



## Review article

# Impact of general cognition and executive function deficits on addiction treatment outcomes: Systematic review and discussion of neurocognitive pathways



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## ABSTRACT

This systematic review aims to examine growing evidence linking cognitive-executive functions with addiction treatment outcomes, and to discuss significant cognitive predictors drawing upon addiction neuroscience theory. We conducted a systematic search to identify studies using measures of general cognition and executive functions in patients with substance use disorders for the purpose of predicting two treatment outcomes: therapeutic adherence and relapse. Forty-six studies were selected, and sample characteristics, timing of assessments, and cognitive measures were analyzed. We observed significant methodological differences across studies, resulting in substantial variability in the relationships between cognitive-executive domains and treatment outcomes. Notwithstanding this variability, we found evidence of associations, of medium effect size, between general cognition and treatment adherence, and between reward-based decision-making and relapse. The link between general cognition and treatment adherence is consistent with emerging evidence linking limited cognitive-executive resources with less ability to benefit from talk therapies. The link between reward-based decision-making and relapse accords with decision neuroscience models of addiction. Findings may inform preclinical and clinical research concerning addiction treatment mechanisms.

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## 1. Introduction

Addiction has been defined as a brain disorder, which reflects a shift from impulsivity to compulsivity and becomes chronic and relapsing along its course (Koob and Volkow, 2010). The unprecedented progress of neuroscience approaches has allowed neuropsychological models, which integrate neurobiological evidence with psychological and psychosocial consequences of neuroplasticity, to provide better explanations of addictive behaviors (Volkow et al., 2016). These integrated models include the Impaired Response Inhibition and Salience Attribution framework (I-RISA; Goldstein and Volkow, 2002), the Vulnerabilities in Decision-Making model (Redish et al., 2008) and the Somatic Marker theory (Verdejo-García and Bechara, 2009), among others. All these models assume that addiction is associated with poorer top-down cognitive control of behavior (executive functions), which ultimately impact on key stages of the addictive cycle, and psychosocial and treatment outcomes.

Systematic reviews and meta-analyses have established the link between drug use and cognitive deficits. Spronk et al. (2013) demonstrated that long-term cocaine use is associated with cognitive impairments in most cognitive domains, with the strongest evidence in executive functions such as sustained attention, response inhibition, working memory and decision-making. Consistent deficits in executive functions have also been shown in users of opiates, methamphetamine or alcohol (Baldacchino et al., 2012; Dean et al., 2013; Stavro et al., 2013). Executive functions are higher-order processes critical for successful goal-directed behavior, including the skills needed to succeed in addiction treatment (Blume and Marlatt, 2009; Loughhead et al., 2015). Thus, from both basic and clinical standpoints, it is crucial to determine if executive deficits have a meaningful impact on addiction treatment.

In recent years, growing studies have examined the relationship between cognitive measures of executive functions and treatment outcomes. A previous review on this topic analyzed the impact of cognitive impulsivity (one of the domains of executive functions), and found evidence of moderate associations between this construct and treatment outcomes (Stevens et al., 2014). However, this review did not analyze other components of executive function linked to drug use (e.g., reasoning, work-

ing memory, flexibility). Moreover, the authors detected significant heterogeneity among existing studies, and raised the need to conduct a more systematic methodological approach to facilitate interpretation of the mounting evidence (Stevens et al., 2014). Specifically, previous studies have not systematically analyzed differences between cognitive predictors of treatment adherence versus drug relapse. Treatment adherence is a measure of treatment progress and a well-established proxy of treatment success (Jackson, 2002; NIDA, 2002). Drug relapse is a direct measure of post-treatment outcomes, linked to remission and long-term recovery (Donovan, 2012). Although adherence and abstinence are meaningfully intertwined in the context of addiction treatment, they are also dissociable from the clinical standpoint: a substantial proportion of patients can achieve abstinence without adhering to treatment (Klingemann and Roserberg, 2009), and many patients adhere to treatment without intending to achieve abstinence (i.e., their goal is to reduce drug use or to ameliorate quality of life). This dissociation has been recently acknowledged by expert consensus statements on selection of appropriate outcomes for addiction treatment studies (Donovan, 2012; Tiffany et al., 2012). The utility of identifying a variable that predicts treatment adherence (but not abstinence) relates to the possibility of improving treatment outcomes other than drug use, such as mood or quality of life (Tiffany et al., 2012). The utility of identifying a variable that predicts abstinence (but not treatment adherence) relates to the possibility of developing self-change interventions, or brief interventions that can rapidly target the identified variable without requiring adherence to intensive treatment regimens. Logically, different cognitive-executive functions would be more relevant to each of these separate outcomes, but this notion needs to be systematically tested.

The overarching aim of this review is to systematically examine the relationship between executive functions and clinically meaningful treatment outcomes. Specific aims are: i) to review existing evidence on the link between executive deficits and treatment outcomes, focusing on methodological aspects among studies; ii) to unravel the differential relationship between executive functions and therapeutic adherence versus drug relapse; iii) to discuss the resulting findings, drawing on integrated neuropsychological models of addiction.

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