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Unveiling synaptic and transcriptomic signatures of approach behavior in medial prefrontal cortex pyramidal neurons: the involvement of excitatory neurotransmission and immune system

Wednesday, September 25, 2024 2:10 PM (20 minutes)

Approaching (AP) and avoiding (AV) tendencies are basic behavioral aptitudes in responding to rewarding and aversive stimuli, and their balancing (BA) is critical for successful adaptation to the environment. The AP tendency, associated with novelty seeking, plays an important evolutionary role in identifying new sources of reward but also heightens the risk of externalizing behaviors like attention deficit/hyperactivity disorder, and addiction. Despite the medial prefrontal cortex (mPFC) being a crucial hub for sustaining attention towards relevant and novel stimuli in AP behavior, its specific synaptic and transcriptomic signatures have not yet been identified. In the present research, we employed an experimental model of individual differences to select a subpopulation of mice that spontaneously responded with AP or BA behaviors toward conflicting emotional stimuli, and expressed yellow fluorescent protein (YFP) in pyramidal neurons of the mPFC. Electrophysiological recordings revealed that AP mice exhibited a significantly higher frequency of spontaneous excitatory post-synaptic currents in mPFC pyramidal neurons compared to BA mice. We isolated YFP-expressing pyramidal neurons from AP and BA mice for cell-specific RNA analysis. The transcriptomic results highlighted differential gene expression between AP and BA mice, particularly in immune system regulation pathways. Notably, AP mice exhibited overexpression of genes related to immune responses, along with changes in cell number and activation of specific peripheral and central immune cells such as CD3+ T lymphocytes and microglia. Overall, our findings suggest that in the mPFC both the increased excitatory neurotransmission and the altered immune response are crucial underpinnings of the AP tendency.

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