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Corresponding Author:	Eamon McCrory, PhD University College London London, UNITED KINGDOM
Order of Authors:	Eamon McCrory, PhD

Investigating the neurocognitive mechanisms that influence how mental health risk can unfold following maltreatment.

Eamon J. McCrory[1,2]

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

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

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Address correspondence to Eamon J. McCrory, Division of Psychology and Language Sciences, University College London, Gower Street, London WC1 6BT, UK; Email: e.mccrory@ucl.ac.uk; Telephone: 02034567890

When working clinically with adolescents who have experienced severe maltreatment, the complexity of each case is invariably striking. No two individuals are the same. Developmental histories are characterized by intricate sequences of risk events, reflecting multiple forms of adversity. Fortunately many affected individuals also typically experience a range of protective influences, particularly in the form of supportive relationships, which serve to buffer the deleterious impact of adversity. A decade ago, it was not at all clear how useful functional neuroimaging would be in helping us understand the basis for the now widely recognized relationship between maltreatment experience and life-long mental health risk. As an early career researcher, I remember clearly the scepticism of some of my more seasoned colleagues about the feasibility of such an endeavour. The population was simply too heterogeneous and the phenomenon too complex: systematic and meaningful research was not really thought to be tenable. However, my clinical experience forced me to challenge this assumption. It was obvious from the developmental history of each individual that the pattern of severe behavioural and emotional problems had not emerged overnight: difficulties had unfolded over time. There were indications of vulnerability and periods of opportunity that had been missed. In other words, it seemed to me that we were failing these children by waiting until full-blown psychiatric disorders had emerged before help was offered.

A decade later the prism through which we understand this complex puzzle has shifted. Arguably neurocognitive research has made three useful contributions. First, there is now evidence that maltreatment is associated with altered functioning in a range of neurocognitive systems including threat processing, reward processing, emotion regulation,

autobiographical memory and executive control (1). These studies, although preliminary in nature, have begun to demonstrate the feasibility of characterizing the specific ways in which a child, following maltreatment exposure, begins to process the internal and external world differently. Second, the nature of these alterations has led a number of researchers to consider the adaptive value of these neurocognitive changes. Mental health risk is postulated to arise from the fact that these adaptations, while helpful at one time in the early atypical home environment, are poorly optimized to negotiate more normative environments. Third, such neurocognitive changes are observable even in the absence of psychiatric disorder and have been shown, in some cases, to predict future symptomatology (2). Moreover, observed changes in neural reactivity are often highly consistent with those seen in individuals presenting with psychiatric disorder. This suggests that neuroimaging has the potential to shed light on the mechanisms implicated in the *pathogenesis* of psychiatric disorder. Collectively, these insights have informed the framework of latent vulnerability (3). This theory offers a system-level approach that places emphasis on the neurocognitive mechanisms that can help us understand how childhood maltreatment and subsequent mental health problems are linked.

Altered threat processing (and poorer emotional regulation more broadly) has emerged as one neurocognitive mechanism that may provide proximal benefits for a child in an early chaotic or violent home environment, but which over time increases the likelihood of internalising and externalising problems. Animal studies have established a strong link between early adverse experiences and alterations in the central and peripheral nervous systems involved in threat processing and stress responses (4). Studies with humans have also indicated heightened electrophysiological responses to negative stimuli, and

preferential attention and enhanced perceptual ability for threat cues, such as angry or fearful faces, in children with maltreatment experiences (5). These behavioural and neurophysiological findings have been complemented by a series of recent functional magnetic resonance imaging (fMRI) studies with children, adolescents and adults who had experienced maltreatment or institutionalization. These fMRI studies have reported increased neural response in the amygdala during the processing of threat cues.[1] Relatedly, other studies have reported atypical activation of regulatory frontal regions in maltreated individuals (6).

In the current issue of Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, Kim et al. (7) investigate the functional significance of these alterations by examining the neural response to threat cues and childhood maltreatment in relation to trait anger. Trait anger refers to the dispositional tendency to find many different situations annoying or frustrating, leading to a low threshold for feeling angry. High levels of trait anger are associated with increased reactive aggression and violence, outcomes also associated with maltreatment. At the same time, we know that maltreatment has been linked to both increased trait anger and increased risk of externalizing problems. Furthermore, a pattern of higher amygdala activity and reduced engagement of prefrontal executive regions to threat-related cues is found in both those with high trait anxiety, and those with maltreatment experience. However, how these two neural circuits jointly modulate the link between childhood adversity and trait anger has not previously been examined. Kim and colleagues therefore set out to investigate if individual differences in threat-related amygdala and executive control-related dlPFC activity modulated the expression of trait anger as a function of childhood adversity. They found that the association between childhood

adversity and later trait anger was moderated by the individual differences in bottom-up threat and top-down executive control activity of the amygdala and dlPFC, respectively. Specifically, the combination of lower amygdala and higher dlPFC activity attenuated the relationship between childhood adversity and trait anger. The authors suggest that this may reflect the possibility that this neural activation pattern 'buffers' individuals against the impact of childhood adversity on trait anger. This raises the important question as to why some people present with this apparently more adaptive pattern following adversity. Kim and colleagues acknowledge however, that such individuals may have had a distinct kind of adverse experience (for example, developmental timing of exposure may have differed). A related possibility is that these individuals benefited from the influence of one or more supportive relationships that helped to promote the formation of stable emotion regulation circuits (8).

By focussing on trait anger, this study investigates an important factor that may mediate the relationship between early adversity and increased mental health risk. While the cross-sectional nature of this study constrains the inferences that can be drawn, it provides an important catalyst for future research into latent vulnerability. For example, we know that maltreatment is associated with increased risk of stressful life events across the lifespan (9) and that stress exposure is in turn associated with increased symptomatology (10). High trait anger may represent one factor that increases risk of 'stress generation' following maltreatment: that is, higher levels of this trait may increase the likelihood of the occurrence of stressor events, such as interpersonal conflict. In other words, neurocognitive changes would increase the likelihood of higher stress exposure that would *in turn* increase mental health risk. An alternative is that high trait anger proceeds an increase in an

individual's susceptibility to stress. Consider for example how neurocognitive changes associated with maltreatment may cumulatively, over time, attenuate an individual's supportive social network because of a reduced capacity to elicit, cultivate and sustain close relationships (1). It is not difficult to imagine how a disposition of high trait anger would make it harder for an individual to build stable social relationships that would be protective in buffering them against future stress. Longitudinal designs are required to test these putative effects of high trait anger on stress generation and susceptibility.

In this issue, Kim et al. (7) demonstrate how neuroimaging can indeed help specify a neurocognitive model of vulnerability following maltreatment, by investigating the relationship between multiple neural circuits and an important dispositional trait. This study, among others, brings us another step closer to understanding why early adversity is so strongly associated with later poor mental (or indeed physical) health. Although progress is incremental, a neuro-cognitively and developmentally informed mechanistic model is essential if we are to develop the targeted forms of help capable of reducing mental health risk following maltreatment. For clinicians and policy makers alike this would help drive an important shift towards preventative help, reducing the individual and societal costs of treating complex difficulties once they have already become entrenched.

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Disclosures

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