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W114. Adolescent Anhedonia Following Early-Life Adversity Involves Aberrant Interaction of Reward and Anxiety Circuits and is Reversed by Knockdown of Amygdala Corticotropin-Releasing Hormone

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Background: Anhedonia, the diminished ability to experience pleasure, is an important dimensional entity linked to depression, schizophrenia and other emotional disorders, but its origins and mechanisms are poorly understood. We have previously identified anhedonia, manifest as decreased sucrose preference and social play, in adolescent male rats that had experienced early-life adversity as a result of fragmented unpredictable sensory signals from maternal care (FRAG). Here we probed the molecular, cellular and circuit processes underlying FRAG-induced anhedonia and tested them mechanistically.  

Methods: We examined functional brain circuits and neuronal populations activated by social play in adolescent FRAG and control rats. Structural connectivity between stress- and reward-related networks was probed using high-resolution diffusion tensor imaging (DTI), and cellular/ regional activation was probed using cFos. We employed viral-genetic approaches to reduce corticotropin-releasing hormone (CRH) expression in amygdalar central nucleus (ACe) in anhedonic rats, and tested for anhedonia reversal in the same animals.  

Results: Sucrose preference was reduced in adolescent FRAG rats (F[1,21] = 8.85, p < 0.01). Social play, generally considered an independent measure of pleasure, activated brain regions involved in reward circuitry in both control and FRAG groups. Compared with controls, social play in the FRAG group activated three times as many CRH-expressing neurons in ACe, a nucleus typically involved in anxiety/fear, indicating aberrant functional connectivity of pleasure/reward and fear circuits (t(7) = 2.45, p < 0.05). DTI-tractography revealed increased structural connectivity of amygdala to medial prefrontal cortex in FRAG rats (t(13) = 2.29, p < 0.05). CRH-shRNA, but not control shRNA, given into ACe reversed FRAG-induced anhedonia (interaction: F[1,17] = 10.42, p < 0.005) without influencing other emotional measures.  

Conclusions: These findings robustly demonstrate aberrant interactions of reward and fear/anxiety networks after chaotic (high-entropy) early-life experience, and suggest mechanistic roles for CRH-expressing amygdala neurons in emotional deficits portending major neuro-psychiatric disorders. Supported by P50 MH096889; NS28912.  

NOTE: this poster is linked to Risbrough et al., a poster focusing on how anhedonia predicts PTSD. Please view poster M22, Poster Session I.  

Keywords: Anhedonia, Reward Circuitry, Amygdala, Corticotropin-Releasing Hormone, shRNA  

Disclosure: Nothing to Disclose.