

The Neuropsychopharmacology of Syndrome E

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ABSTRACT

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Syndrome ‘E’ comprises a set of symptoms, at least some of which can be related to aspects of anti-social behaviour, as defined by DSM5, as well as some of its constituents such as conduct disorder or psychopathy. Some of the component symptoms of Syndrome E resemble those acquired through lesions of the ventromedial or lateral orbitofrontal cortex or via pharmacological agents affecting dopamine function known to be abused by terrorist groups, such as methamphetamine and Caprogan (CCT or fenethylamine). Thus frontal lobe damage can lead to a pseudo-psychopathic syndrome in the absence of gross cognitive deficit, including enhanced reactive aggression and reduced empathy which can

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readily be interpreted as a form of ‘top-down’ loss of executive control over subcortical systems including the amygdala, hypothalamus and brainstem.

Moreover, chronic methamphetamine has been shown to lead to alexithymia, a dysfunction in emotional awareness, social attachment, and interpersonal relations, as well as enhanced reactive aggression. Methamphetamine abuse also leads to serotonin depletion, especially in the orbitofrontal cortex which is associated in humans and other animals with reduced harm aversion (in tests of social cognition) and impaired responses to punishment and inflexibility of responding when reward and punishment contingencies change (as in reversal learning). Exposure to stress in otherwise healthy animals has been shown to exaggerate some of these effects and this may be relevant to the human situation.

Whilst it would appear therefore that we have the beginnings of a neural account of symptoms of Syndrome ‘E’, there are in fact many issues that require debate and resolution by appropriate experimentation: (i) if its symptoms can be indeed related to these neural and neurochemical changes (ii) if the changes in the brain are causes or effects of the symptoms (iii) consideration of whether an approach based on Research Domain Criteria might be more useful to define Syndrome ‘E’ than DSM-type categorical diagnosis (iv) alternative conceptualizations of how the prefrontal cortex controls behaviour, which include imbalance and competition between different frontal circuits, for example mediating rule governed and social behaviour, or goal-directed versus habitual responding; and (v) enhanced scientific understanding of how the formation of ideological beliefs and their representation in the brain interact with neural systems controlling social behaviour and rational cognition, and to what extent neuro behavioural endophenotypes and environmental circumstances may enhance such vulnerability.

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