreated children developing subsequent mental health difficulties. Third, this understanding provides a clear rationale for rethinking service design and delivery, with a much greater focus on the prevention of mental health problems.

[Figure 1]

Functional magnetic resonance imaging studies of childhood maltreatment

This review explores changes to neurocognitive processes that may increase risk of mental health problems following maltreatment experience. There is a wide range of methods and

paradigms that have been used to investigate the neurobiological impact of childhood maltreatment. These include the measurement of neuroendocrine stress and inflammatory responses (Coelho et al., 2014), the detection of neuroanatomical changes via Structural Magnetic Resonance Imaging (sMRI) and Diffusion Tensor Imaging (DTI) (Kelly et al., 2015; Puetz et al., 2017), as well as functional brain alterations, using electroencephalography (EEG) (Curtis and Cicchetti, 2013) and Functional Magnetic Resonance Imaging (fMRI) (McCrory et al., 2017). In our view task-based fMRI has the greatest potential to help refine our understanding of the underlying neurocognitive differences in processing that may not be otherwise detectable, with more direct implications for practice (e.g. Gerin et al., 2017; McCrory et al., 2013). Therefore, in order to focus this paper, we will confine our consideration to fMRI findings, reviewing *all* extant fMRI studies of children and adolescents with histories of maltreatment relating to four key areas: threat processing, reward processing, emotion regulation and executive control - we refer readers to McCrory et al (2017) for a more comprehensive review and methodological critique of the literature. To help put these findings into context, we first provide a brief description of each system and then summarise how each has been implicated in common mental health difficulties before considering the evidence from studies of maltreatment or adverse early life experience.

In brief, the studies discussed here support the notion that some individuals with histories of childhood maltreatment, even in the absence of manifest clinical symptoms, may present with changes in brain function across several cognitive, social and emotional domains. These changes are often consistent with neural signature observed in individuals with anxiety, depression and conduct problems (McCrory et al., 2017).

1. Threat Processing

What is threat processing? Survival is dependent on the ability to detect and respond to dangerous and aversive stimuli in the environment. For this reason, it is not surprising that both animal and human studies have revealed that a large amount of cognitive resources and

neurobiological systems are dedicated to threat detection (LeDoux, 2000). Within the central nervous system the amygdala is one of the core structures dedicated to the processing of danger and to the detection of salient information more broadly (LeDoux, 2000). The amygdala is part of an integrated network comprising several cortical and subcortical brain regions involved in fear conditioning, stress responses and salience detention, such as the hippocampus, the striatum, the anterior insula and the dorsal anterior cingulate cortex (ACC) (Shin and Liberzon, 2010).

How is altered threat processing implicated in mental health difficulties? In recent years, neuroimaging findings have shown that alterations in amygdala and anterior insula activation are implicated in several disorders, including posttraumatic stress disorder (PTSD), mood and anxiety disorders (Etkin and Wager, 2007; Kerestes et al., 2014; Patel et al., 2012), drug addiction (Sripada et al., 2011) and conduct problems (Viding et al., 2012). Crucially, recent longitudinal studies of healthy individuals exposed to different kinds of environmental stressors have shown that baseline hyper-responsiveness (i.e. increased responsiveness) to threat in the brain is associated not just with current, but also with future symptoms (Admon et al., 2009, 2013; Swartz et al., 2015).

Functional neuroimaging studies of threat processing in maltreated children and adolescents. Animal studies have established a strong link between early adverse experiences (such as early separation from a caregiver, social isolation, or reduced maternal care and sensitivity) and neurophysiological long lasting alterations in the central and peripheral nervous systems involved in threat processing and stress responses (Caldji et al., 2003; Meaney, 2001; Rosenblum et al., 1994). Behavioural and electrophysiological studies with humans also suggest that abuse and neglect are associated with long lasting alterations in threat processing that can be detected as early as infancy. These changes include heightened electrophysiological responses to negative stimuli, and preferential attention and enhanced perceptual ability for threat cues,

such as angry or fearful faces (Curtis and Cicchetti, 2013; Pollak et al., 2005; Pollak and Sinha, 2002).

These behavioural and neurophysiological findings have been extended by a series of recent functional magnetic resonance imaging (fMRI) studies with children and adolescents. These have found a pattern of increased neural response during the processing of threat cues (e.g. angry faces) in the amygdala, and other subcortical neighbouring regions, such as the anterior insula and hippocampus (Maheu et al., 2010; McCrory et al., 2011, 2013; Tottenham et al., 2011). Such neural alterations seem to be shared across individuals with different experiences of early adversity, ranging from severe institutional neglect (Maheu et al., 2010; Tottenham et al., 2011), substantiated maltreatment in community settings (McCrory et al., 2011, 2013) and also less severe experiences of neglect (White et al., 2012). Importantly, by using well matched control groups, these studies suggest that increased threat-related neural responses among maltreated children and adolescents is independent from potentially confounding factors, such as IQ, socioeconomic status, pubertal status and concurrent psychopathology (e.g. Maheu et al., 2010; McCrory et al., 2013). Moreover, by showing that both amygdala and insula hyperactivity have a dose-dependent relationship with the severity / duration of maltreatment (Maheu et al., 2010; McCrory et al., 2011, 2013), these findings point to a pattern of neural calibration directly related to the degree of early adversity. Finally, it is worth noting that a similar pattern of findings comes from studies with adults with a history of childhood maltreatment, suggesting that abuse and neglect can have a long-lasting impact on the threat-processing system (e.g. Dannlowski et al., 2012).

Summary. It has been shown that different forms of early adversity alter the neural reactivity of the threat system, especially amygdala activation, even in children and adolescents who are not presenting with overt psychiatric symptomatology. Crucially, this association seems to be directly related to the severity of maltreatment (Maheu et al., 2010; McCrory et al., 2011;

White et al., 2012). Interestingly, similar findings have been reported in adults who experienced maltreatment during childhood (see Hein & Monk, 2016), suggesting that such alterations can be long lasting. Given that hyper-responsiveness of the amygdala and anterior insula have been associated with several psychiatric conditions, including depression, anxiety and PTSD, it is possible that altered threat processing may increase the risk of future mental health problems. However, longitudinal studies are required to confirm this hypothesis. Ways in which this risk might become instantiated are discussed in the clinical implications section below.

2. Reward Processing

What is reward processing? Learning which stimuli and actions are associated with attaining rewarding objects, experiences or events is essential to motivate and guide adaptive decision-making and behaviour. The main network underpinning the processing of reward is the mesocorticolimbic dopaminergic neural pathway. This includes brain-stem regions, such as the ventral tegmental area, which project to basal ganglia nuclei, especially the striatum, and terminate in prefrontal regions, including the orbitofrontal cortex (Clithero and Rangel, 2013; O'Doherty, 2011).

How is altered reward processing implicated in mental health difficulties? Neural alterations in the reward system have been associated with suboptimal decision-making and psychological distress, such as the emergence and maintenance of anxiety, mood, conduct and substance abuse disorders (Balodis and Potenza, 2015; Stringaris et al., 2015; White et al., 2013; Zhang et al., 2013). For example, neuroimaging findings show a consistent pattern of reduced activation in the striatum during reward processing among depressed individuals (Forbes and Dahl, 2012; Pizzagalli et al., 2009; Ubl et al., 2015). Interestingly, this predicts not only current but also future clinical status and symptoms level (Morgan et al., 2013; Telzer et al., 2014), even in those who were previously "healthy" (Stringaris et al., 2015). Neuroimaging studies suggest that this pattern of blunted neural activation may be associated with difficulties in computing reward anticipation and detecting

differences between expected and actual rewards (prediction-error signalling). In the context of depression, this might entail reduced sensitivity to rewards and limited motivational response (i.e. anhedonia) (Gotlib et al., 2010; Stringaris et al., 2015; Ubl et al., 2015); in the context of conduct disorder, this may suggest difficulties in integrating and updating reward (and punishment) information (White et al., 2013, 2016).

Functional neuroimaging studies of reward processing in maltreated children and adolescents. Researchers have been motivated to investigate reward processing in maltreated individuals for two reasons. First, the clinical literature described above suggests that altered reward processing may be associated not just with current symptoms, but also with the development of mental health problems. Secondly, we know that the familial environment experienced by maltreated children is often characterised by the erratic and infrequent availability of rewards. To date most neuroimaging studies of maltreatment have found reduced activation during reward processing, especially in the striatum and the orbitofrontal cortex (McCrory et al., 2017). This pattern of findings has been found both in individuals who have experienced extreme forms of institutional deprivation (Goff et al., 2013; Mehta et al., 2010) or maltreatment in community settings, especially neglect (Gerin et al., 2017; Hanson et al., 2015). Notably, this pattern of findings remains even after controlling for the presence of overt psychological disorders or symptoms severity for conditions commonly associated with blunted reward-related neural response, such as depression (e.g. Gerin et al 2017). Dennison et al., (2016) did not find this effect but nevertheless found that higher neural response to reward was linked to better future mental health outcomes. Overall these findings suggest that increased / decreased activation in the striatum may represent a marker of resilience / risk to psychopathology. In particular, the pattern of lower neural response in maltreated individuals may reflect neural calibration to reduced opportunities for reward-based learning. Such alterations may represent an adaptive regulatory mechanism which reduces disappointment in the context of inconsistent and insensitive parenting (McCrory et al., 2017). However, these neurocognitive alterations may also hamper functioning in more normative

situations. For example, they may hinder exploratory behaviour, thus decreasing the opportunities for learning and for motivating the search of alternative sources of reward outside the home environment.

Summary. Overall, these findings suggest that maltreatment - especially neglect and institutional deprivation - is associated with a blunted neural response to reward cues in the orbito-striatal network. This neural profile, which may be shaped by familial environments characterised by erratic and infrequent availability of rewards, is also known to be associated with common mental health problems, particularly depression and conduct disorder. Therefore, alterations in reward processing following maltreatment may represent a potential neurocognitive vulnerability to mental health difficulties. Initial longitudinal evidence also suggests that higher levels of neural response in this network may be a marker of *resilience* to future psychopathology.

3. Emotion Regulation

What is emotion regulation? The ability to regulate affect entails the modification of an emotion by producing changes to its intensity, duration or valence (Eisenberg and Spinrad, 2004; Ochsner et al., 2012). Various strategies can be used for emotion regulation, such as emotional distancing, suppression, social support, reappraisal and attention modulation, just to mention a few (Koenigsberg et al., 2010; Ochsner et al., 2012). Crucially, such processes may involve explicit effort or occur implicitly and outside conscious awareness (Gyurak et al., 2011). A large neural network is linked to affect regulation. Broadly speaking, prefrontal regions are understood to have top-down regulatory control over regions implicated in emotional reactivity, impulsivity and negative affect, such as the amygdala, insula, striatum and the dorsal anterior cingulate cortex (dACC) (Etkin et al., 2015; Ochsner et al., 2012). In particular, the ventral anterior cingulate cortex (vACC) and medial prefrontal cortex (mPFC) seem to be more involved in the implicit and automatic regulation of affect, while latero-prefrontal (lPFC) and also latero-parietal (lPC) cortices seem to be necessary for more explicit and volitional forms of emotion regulation (Etkin et al., 2015).

How is altered emotion regulation implicated in mental health disorders? Many psychological difficulties involve altered affect regulation (e.g. anxiety, conduct disorder and depression) (Aldao et al., 2010; Mennin et al., 2007). Moreover, difficulties in emotion regulation have been shown to represent a risk factor for developing mental health problems in the future among those individuals who have suffered early adversity (Kim-spoon et al., 2013; Kim and Cicchetti, 2010) and/or who do not present with current clinical symptoms (Folk et al., 2014; Michl et al., 2013; Wirtz et al., 2014).

Functional neuroimaging studies of emotion regulation in children and adolescents exposed to maltreatment. Three studies of functional *connectivity* have reported that maltreated children and adolescents present with atypical connectivity between regulatory frontal regions (such as vACC and mPFC) and subcortical brain areas, such as the amygdala (Gee et al., 2013; Lee et al., 2015; Marusak et al., 2015). In addition, five studies that investigated *focal* brain activity have also reported alterations in the same frontal regulatory network, including the mPFC, vACC, dACC and also the lPFC (Elsey et al., 2015; Marusak et al., 2015; McLaughlin et al., 2015; Puetz et al., 2014, 2016). However, despite the fact that these studies have reported altered functioning in a consistent set of brain regions during emotion regulation, the direction of these alterations has been inconsistent (i.e. increased vs. decreased activity and stronger vs. weaker connectivity). These discrepancies are not entirely unexpected given the spectrum of participants recruited in these studies. Participants varied in terms of developmental stage and type of early adversity (e.g. physical abuse, verbal abuse, institutionalisation, neglect in community settings, etc.). Moreover, different emotion regulation paradigms were implemented, with some requiring simple or automatic emotional processing and others requiring more explicit and higher order regulatory demands. It has been suggested that these different task demands may be helpful in understanding the differences across studies (McCrory et al., 2017). When a task explicitly requires participants to attend to aversive stimuli or to consciously modulate affective responses (Elsey et al., 2015; McLaughlin et al., 2015) one tends to see a pattern of *increased activation* in

regulatory frontal regions in maltreated individuals that may reflect increased effort. On the other hand, on those tasks where it is possible to shift attention away from the processing of aversive stimuli, maltreated individuals show a pattern of *reduced activation* and connectivity (Gee et al., 2013; Lee et al., 2015; Puetz et al., 2014, 2016). This pattern of hypo-activation is consistent with the use of avoidant and dissociative regulatory strategies (McCrory et al., 2017) that can often be unhelpful in the longer term and are associated with increased risk of anxiety, depression, self-harm and PTSD (Kaplow et al., 2005; Karstoft et al., 2015; Wirtz et al., 2014; Yates et al., 2008).

Summary. Overall, the neuroimaging studies of emotion regulation in maltreated children and adolescents suggest that the network traditionally involved in self-regulatory processes shows a pattern of atypical focal activation and connectivity. Medial frontal regions (e.g. vACC and mPFC) and the lPFC seem to be particularly implicated, as well as the frontolimbic neural network (e.g. amygdala-vACC connectivity). Taken together with the neuroimaging studies of mental health disorders, these findings suggest that emotion regulation processing changes may confer risk. However, longitudinal studies are still required to test this hypothesis directly. The heterogeneity in the neurocognitive findings to date probably reflects differences in the type and timing of early adversity, and the specific computations (simply put, explicit vs. implicit) engaged during different emotion regulation tasks.

4. Executive Control

What is executive control? Executive control broadly refers to three interrelated cognitive functions: inhibiting (the ability to constrain automatic and dominant responses irrelevant to a given goal), updating (the ability to maintain, monitor and quickly add/delete information), and shifting (the ability to flexibly switch between different tasks) (Miyake et al., 2000). These functions are important for adaptive behaviour and effective decision-making. Neuroimaging studies have found that these functions are underpinned by a central executive network, whose central nodes include

the dorsolateral prefrontal cortex (dlPFC) and posterior parietal cortex. Brain areas engaged during error monitoring, such as the dACC and mid cingulate cortex (MCC), are also involved in executive control functions.

How is altered executive control implicated in mental health difficulties? Cross-sectional and longitudinal evidence suggests that alterations in executive control may be involved in the development of depression, anxiety, conduct problems, ADHD and PTSD (Cortese et al., 2012; Evans et al., 2015; Parslow and Jorm, 2007; Snyder, Kaiser, et al., 2015). The association between atypical executive control and mental health problems may (for example) be mediated by alterations in several cognitive, emotional and social processes which rely upon executive functions, such as suppression of ruminative thinking, problem solving and regulation of affect (Snyder, Miyake, et al., 2015).

Functional neuroimaging studies of executive control in maltreated children and adolescents. Two studies have found that exposure to early adversity is associated with increased activation during tasks requiring executive functions (such as error processing, cognitive shifting and inhibition) in brain areas linked with executive control, including the dACC/MCC and lateral frontal regions (Lim et al., 2015; Mueller et al., 2010). This increased activation may reflect decreased neural efficiency and increased effort to attain the same performance as their non-maltreated peers. Notably, these findings are in line with the neuroimaging clinical literature of several disorders associated with maltreatment, such as anxiety (Basten et al., 2011), depression (Harvey et al., 2005) and ADHD (Cortese et al., 2012),

Summary. To date, two fMRI studies have investigated executive control in maltreated youth (Lim et al., 2015; Mueller et al., 2010). Both studies identified a pattern of increased brain activation in regions involved in executive functions such as inhibition and performance monitoring/updating, including the dACC/MCC and the fronto-lateral cortex. These findings, in conjunction with the clinical neuroimaging literature suggest that neurocognitive alterations in

executive control may increase the risk of mental health problems. However, a recent study by Danese and colleagues (Danese et al., 2017) suggests that we should be cautious in assuming a causal link between maltreatment experience and alterations in executive function, as these may instead result from the socioeconomic and genetic factors that commonly co-occur with maltreatment. Indeed, similar limitations may apply to the other neurocognitive domains of interests. However, to the best of our knowledge, this has not yet been investigated in population-representative birth cohort samples.

Conclusions: Clinical Implications

The functional neuroimaging literature suggests that the experience of abuse and neglect can influence the development of specific aspects of cognitive and affective functioning, which may increase vulnerability to future mental health problems. However, there are still common methodological shortcomings that characterise the neuroimaging literature of maltreatment that need to be addressed in future research if stronger causal inferences are to be made. Some of the most common limitations include small sample sizes, the lack of prospective/longitudinal designs and the conflation of severe maltreatment experience with adversity in the normal range. Moreover, it is essential that future studies aim to control for relevant confounding variables, such as IQ, pubertal status, age, gender, socio-economic status and the presence of a frank mental health disorders, which are known to co-occur with the experience of maltreatment - see McCrory et al (2017) for a more comprehensive critique of these methodological concerns. Despite these limitations, the emerging pattern of findings reviewed here complement and extend those from wider psychological research, indicating for example, increased hypervigilance and compromised emotion regulation skills in maltreated children (Curtis and Cicchetti, 2013; Kim-spoon et al., 2013; Romens and Pollak, 2012)

From a clinical perspective, two aspects of the findings we have reviewed merit particular attention. First, maltreatment-related changes resemble the neurocognitive profile associated

with mental health disorders commonly associated with maltreatment, such as anxiety and depression. Second, these alterations are already present before a *manifest* clinical disorder. As such, they can be considered markers of *latent* psychiatric vulnerability since they may have prognostic value, but do not reflect *overt* symptomatology. Another important implication emerging from these findings is that, despite the link with mental health problems, these neurocognitive changes should not be readily interpreted as a sign of 'damage'. Rather, in line with the theory of Latent Vulnerability (McCrory et al., 2017; McCrory and Viding, 2015), they may in many instances be understood as the outcome of a complex set of adaptive processes which may confer short-term advantages for the child in the context of abusive and neglectful environments. However, they may equally incur long-term costs as an individual may not be equipped to deal with more normative challenges.

The neurobiological and psychological alterations which can follow experiences of maltreatment can be understood to increase mental health risk, particularly following exposure to future stressors, in both direct and indirect ways (McCrory et al., 2017). Alterations in the way we process our internal and external worlds can have immediate repercussions: this can be understood as the direct effects of latent vulnerability. An example is the established pattern of hypervigilance to threat cues. While helpful to the child in a chaotic or dangerous home environment, such a response may curtail attentional resources available for the processing of other potentially helpful environmental cues, limiting the opportunities for learning and developing other cognitive and affective functions. Heightened response of the threat system may also lead to increased stress reactivity and experience of negative emotions – in other words, it serves to potentiate the negative impact of new stressor experiences. In this way, adaptation of the threat system may have 'real-time' implications for how the child negotiates their experience inside and outside the home.

In parallel, there are likely to be indirect effects that over time can compromise psychological and social functioning. Alterations of the threat system may undermine a child's ability to develop positive peer friendships and social support networks which may help buffer their experience of future stressors. It may also lead them to act in ways that increase the likelihood of future stressor exposure, for example, because of relationship breakdown or exclusion from school. This may unfold because heightened threat reactivity serves to increase the likelihood of misinterpreting ambiguous cues, and over-responding to negative cues in ways that lead to more conflictual interactions. Equally, avoidance of threat or aversive cues (both internal and external) via dissociation and cognitive and behavioural strategies, whilst reducing distress in the short-term, may impair the development of important skills, such as the effective detection of threat, in the longer term (e.g. DePrince, 2005).

When and how to intervene?

Currently (notwithstanding some exceptions), statutory interventions happen mainly at two stages. Once the maltreatment has been substantiated, professionals seeks to ensure safety and the stability of the child's placement. Then, if an individual meets clinical criteria for a mental health problem, they may be offered treatment from mental health services. However, extant neuroimaging findings are beginning to show that neuro-cognitive vulnerabilities are present *before* manifest behavioural symptoms emerge. These findings, alongside those indicating a variety of other psychological mediators between maltreatment and mental health difficulty, provide the motivation and the rationale to pursue a preventative care approach. In other words, help could be provided proximate to the detection of maltreatment experience to those most at risk of a worsening mental health trajectory.

Therefore, the natural next step would be to seek to develop a psychometric tool designed to screen for latent vulnerability that could help as part of a formal assessment process, identify those children at most risk for later poor outcome. However, the degree to which the extant

neuroscience findings can shed light on models of prevention and intervention is much less clear; our view is that the field has not matured to this point. Rather, in the medium term we would hope that systematic neurocognitive research could help identify specific mechanisms that could be targeted in treatment. Further work is required, particularly within a longitudinal framework, in order to investigate the degree to which alterations of the systems reviewed here are implicated in the pathways to overt mental health problems and furthermore, whether they are amenable to change. Such targeted mechanistic approaches are necessary given that 'treatments as usual' (Nanni et al., 2012) and general parental caring (Rothman and Silverman, 2007) may not be enough to prevent and ameliorate symptoms among individuals who have suffered early abuse and neglect. If we are able to accurately delineate which neurocognitive systems are altered following maltreatment, an important next question is how to promote adaptive change in these systems or compensatory protective neurocognitive functions which can foster resilience (McCrory et al., 2017).

Future studies should systematically investigate the impact of a variety of positive relationships (involving peers, carers and others) and what factors promote the child's ability to learn from these (Toth et al, 2013). Positive, predictable and safe relationships may help shift the child's expectations of other people and build a foundation of trust. Repeated interactions within such relationships might create the conditions that could facilitate recalibration of the threat and reward processing systems. Alternatively, such relationships could foster development of compensatory strategies that counteract the affective processing biases. However, engaging in a positive, warm, consistent and constructive way with children who have experienced maltreatment can be challenging to their carers. If a child is hypervigilant to threat, less sensitive to reward, and has fewer emotion regulation and executive functioning skills, this can often evoke negative feelings and a sense of inadequacy in those who are trying to meet their needs. We argue that a more comprehensive understanding of the neurocognitive impact of maltreatment can help clinicians and carers to reframe the child's behaviour and develop strategies that are helpful in 'unhooking' them from maladaptive patterns of interaction. Building positive peer cultures and harnessing the

potential of digital technology are also important areas for future research and innovation. In relation to technology, certain apps can support self-reflection and emotion regulation, and can enable connections with supportive peers and others - this being especially useful if young people are experiencing isolation or ostracism elsewhere (McGeeney and Hanson, 2017).

One key factor that may be important in fostering recalibration of the neurocognitive systems impacted by maltreatment through relational experiences is the development of *epistemic trust.* This is the ability to use others to acquire new knowledge about the internal and external world – a capacity that has typically been compromised during maltreatment (i.e. the child comes to mistrust information from adults, closing down the ability to learn from others and the cultural world) (Fonagy and Allison, 2014). Children and adults privilege information from a trusted person in guiding their everyday interactions with others and participation in life. In other words, a foundation of epistemic trust with a caregiver can help promote positive interactions that facilitate the acquisition of new knowledge. In developing such carer- and peer-group approaches, it may be useful to draw on the knowledge surrounding a variety of evidence-based interpersonally focused therapies that apply an understanding of epistemic trust (Toth et al., 2013).

There are also other promising approaches that more directly target some of the neurocognitive alterations reviewed in this paper. For example, DePrince et al (2015) found that a 12 session 'risk detection/executive functioning' group intervention with maltreated adolescents, which included teaching mindfulness, problem-solving and accurate threat detection, led to nearly 5-fold decrease in reports of sexual victimization in the following six months. It will be important to establish what precise neurocognitive mechanisms underpinned the improved outcome for the maltreated adolescents with this approach. More broadly, it may be fruitful to review techniques and approaches that have been developed in the context of treatment for manifest disorders and consider how these might be adopted or incorporated within a preventative model designed to enhance resilience. Dialectical Behavioural Therapy (DBT) for example, comprises a number of

elements addressing emotion regulation, tolerating distress and improving interpersonal skills that may be extremely useful to consider.

As a final note, the ethical implications of any preventative strategy must be carefully considered in order to minimize risk of stigmatization. How will deviation from normative development be explained and understood? How will individuals (who have been exposed to abuse and neglect) be screened? And how will they be engaged as active partners in any process of seeking and receiving support or help? Should this help be framed as promoting a resilient outcome? These, and other important issues, will require collaborative engagement with the young people and their families as active participants and careful consideration by professionals. In our view, such a collaborative approach has a greater chance of not only being more ethically grounded, but also of having greater efficacy in enabling and promoting agency and empowerment.

In summary, the acquisition of specific knowledge regarding neurocognitive processes impacted by early adverse experiences can help us understand how children who have been maltreated see the world around them and why they are often more vulnerable to developing mental health problems. In the longer term this knowledge can inform the development of both a screening tool to identify those at most high risk and preventative approaches that effectively promote resilience and increase the likelihood of positive outcomes following childhood maltreatment.

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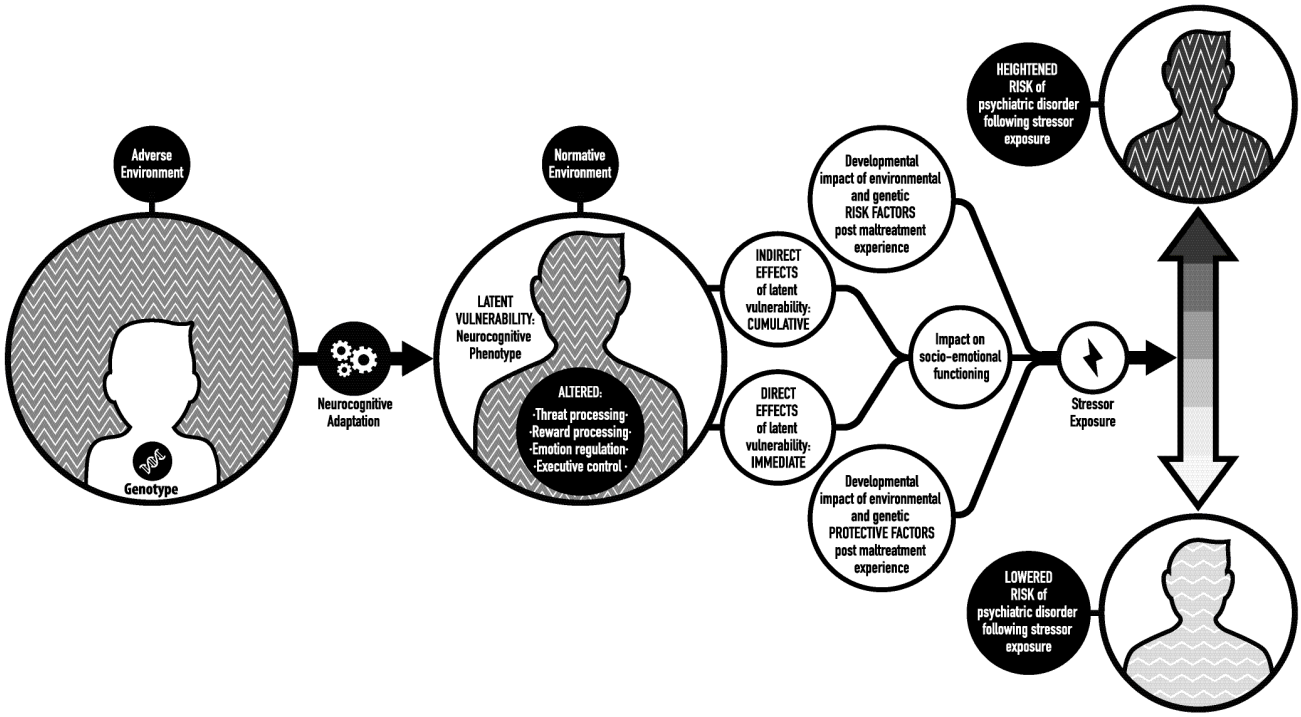

Figure 1. A schematic illustration - taken from McCrory et al (2017) - depicting how latent vulnerability can become instantiated at the neurocognitive level with both direct and indirect effects on socio-emotional functioning. Differential outcomes are shown in relation to mental health risk and resilience depending on protective factors, stressor exposure and genotype.