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Cognitive mechanisms and therapeutic targets of addiction

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Fundamental to cognitive models of addiction is the gradual strengthening of automatic, urge-related responding that develops in tandem with the diminution of self-control-related processes aimed at inhibiting impulses. Recent conceptualizations of addiction also include a third set of cognitive processes related to self-awareness and superordinate regulation of self-control and other higher brain function. This review describes new human research evidence and theoretical developments related to the multicausal strengthening of urge-related responding and failure of self-control in addiction, and the etiology of disrupted self-awareness and rational decision-making associated with continued substance use. Recent progress in the development of therapeutic strategies targeting these mechanisms of addiction is reviewed, including cognitive bias modification, mindfulness training, and neurocognitive rehabilitation.

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Introduction

Addiction is a brain disease characterized by the compulsion to use psychoactive substances despite negative consequences. Although different methods and models have been used to explain addiction, its etiology is generally attributed to neurobehavioral adaptations resulting from a combination of predisposing factors and chronic substance use that gradually strengthen the urge to use substances, weaken willpower and resolve to resist these urges, and diminish critical awareness of the growing strength and range of stimuli that trigger these urges.

Recent conceptualizations of addiction [1•,2•,3•] include three disparate but interactive sets of mental processes instrumental to the initiation, progression, and maintenance of addiction[3]: first, implicit cognitive processes, which encompass learning and memory; second, metacognitive processes, including self-awareness, reflective thinking, and superordinate self-regulation; and third, executive function, which includes other higher order mental processes necessary for the planning, execution, and monitoring of goal-directed behavior. Central to the compulsive nature of addiction is the gradual strengthening of stimulus-driven implicit processes, which overwhelm a progressively weaker executive control system and interfere with awareness and rational thinking about the costs and benefits associated with continued substance use. The purpose of this paper is to provide a concise yet integrative review of the literature since 2014 that has contributed to a greater understanding of these cognitive processes both as mechanisms of addiction and as therapeutic targets.

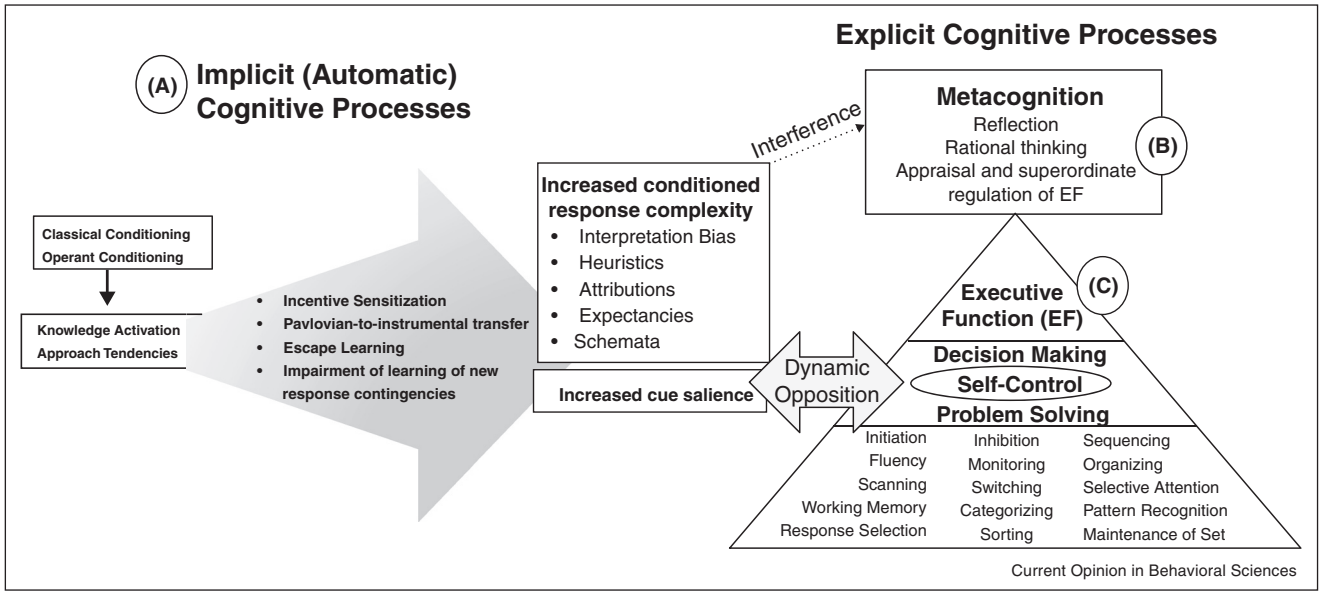
Implicit cognitive processes

Implicit, or automatic, cognition includes classically and operantly conditioned responses, which are controlled respectively by repeated pairings with their antecedents and consequences. Implicit responding is generally measured indirectly as central task disruption or facilitation, or the degree to which drug-or-alcohol-related cue responding impedes or facilitates performance of (i.e. increases or decreases latency to complete) a goal-directed task. The three most common implicit cognition paradigms examined in addiction literature include spontaneous memory association (i.e. memory bias), attentional capture (i.e. attentional bias), and action tendency (i.e. approach-avoidance biases). These are sometimes referred to collectively as measures of cognitive bias. It is, however, important to differentiate cognitive bias paradigms, that vary the type of central task, from the underlying cue-reactivity, or implicit processing, which influences central task performance (Figure 1).

Recent studies provide evidence in support of [4], in partial support of [5] and contrary to [6] the validity and clinical relevance of specific cognitive bias measures. Recent papers have also reviewed the clinical relevance

[3] These authors present cognitive models of addiction whose elements are not necessarily named the same, but include similar characteristics. The labels, *implicit*, *metacognitive*, and *executive* were selected for this review because they appear with greater frequency as PubMed keywords in the context of addiction than do alternative search terms of similar meaning.

Figure 1



Visual representation of the cognitive mechanisms of addiction. **(a)** Implicit, or automatic, cognition includes classically and operantly conditioned responses that strengthen over time, resulting in increased cue salience and conditioned response complexity; **(b)** Metacognition is a subdivision of explicit, or controlled, cognitive processes, and includes subjective, self-reflective and rational thinking, and appraisal and superordinate regulation of executive function. Complex conditioned responses (i.e. automatic information processing) happen outside of metacognitive self-awareness and can bypass reflective thinking. **(c)** Executive function represents the second sub-division of the explicit system, and includes mental operations that are value free, purposeful, and algorithmic. Fundamental to cognitive conceptualizations of addiction is the dynamic opposition between self-control and implicitly strengthened urge-related responding.

of attentional bias in substance use disorders (SUD) in general [7,8] and in cocaine use disorder specifically [9].

There is no universal consensus regarding how implicit processes are strengthened over the course of addiction, but the progression appears to be multidetermined. One way implicit processes are regarded to strengthen over time is through incentive sensitization [10], in which chronic substance use is posited to hypersensitize mesocorticolimbic reward pathways resulting in enhanced incentive motivation (i.e. 'wanting'). Recent studies provide evidence in support of incentive sensitization theory. For example, repeated exposure to amphetamine in a human laboratory study resulted in increased fMRI BOLD activation in the caudate nucleus during reward anticipation that was correlated with enhanced subjective amphetamine-like responding [11••]. Other clinical studies similarly identify reward pathway hypersensitivity associated with quantity of recent cannabis use [12] and duration and severity of alcohol dependence [13]. Furthermore, across twenty-four neuroimaging studies of cognitive interventions for addiction, the reduction of reward pathway sensitivity was identified as one of two brain changes common to successful treatment outcomes [14].

Another mechanism by which implicitly learned habits become increasingly resistant to extinction is through Pavlovian-to-instrumental transfer (PIT). Closely related to incentive sensitization, PIT represents a shift over the course of addiction in which increasingly stronger incentive motivation in response to predictive cues maintains operantly conditioned habits in the apparent absence of a reinforcement mechanism. A recent study showed PIT associated BOLD activation in the nucleus accumbens that was predictive of subsequent relapse in alcohol dependent individuals [15]. Central to PIT is the maintenance of habit via predictive, or anticipatory, responding. Investigators in another study examined anticipatory cue responding using a modified alcohol approach-avoidance task, and found cue-reactivity to be associated with strength of anticipatory processing as measured by EEG beta-band event-related desynchronization [16].

Although no reinforcement mechanism may be apparent in PIT, hedonic shifting over the course of addiction [17] suggests that drug-and-alcohol-related predictive cues trigger avoidance responding, which is a negatively reinforced behavior. This would provide an additional mechanism for the further strengthening of learned habits. Potential support for this mechanism is provided by a recent study in which reward anticipation was associated with anhedonia in cocaine users, suggesting implicit responding may be driven by 'wanting' to alleviate a negative affective state [18].