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Circuitry of self-control and its role in reducing addiction

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We discuss the idea that addictions can be treated by changing the mechanisms involved in self-control with or without regard to intention. The core clinical symptoms of addiction include an enhanced incentive for drug taking (craving), impaired self-control (impulsivity and compulsivity), negative mood, and increased stress reactivity. Symptoms related to impaired self-control involve reduced activity in control networks including anterior cingulate (ACC), adjacent prefrontal cortex (mPFC), and striatum. Behavioral training such as mindfulness meditation can increase the function of control networks and may be a promising approach for the treatment of addiction, even among those without intention to quit.

Intention and self-control in behavioral change

Traditionally, intentions are viewed as being crucial for behavioral change [1]. However, many influences on behavior are not conscious. Dual process models provide a role for both automatic (implicit) and controlled (explicit) processes that make complementary and possibly interactive contributions to changing addictive behavior [2]. 'Automatic' usually refers to either attention or memory bias toward the substance cues related to the addiction, whereas 'controlled' involves motivation and refers to a conscious intention that can be reported by the person [2]. Both automatic and controlled processes are involved in attempts to modify addiction. In the case of alcohol addiction, pharmacological therapies have been used to induce change automatically in animals and humans [3]. Behavioral methods have also been used to induce changes in addictive behavior without a specific intention. For example, one study used evaluative conditioning to associate drinking with unpleasant experience, and found a reduction in craving and consumption [4]. In another study, smoking behavior was reduced by an association induced during sleep in subjects who wished to quit smoking [5]. A recent review of decision making indicates that behavioral changes can occur with or without conscious intention [6].

In this opinion article, we examine how behavioral training methods may be used to induce automatic changes in smoking addiction by targeting neurobiological circuits involved in self-control that have been shown to be disrupted in addictions [7,8]. Brain self-control networks mainly include the ACC, mPFC, and striatum. Support for this network comes from many fMRI studies of activation of these areas during tasks involving the resolution of conflict [9] and control of thoughts and feelings [10]. A recent developmental study highlighted reduced white matter in these same networks in vulnerability to smoking addiction [11].

The relation of control networks to the instantiation of goals is supported by the finding that lesions of the frontal lobes are associated with a tendency to neglect goals during task performance [12]. Goals often involve a complex hierarchy of subgoals, which must be implemented in a

Glossary

Cortisol: a steroid hormone, more specifically a glucocorticoid, is produced by the adrenal cortex. It is released in response to stress and to a low level of blood glucose. Its functions are to increase blood sugar and suppress the immune system.
Dopamine receptor type 2 (D2R): one subtype of dopamine receptors. Dopamine receptors are implicated in many neurological processes, including motivation, pleasure, cognition, memory, learning, and fine motor control, as well as the modulation of neuroendocrine signaling.
Fractional anisotropy (FA): a parameter in diffusion tensor imaging that images brain structures by measuring the diffusion properties of water molecules. Higher FA indicates more-efficient connectivity and provides information about the microstructural integrity of the white matter.
Frontal theta: the theta rhythm is 4–8 Hz oscillatory pattern in EEG signals recorded either from inside the brain or from scalp electrodes. Frontal theta appears to reflect a computation related to cognitive control.
Integrative body–mind training (IBMT): a form of mindfulness meditation that originates from ancient Eastern tradition. IBMT stresses less effort to control thoughts and the achievement of a state of restful alertness, allowing a high degree of awareness and balance of the body, mind, and environment. Several randomized trials indicate that IBMT improves attention and self-regulation and induces neuroplasticity through interaction between the central nervous system and autonomic nervous system.
Mindfulness meditation: a form of mental training that originally stems from Buddhist meditation traditions and is often described as non-judgmental attention to experience in the present moment.
Oligodendrocytes: a type of neuroglia that function to help create a myelin sheath insulating axons in the central nervous system.
Network training: repeated practice of a specific cognitive task (e.g., Stroop task, N-back working memory task) that thus exercises its specific brain network (e.g., a network related to resolving conflict or working memory).
Parasympathetic function: a division of the autonomic nervous system that is responsible for regulating the unconscious actions of the body.
Relaxation training (RT): a behavioral therapy focuses on relaxing different muscle groups in turn. With eyes closed, and in a sequential pattern, one is instructed to concentrate on the sensation of relaxation, such as the feelings of warmth or heaviness.
State training: practice to develop a brain state that may influence the operations of many networks. This state involves networks, but is not designed to train networks using a cognitive task.

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sequence. An fMRI study in which participants carried out a task involving multilevel goals [13] found that the ACC and anterior insula are core areas involved in switching between subgoals. As more complex switches are carried out, lateral frontal and parietal areas are recruited. Research on the regulation of action control has revealed a substantial gap between intentions and action [14,15]. A meta-analysis showed that a medium-to-large change in intention only leads to a small-to-medium change in behavior [15].

In the next section we discuss neurobiological findings from imaging studies of addiction. We then examine what is currently known about the development of the brain circuits (or functional networks) that are necessary for self-control and the transition of self-control from infancy and childhood to adulthood. Next we introduce mindfulness meditation methods that have been shown to modify brain regions within the self-control network, and demonstrate the promise of these methods in reducing drug-taking behaviors such as smoking. Finally we discuss future directions that may allow us to better understand the influence of intention in efforts to overcome addiction.

Addiction networks and deficits of self-control

Studies of humans are revealing neuroadaptations in frontocortical regions of the brain that underlie compulsive drug-seeking behaviors in addiction [16]. Imaging studies have provided compelling evidence for the involvement of the brain control network areas, such as ACC and adjacent mPFC, in the addiction process [17,18].

Dopamine

Humans addicted to drugs display a significant reduction in dopamine receptor type 2 (D2R) function in the striatum (including the nucleus accumbens, NAc) that is associated with reduced activity in ACC and adjacent prefrontal regions. The reductions in striatal D2R, which modulate the indirect striato-cortical pathway, have been implicated in impulsive and compulsive behaviors [7,19]. In addition, the capacity of cocaine addicts to control craving and reduce activation of the NAc upon exposure to drug cues is dependent on the proper activity of the prefrontal cortex [20]. Targeting the frontal impairments in addiction has been proposed as a therapeutic strategy to improve self-control [21,22]. Figure 1 illustrates the connection of the self-control circuits and those crucial for reward.

The circuits illustrated in Figure 1 are associated with compulsive behaviors and impulsivity, and impaired dopamine modulation of these regions is likely to contribute to the drug intake seen in addiction [18]. Low dopamine tone could also represent a pre-existing vulnerability for drug use, albeit one that is likely to be exacerbated with the further decreases in striatal D2R that are associated with repeated drug exposure.

Craving

A major problem in overcoming addiction is craving. Craving can lead to relapse during attempts to quit smoking. Craving is associated with activation in ACC, mPFC, orbitofrontal cortex (OFC), striatal areas [23], and insula [24]. Trying to resist the urge to smoke is almost always

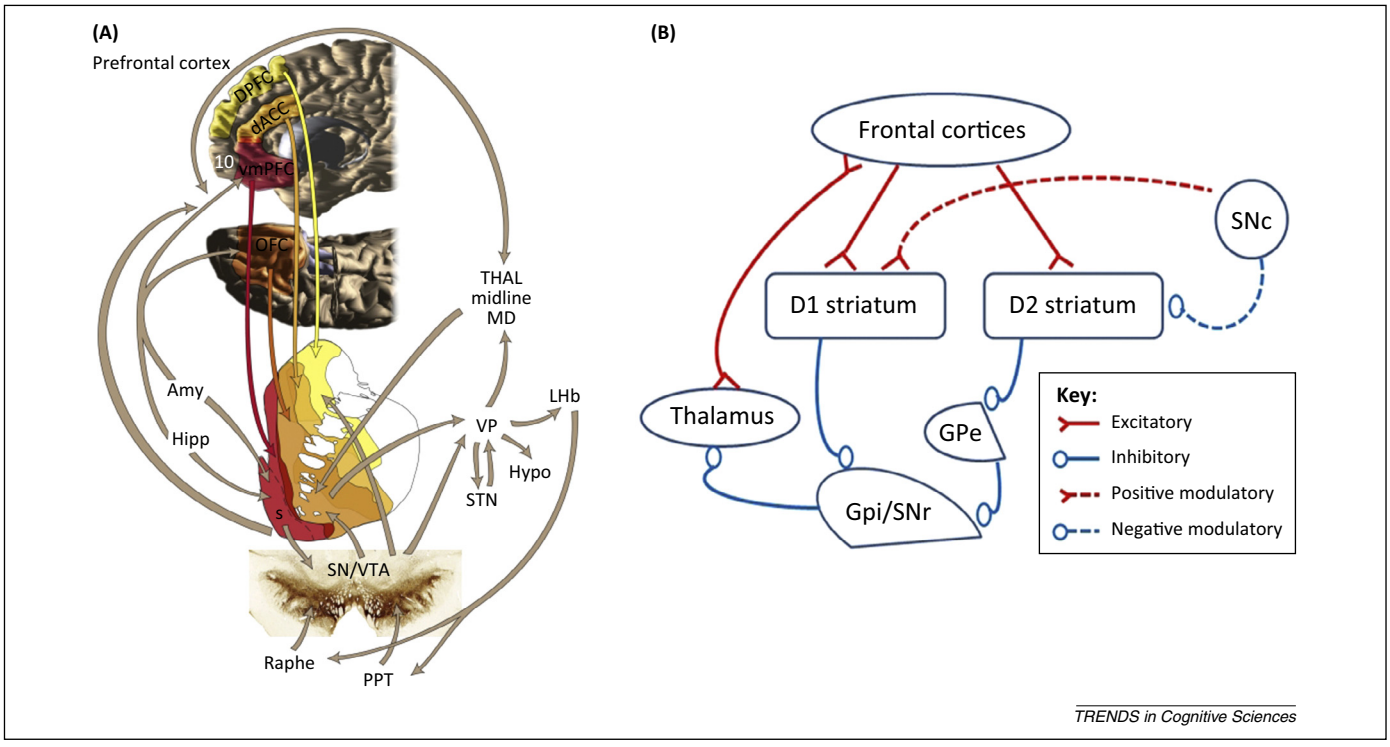

Figure 1. Reward circuits and pathways of basal ganglia. **(A)** Key structures and pathways of the reward circuit. Arrows indicate main connections of the reward circuit. Abbreviations: Amy, amygdala; dACC, dorsal anterior cingulate cortex; dPFC, dorsal prefrontal cortex; Hipp, hippocampus; hypo, hypothalamus; LHb, lateral habenula; OFC, orbital frontal cortex; PPT, pedunculopontine nucleus; S, shell, SNc, substantia nigra, pars compacta; STN, subthalamic nucleus; Thal, thalamus; vmPFC, ventral medial prefrontal cortex; VP, ventral pallidum; VTA, ventral tegmental area. Reprinted from [74] with permission from Nature Publishing Group. **(B)** Direct and indirect pathways of the basal ganglia (BG). The principal input of BG is the striatum, receiving excitatory inputs from most cortical areas. The output nuclei of BG are the internal globus pallidus and substantia nigra reticulate (GPi/SNr), which send processed information to the thalamus to eventually feed back an excitatory projection to the cortex. Within this circuitry there are two pathways: a direct pathway that expresses dopamine D1 receptors and an indirect pathway that expresses D2 receptors. D1 striatal neurons inhibit GPi/SNr cells forming the direct pathway. D2 striatal cells inhibit an intermediate relay, the external globus pallidus (GPe), which ultimately provides inhibition to GPi/SNr. Reprinted from [75].