Perspective

Neurobiology

Is Addiction being Memorized?

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Addiction study has switched to the realm of modern neuroscience, with the most recent and cutting-edge studies focusing on the behaviors that contribute to addiction. Addiction memory is a series of specific plastic changes at the synaptic level caused by long-term drug stimulation through gene transcription and expression. Based on clinical observations, addictive memory is viewed as a dysregulation of independent acquisition associated with the integration of choice lines in the "feedback loop" and "comparative system" of the hippocampus during neural information processing. Two meanings of the addition memory as (i) memory unrelated to the loss of drug control and (ii) drug-specific memory of the addicted drugs.

Keywords: Drug Addiction; Memory Theory; Neuronal Plasticity; Neuromodulation

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STUDIES have shown that the process of drug addiction may have the same neurobiological basis as learning and memory (1). Most of the changes in the brain's neurotransmitter system caused by addictive drugs are related to the activation and molecular changes of learning and memory circuits (2). It is believed that the molecular pathways and neural circuits of learning and memory and the molecular pathways and neural circuits of drug addiction all have substantial intersections (3). The molecular pathways of learning and memory intersect with those of drug addiction in that both are regulated by the same neurotrophic factors, share intracellular signaling flows, depend on the same neural transcription factors, and are surprisingly accompanied by the same changes in neuroplasticity at glutamate synapses (4). For example, the long-term potentiation and long-term depression of the post-synaptic membrane of glutamatergic neurons, which were originally considered to be an important basis for memory formation, have been found to be involved in the process of drug addiction (5). In addition, the neurons involved in learning and memory circuit also intersects with the neural circuit of drug addiction (6, 7). It is well known that the amygdala plays an important role in addictive behavior, and it is also an important brain organization for recognizing emotions and regulating emotions, especially negative emotions (8). Furthermore, the key to the neural circuit is the mesolimbic dopamine system, which consists of the ventral tegmental area and its prefrontal cortical regions, such as the nucleus accumbens (NAc, aka the ventral striatum). The NAc regulates emotional valence and the strength of memory encoding in the hippocampus, which is critical not only for declarative and spatial learning and memory but also controls compulsive behaviors associated with addiction (9, 10). In self-stimulated experimental animals, the importance of the hippocampus in the reward system was testified (11). In addition, NAc neurons guide the formation of habitual memory and regulate compulsive be-

havior (12, 13) suggesting that the neurons related to memory also are involved in the process of drug addiction.

It has been demonstrated that a marked state of craving can be induced by activating part of the memory circuit in mice. Mice previously subjected to the cocaine rod-pressing test exhibited intense rod-pressing behavior for as long as 5 minutes when the ventral part of the mouse hippocampus was stimulated; in contrast, the reward centers were not found to be electrically stimulated over the effect (14). The above experiments support the view of the American Institute on Drug Abuse: two key processes exist in the formation of drug addiction, i.e., one is the "passive neuronal adaptive changes" in the neural circuit; the other is the "memory trace construction" in the hippocampus. We can think that these two processes should be independent and parallel. The former is the condition and basis of the latter, and the latter is likely to be the underlying cause of addiction.

Synaptic Plasticity: The Underlying Reason of Addiction Memory

Synaptic plasticity refers to the variability and modifiability of synapses in terms of morphological structure and function, including the plasticity of morphological structure and function, which is the basis of brain remodeling and the neurobiological basis of learning and memory (15). Synaptic plasticity can be divided into morphological plasticity related to information storage and functional plasticity related to transmission efficiency (16, 17).

The plasticity of synaptic morphological structure is mainly manifested in the formation, rearrangement, and structural modification of new synapses (18), while the plasticity in synaptic function refers to the enhancement and weakening of synaptic transmission efficiency, mainly including synaptic transmission of long-term potentiation (LTP) and long-term depression (LTD) (19). LTP refers to the continuous enhancement of synaptic efficacy after high-frequency stimulation of afferent nerve fibers (20); LTD refers to the long-term reduction of synaptic transmission efficiency (21). As two important forms of synaptic plasticity, almost all excitability in the brain synapses can both express LTP and LTD, and in drug-dependent animal experiments, it was also found to exist in the addicted brain, but compared with the normal animal brain, the form has changed (22).

Chronic drug addiction is an abnormal form of learning and memory. The long-term abuse of addictive drugs not only activates the mesolimbic dopamine system involved in motivation and reward but also causes continuous antagonistic adaptation of relevant nuclei or neuron synapses (23). Under the repeated action of drugs, especially dopamine (DA) receptors, they will undergo a series of adaptive and plastic changes involving the number or activity of receptors, the activity of intracellular signal transduction molecules or signal transduction pathways (24). Further changes in gene expression results in abnormal learning and memory processes, abnormal behavior, and drug-related cues thus induce cravings, compulsive drug-taking behavior, and uncontrolled overdose (25).

Studies on animal and human drug addiction behaviors have confirmed that addiction memory plays a pivotal role in the maintenance of learned addiction behavior or the recurrence of addiction behavior, and it is the long-term and even life-long abnormal. Therefore, addiction is a kind of deformed learning and memory, which is a long-term conditioned reflex caused by repeated drug intake, and this is controlled by the memory of addiction. In other words, the real physiological basis of addictive behavior is addictive memory.■

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