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HOT TOPICS

Synaptic plasticity of the orbitofrontal cortex in obesity

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Complex interactions of internal and external factors drive overeating which leads to increased body weight and obesity. In our modern food environment, energy dense foods are typically overconsumed because they are easily accessible and highly palatable. Preclinical models of obesity have begun to examine how diet induced obesity impacts synaptic plasticity in brain regions that guide decision making and motivated feeding behavior. The orbitofrontal cortex (OFC) can influence food intake decisions as it integrates sensory information with limbic, prelimbic, and basal ganglia regions [1, 2]. Rats with OFC lesions consume food regardless of the updated sensory features and motivational value of the outcome, in a habit-like fashion [2]. Given that habit-like eating is associated with obesity [1], it is possible that access to an obesogenic diet can influence OFC synaptic function. Here, we briefly summarize emerging evidence on how obesity alters synaptic plasticity in the lateral OFC (lOFC).

The lOFC consists of pyramidal output neurons arranged in layers along with inhibitory GABAergic interneurons and astrocytes. Rats with prolonged extended access to a cafeteria diet leading to obesity have decreased basilar spines and increased dendritic branching of lOFC pyramidal neurons compared to lean rats [3]. Furthermore, obese rats have decreased frequency, but not amplitude of miniature inhibitory post synaptic currents projecting onto layer II/III lOFC pyramidal neurons [3, 4]. This was supported by a paired-pulse facilitation, consistent with a decrease in presynaptic GABAergic release probability [3, 4]. Decreased inhibitory synaptic transmission could be associated with increased endocannabinoid signaling, as diet alters endocannabinoid levels in other parts of the brain and body [5]. Indeed, obesity increases endocannabinoid-mediated inhibitory synaptic plasticity [4]. Elevated endocannabinoids were due to activated mGluR5 receptors on layer II/III lOFC pyramidal neurons from increased extrasynaptic glutamate [4]. Additionally, obese rats had hypertrophic astrocytes and reduced astrocytic glutamate transporter, GLT-1 function, underlying the increased extrasynaptic glutamate [4]. These synaptic changes were restored by N-acetylcysteine, a substrate of the cystine-glutamate transporter which increases astrocyte GLT-1 function [4], suggesting a potential therapeutic mechanism to restore synaptic changes associated with obesogenic diet exposure. Taken together, obesity alters inhibitory signaling through disrupted endocannabinoid signaling as well as astrocytic changes in morphology and function.

These synaptic changes may lead to a disinhibition of lOFC pyramidal neurons resulting in changes in firing pattern and consequent output to projection targets. Ongoing studies are aimed to address how this disinhibition influences lOFC neuronal activity and behavior. Obesity induced disruption of synaptic transmission in the OFC could lead to changes in reward devaluation tasks, as chemogenetic alteration of OFC circuits in lean mice shifts goal-directed behavior to habitual [6]. Notably, obese rodents and humans have impairments in goal directed behavior [1]. Future work will address if these effects are mediated by disinhibition of the OFC. Despite the motivation to lose weight, many dieters return to habitual eating behaviors. These findings support the hypothesis that obesity alters synaptic function in the lOFC, a brain region that encodes decisions about food rewards and may underlie one of the challenges with maintaining healthy eating habits.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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