Review

# Personalizing substance use treatment based on pre-treatment impulsivity and sensation seeking: A review

Rachel L. Tomko*, Kaitlin E. Bountress, Kevin M. Gray

Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, 67 President Street, Charleston, SC 29425, USA

## ARTICLE INFO

## ABSTRACT

*Background:* Theoretically, substance use disorder (SUD) treatment that matches an individual's etiology and/or maintaining factors should be more effective than a treatment that does not directly address these factors. Impulsivity and sensation/reward seeking may contribute to the development and maintenance of SUDs, and are potential candidate variables for assigning patients to treatment. The goal is to identify whether current research can provide insight into which treatments may be most effective for individuals high in impulsivity or sensation seeking, relative to other treatments. A secondary goal is to provide recommendations for personalizing SUD treatment based on etiology or maintaining factors.
*Method:* This review summarizes clinical trials that speak to the differential effectiveness of two or more treatments for alcohol, tobacco, and other drug use disorders, based on pre-treatment impulsivity, sensation seeking, or related constructs.
*Results:* Few studies examine the differential effectiveness of two or more treatments for individuals high in impulsivity or sensation seeking. Very preliminary evidence suggests that contingency management may hold promise for individuals high in impulsivity. Pharmacological trials were under-represented in the current review, despite evidence that the effectiveness of some pharmacological interventions may be moderated by impulsivity.
*Conclusions:* Potential reasons for slow rate of progress to date are provided. Given slow accumulation of evidence, an alternative method for personalizing treatment based on pre-treatment psychosocial factors, including impulsivity and sensation/reward seeking, is proposed. Future research may explore the role of contingency management for SUD among individuals with high pre-treatment impulsivity or sensation seeking. Finally, novel, technology-enhanced behavioral mechanisms are discussed as an adjunct to SUD treatment for these high-risk populations.

## 1. Introduction

Alcohol, tobacco, and illicit drug use disorders are highly prevalent. It is estimated that 13.9% of adults in the United States meet criteria for a current alcohol use disorder (AUD; Grant et al., 2015), 13.7% are daily cigarette smokers (Jamal et al., 2014), and 2.6% meet criteria for a current drug use disorder (Substance Abuse and Mental Health Services Administration, 2014). Patients and clinicians have numerous pharmacological and psychosocial treatment options for substance use disorder (SUD). Unfortunately, treatment non-completion and relapse rates are high (Moos and Moos, 2006; Borland et al., 2012; Brorson et al., 2013). An effective system for matching individuals to a particular treatment has several potential advantages. If clinicians are able to assign a patient to the treatment that is most likely to be effective for him/her, patients and clinicians can avoid the "trial and error" approach that is commonplace in SUD treatment and maximize treatment response. Further, this approach is consistent with an ongoing precision medicine initiative in the United States (see Ashley, 2015) which "includes precisely tailoring therapies to subcategories of disease" (Ashley, 2015).

Advances in genetics have led to increasing emphasis on precision medicine, however, the concept of personalizing treatment is not new. The *specificity hypothesis* (e.g., Morgenstern and McKay, 2007) suggests that treatments, have "active ingredients" and that these active ingredients vary across treatments. Morgenstern and McKay (2007) argue that one tenet of the specificity hypothesis is that when a patient is well-matched to a treatment based on individual characteristics and the etiology or maintaining

* Corresponding author.
E-mail addresses: tomko@musc.edu (R.L. Tomko), bountres@musc.edu
(K.E. Bountress), graykm@musc.edu (K.M. Gray).

characteristics of the disorder, outcomes should be improved. Historically, there have been numerous attempts to discover which psychosocial substance use treatments work for whom. However, several large-scale tests of patient-treatment matching hypotheses found minimal evidence of matching effects based on patient characteristics, such as psychiatric severity, severity of substance use problems, gender, readiness to change, sociopathy, and social support for drinking (e.g., Longabaugh and Wirtz, 2001; UKATT Research Team, 2007; Crits-Christoph et al., 1999). Several researchers have concluded that matching patients to psychosocial treatments has been largely ineffective to date (Morgenstern and McKay, 2007; Mann and Hermann, 2010). However, Mann and Hermann (2010) suggest that as the field's understanding of genetic and neurobiological underpinnings of addiction improves, matching patients to pharmacological treatments may become more feasible. Thus, recent focus has been on behavioral and pharmacological substance use interventions that target neurobiological pathways of addiction (Kranzler and McKay, 2012).

Dysregulation of inhibitory control (i.e., impulsivity) and reward pathways are prime neurobiological targets in addiction. Impulsivity and reward seeking directly confer risk for the development of SUDs (Littlefield and Sher, 2010; Verdejo-García et al., 2008) and have been shown to moderate SUD treatment outcome (Hutchison, 2010; Kranzler and McKay, 2012; Loree et al., 2015; Stevens et al., 2014). Therefore, we propose that risk factors associated with poor impulse control and dysregulation of reward pathways may be prime candidates for both pharmacological and psychosocial treatment-matching.

### 1.1. Impulsivity and reward

Neurocognitive theories suggest that the brain's reward system, mediated by subcortical areas such as the amygdala, overrides an executive control system mediated by the lateral prefrontal cortex to result in risky behaviors, such as substance use (Casey et al., 2008; Steinberg et al., 2008). These two systems are complementary such that an overactive reward system (referred to as "bottom-up processing") or an underactive executive control system (referred to as "top-down processing") could lead to this imbalance. Impulsivity and sensation/reward seeking are behavioral manifestations of these neurocognitive systems. An inability to inhibit behavioral responses or regulate urges is a failure of top-down processes, which we will refer to as "impulsivity." This term is multi-faceted and has been used to describe constructs such as poor response inhibition, acting without forethought, difficulty with task persistence, and a preference for an immediate, smaller reward over a delayed, larger reward (Evenden, 1999). Intense desire for reward is a function of bottom-up processes, which we will refer to as "sensation seeking", reflecting an individual's preference for new and exciting experiences, regardless of risk involved (Zuckerman, 1979). For the purpose of this review, novelty seeking, or the desire for novel experiences, will also be included in this category.

### 1.2. Purpose of current review

Because dysregulation in impulse control and reward pathways may place individuals at risk for poor response to SUD treatment (i.e., Loree et al., 2015; Stevens et al., 2014), the identification of optimal treatments for this sub-population is essential. The primary goal of this review is to identify whether particular treatments have a relative advantage over other treatments for individuals with dysregulation in impulse control or reward systems, as measured via self-report and behavioral tasks (Aim 1).

A secondary goal is to evaluate the current use of a personalized medicine approach for treatment of SUDs based on a single characteristic, such as dysregulation in impulse control or reward

pathways, and to provide recommendations for future personalized medicine research (Aim 2). Historically, researchers have concluded that matching an individual to substance use treatment based on psychosocial characteristics has limited utility. Thus, we discuss whether a movement toward assigning treatments based on endophenotypes (presumed to be closer to the biological basis of SUD) has greater utility.

## 2. Review of literature on impulsivity, sensation seeking, and SUD treatment matching (Aim 1)

### 2.1. Study inclusion

Though other methodologies exist, many researchers examine treatment matching effects retroactively, after a randomized controlled trial has been conducted, by examining whether the interaction between patient characteristics and treatment type predicts treatment outcome (i.e., hindsight matching design; Miller and Cooney, 1994). Importantly, these studies compare active treatments, allowing investigators to determine whether one is superior to the other for a sub-population of interest. Previous research has established that certain aspects of impulsivity and reward seeking place individuals at greater risk for SUD and poor treatment response. Thus, we expect that low impulsivity and low sensation seeking will be associated with better treatment outcomes when individuals are provided with most active treatments, but this may be a function of the severity of the disorder and not a function of the specific treatment. The goal of this review was to identify which treatments have the most favorable response for individuals high in impulsivity or sensation seeking. We decided to only include studies that compare two or more active treatments and the rationale for this decision was two-fold. First, we wanted to ensure that any differences in treatment outcome between high and low risk groups are attributable to *differences in treatment effects* and not differences in baseline risk. And, second, we were interested in the relative efficacy of treatments for the population of interest, in order to inform treatment recommendations for this population.

Studies may also limit the sample to the population of interest (e.g., individuals recruited based on high baseline impulsivity), to compare two or more active treatments and determine which is more effective; however, no studies of this nature were identified in the current review.

An active SUD treatment was defined as a treatment other than placebo or treatment as usual. A number of pharmacological trials have randomized participants to receive an active medication or placebo, but also concurrently administered a manualized, behavioral intervention to all participants. These studies were considered to compare two active treatments. To be included, however, the behavioral intervention must be based at least partially on known, evidence-based treatments. If no reference to an evidence-based treatment (e.g., relapse prevention, cognitive-behavioral therapy, motivational enhancement therapy) was made, the study was excluded. Manualized behavioral interventions with the goal of improving medication compliance only were excluded. Additionally, pilot studies with small sample sizes ($n < 25$) were excluded.

Searches were conducted by the first author on 3/22/16 and again on 6/13/16 (to locate any new publications) using the following terms in PubMed search engine: (1) "impulsivity", "sensation seeking", "novelty seeking", "delay discounting", AND (2) "substance use disorder", "substance dependence", "addiction", "smoking cessation", "drug use disorder", "drug dependence", "alcohol use disorder", "alcohol dependence", "opioid use disorder", "opioid dependence", "heroin use disorder", "heroin dependence", "cocaine use disorder", "cocaine dependence", "methamphetamine use disorder", "methamphetamine