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Severe stress switches CRF action in the nucleus accumbens from appetitive to aversive.

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Source

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Abstract

Stressors motivate an array of adaptive responses ranging from 'fight or flight' to an internal urgency signal facilitating long-term goals. However, traumatic or chronic uncontrollable stress promotes the onset of major depressive disorder, in which acute stressors lose their motivational properties and are perceived as insurmountable impediments. Consequently, stress-induced depression is a debilitating human condition characterized by an affective shift from engagement of the environment to withdrawal. An emerging neurobiological substrate of depression and associated pathology is the nucleus accumbens, a region with the capacity to mediate a diverse range of stress responses by interfacing limbic, cognitive and motor circuitry. Here we report that corticotropin-releasing factor (CRF), a neuropeptide released in response to acute stressors and other arousing environmental stimuli, acts in the nucleus accumbens of naive mice to increase dopamine release through coactivation of the receptors CRFR1 and CRFR2. Remarkably, severe-stress exposure completely abolished this effect without recovery for at least 90 days. This loss of CRF's capacity to regulate dopamine release in the nucleus accumbens is accompanied by a switch in the reaction to CRF from appetitive to aversive, indicating a diametric change in the emotional response to acute stressors. Thus, the current findings offer a biological substrate for the switch in affect which is central to stress-induced depressive disorders.

Comment in

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