

THE NEURAL BASES OF EMOTION, MEMORY, AND DEPRESSION

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The orbitofrontal cortex is the key brain region in emotion and reward value-based decision-making in primates including humans (Rolls, 2019). Evidence for this, including its connectivity, neurophysiology, and functional neuroimaging will be described. The medial orbitofrontal cortex represents many rewards, and the lateral orbitofrontal cortex non-reward (not receiving an expected reward) and punishers. In a new theory of depression, it is proposed that cortical attractor networks in the lateral orbitofrontal cortex, where not receiving expected rewards is represented, are over-responsive or over-connected (Rolls 2016, 2017, 2018). Supporting evidence based on functional connectivity in more than 600 participants with depression and controls is described. Functional connectivity (measured by correlations with resting-state fMRI) of the lateral orbitofrontal cortex (OFC) was increased in depression with the temporal lobe cortex (which provides inputs to the OFC); the angular gyrus (involved in language and providing a long loop for rumination); and the precuneus and posterior cingulate cortex (involved in the sense of self and low self-esteem in depression). The lateral OFC non-reward system has increased functional connectivity with the parahippocampal gyrus and medial temporal lobe memory system, which is believed to increase sad memories in depression. The medial OFC has reduced functional connectivity with the medial temporal lobe memory system in depression, contributing it is believed to fewer happy memories in depression. In an activation study with 1140 participants, it was found that those at high risk of depression have greater activation in the lateral OFC to not winning in the monetary incentive delay task, and that the medial orbitofrontal cortex is relatively insensitive to differences in reward value. This evidence that the non-reward lateral OFC is over-connected and over-responsive to non-reward in depression, and the medial OFC is under-connected and under-sensitive to reward in depression, is leading to new treatments for depression.

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