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Personalizing Substance Use Treatment Based on Pre-Treatment Impulsivity and Sensation Seeking: A Review

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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 to date, and alternative method for personalizing treatment based on pre-treatment psychosocial factors, including impulsivity and sensation/reward seeking, is proposed. Future research may further explore the role of contingency management for SUD among individuals with high pre-treatment impulsivity or sensation seeking. Finally, novel, technology-

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Conflict of interest

The authors have no conflicts of interest to declare.

Contributors

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enhanced behavioral mechanisms are discussed as an adjunct to SUD treatment for these high-risk populations.

Keywords

Precision Medicine; Treatment Matching; Substance Use Disorders; Impulsivity; Sensation Seeking

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 ongoing precision medicine initiatives in the United States (see Ashley, 2015) which “includes precisely tailoring therapies to subcategories of disease” (Ashley, 2015, p. 2119).

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 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 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 comparing treatments 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 study 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 is 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 are 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 dependence", "stimulant use disorder", "stimulant dependence", "cannabis use disorder", "cannabis dependence", "marijuana use disorder", "marijuana dependence", AND 3) "treatment", "randomized controlled trial", "clinical trial", "intervention". The results list was further reduced by eliminating all literature reviews and non-English articles. This resulted in 456 articles. Of these, 5 articles met criteria for inclusion; the majority of articles were excluded because they were not randomized controlled trials for problematic substance use (87.8% of excluded articles). Articles were also excluded because substance use or treatment retention was not examined as an outcome (3.8%), an evidence-based treatment control was not used (3.3%), sample size was less than 25 (0.2%), or because the differential efficacy of treatments based on impulsivity/sensation seeking was not directly examined (5.1%). Empirical studies included in two recent literature reviews (Loree et al., 2015; Stevens et al., 2014) were also reviewed for eligibility, which resulted in 4 additional articles. This resulted in 9 eligible empirical studies for review.

2.2. Results

Though research suggests that impulsivity and sensation/reward seeking are independent constructs (Casey et al., 2008; Steinberg et al., 2008), many of the studies reviewed used assessment instruments that do not distinguish between the two constructs. Because the measures used to assess sensation seeking/novelty seeking were confounded with impulsivity, we present all results together.

With regard to impulsivity/sensation seeking, studies comparing two or more active treatments and examining the interaction between treatment type and impulsivity or sensation seeking/novelty seeking are extremely limited. Of the 9 reviewed studies examining impulsivity or sensation/novelty seeking (see Table 1), one study examined delay discounting (Washio et al., 2011), three studies used the BIS-11 (Bentzley et al., 2016; Morean et al., 2015; Schmitz et al., 2009), four studies used the Tridimensional Personality Questionnaire (TPQ)- Novelty-Seeking subscale and/or Zuckerman-Kuhlman Personality Questionnaire Impulsivity-Sensation Seeking subscale (Feldstein Ewing et al., 2009; Helmus et al., 2001; Helstrom et al., 2007; Kravitz et al., 1999), and one study used discriminant analysis of multiple impulsivity, hyperactivity, and novelty seeking measures to create a novelty seeking/hyperactivity profile (Batra et al., 2010) as a predictor of treatment outcome.

Over half of the studies (5 out of 9) did not find support for differential treatment efficacy based on pretreatment impulsivity/sensation seeking-treatment (Batra et al., 2010; Bentzley et al., 2016; Helmus et al., 2001; Kravitz et al., 1999; Schmitz et al., 2009). Of the few studies that examined interactions between pharmacological treatment and impulsivity and/or sensation seeking, no significant matching effects emerged. With regard to psychosocial treatments, one study found that contingency management (CM), with or without cognitive behavioral therapy (CBT) may be superior to CBT only for highly impulsive individuals seeking treatment for tobacco use disorder (Morean et al., 2015). In addition, Washio and colleagues (2011) suggest that the more a cocaine user discounts a reward as a result of a delay, the greater in value abstinence-contingent rewards must be in

order to effectively promote abstinence. Finally, when comparing CBT + CM + Citalopram to CBT + CM + placebo for cocaine use disorder, Schmitz and colleagues (2009) found that high impulsivity was associated with *better* treatment outcome across both conditions. Though there was not a significant differential treatment effect, the authors suggest that CBT + CM may be a particularly effective combination for highly impulsive individuals since the high impulsivity is generally associated with *worse* treatment outcomes. However, it is impossible to rule out that CBT or CM alone resulted in this effect. In sum, there is some initial evidence to suggest that external incentives, particularly at higher values, may produce more favorable outcomes for highly impulsive individuals (Morean et al., 2015; Schmitz et al., 2009; Washio et al., 2011). Though replication is necessary, this may suggest that highly impulsive individuals are more likely to respond to *modifications to external reinforcement of drug use.* It is unclear whether the combination of CM + CBT is more effective than CM alone for this population, however.

In addition, one research group found that adolescents and college students high in novelty seeking may have better outcomes with educational interventions rather than one-session motivational enhancement therapy (MET) for alcohol and tobacco use (Feldstein Ewing et al., 2009; Helstrom et al., 2007). In fact, both studies found that while low impulsivity individuals did better with MET, high impulsivity individuals fared better with educational interventions. Perhaps a more structured and didactic intervention is superior to a single session of MET for more impulsive/sensation seeking individuals. Motivational interventions, which emphasize personal choice, may be less effective for more impulsive/sensation seeking individuals; however, this is speculative and further research is necessary. These were the only two studies in this review to examine MET and replication is necessary, particularly because both studies were conducted by the same research group.

2.3. Summary

Previous reviews have shown that more impulsive individuals tend to have poorer outcomes in substance use treatment (e.g., Loree et al., 2015; Stevens et al., 2014); however, the results of this review suggest that it is premature to identify “ideal” treatments for individuals high in impulsivity and/or sensation/reward seeking (Aim 1). Very preliminary evidence suggests that external incentives may be effective in reducing substance use for highly impulsive individuals. We interpret this as evidence that modifications to the environment that alter the reinforcing value of substance use may be most beneficial with this population. Replication is necessary, however.

3. PERSONALIZED TREATMENT FOR SUD (AIM 2)

3.1. Utility of a Personalized Approach

Given the minimal number of eligible studies in this review, we conclude that current approaches for examining relative efficacy of SUD treatment are unlikely to efficiently produce knowledge and replicable results. Too few studies randomize participants to two or more active treatments. Further, variation in baseline measures preclude pooling of data. For example, the size of the current review could be expanded if more researchers examined impulsivity/sensation seeking as a predictor of treatment outcome. However, even within

eligible studies, variation in the tools used to measure constructs of interest limits comparison across studies. Precision medicine for SUDs may be improved by standardization of predictive constructs and instruments across clinical trials, as this would allow for pooling data to create larger sample sizes.

One approach for standardizing predictive constructs across studies would be to use a framework such as the ASPIRE model (Ghitza, 2014), which highlights specific risk categories that may be the basis for SUD treatment recommendations. These categories include: anhedonia/reward-deficit (which is conceptually related to sensation/reward seeking), stress, pathological (lack of) self-control (e.g., impulsivity), insomnia, restlessness, and excessive/compulsive preoccupation with seeking the drug. These risk categories represent common maintaining factors for substance use behavior, and many also may contribute to the etiology of SUD. Standardization of predictive instruments can be implemented via initiatives such as PhenX Toolkit (see Conway et al., 2014). If researchers conducting clinical trials for SUD strive to 1) measure constructs in these risk categories using standardized instruments, and 2) report differential efficacy of treatments based on these constructs, we may be able to pool data to more rapidly advance precision medicine initiatives for SUD.

Additionally, improvement in measurement of SUD risk categories, such as those identified in the ASPIRE model, is essential for precision medicine. While we encourage use of standardized measures, we also encourage further refinement of measurement instruments. Assessments that take into account individualized substance use contexts are particularly needed. Using a person-centered framework, researchers can examine whether a specific, presumed risk factor for SUD is actually associated with higher risk of substance use for that specific individual. For example, repeated, real-world assessment (i.e., ecological momentary assessment; Stone and Shiffman, 1994) of substance use and stress in “real-time” using a mobile device allows researchers to examine to what extent stress is a risk factor for substance use *for a specific individual*. Assuming that this context-specific assessment rules out cases for whom stress and substance use are independent, this assessment may explain more variation in treatment outcome.

Treatments may also be designed with SUD risk categories in mind. For example, as noted by Stevens and colleagues (2014), existing psychosocial and pharmacological treatments require planning and perseverance on the part of the patient (e.g., refilling and taking medications as prescribed, selecting appropriate skills to use). And, while the goal of psychosocial treatment is often to increase planning/executive control, patients that struggle with impulsivity may be less likely to “receive a full dose” of treatment due to these difficulties, therefore reducing the likelihood of favorable treatment outcomes for this population without additional supports in place. Perhaps a paradigm-shift is necessary in which special attention is paid to structuring the patients’ environments to increase likelihood of success, particularly early in abstinence. Currently, patients are often encouraged to avoid substance use cues that may activate the reward system (“bottom up” processing). In addition, “real-time” interventions may serve as a reminder to patients to plan or “think through” decisions. Technology can be used to provide interventions as they are needed, via electronic prompts. For example, whenever a patient has a physiological

response consistent with craving (Boyer et al., 2012) or approaches a personal high-risk location (Epstein et al., 2014), patients may be asked questions that force them to "think through" choices before acting. In other words, until bottom-up processes are less dominant, as is often the case in early recovery with intense cravings and withdrawal, real-time or "ecological momentary interventions" (Heron and Smyth, 2010) may temporarily serve to activate or strengthen top-down control processes. Though this example applies specifically to the self-control/reward risk categories (impulsivity and sensation/reward seeking, respectively), other treatments tailored to other risk categories may be developed.

Finally, as pointed out in response to earlier large-scale matching studies (e.g., Longabaugh and Wirtz, 2001), multivariate approaches are likely necessary to effectively tailor SUD treatments to a specific individual. Batra and colleagues provide a great illustration of one multivariate approach (Batra et al., 2008; Collins et al., 2008; Batra et al., 2010). First, they use cluster analysis to identify smoker profiles. They replicate these profiles on an independent sample and then test the efficacy of tailored smoking treatments for the various profiles. Though Batra and colleagues (2010) did not find differential treatment effect for the novelty-seeking/hyperactivity smoker profile, they did find differential efficacy across treatments for the depressive smoker profile. Again, using Ghitza's (2014) ASPIRE model as an example, future research may create profiles based on the level of various risk within each category (e.g., level of anhedonia, stress, self-control). It is critical for researchers to publish specific information on the profiles obtained and classification algorithms used so that other researchers may replicate and refine these classification procedures.

3.2. Limitations to the Current Review

Impulsivity is multi-faceted and impulsivity and sensation/reward seeking are considered unique constructs. However, there were too few articles to break impulsivity down into its relevant sub-facets. Also, as previously mentioned, impulsivity and sensation seeking were often confounded in the measures utilized by investigators. As such, these constructs were not separated for the review. However, this may limit the interpretability of results.

The decision to include only clinical trials which compared two or more active treatments resulted in only a small number of eligible articles. This was done to compare the relative efficacy of treatments for the population of interest. Alternatively, relative efficacy of treatments may also be examined by comparing effect sizes of treatments obtained by using meta-analysis. In this case, a no-treatment control group is often used; however this method is not without limitations (see Wampold and Imel, 2015). Further, no-treatment controls are also limited, as researchers are ethically obligated to provide treatment to individuals desiring treatment, in most scenarios.

Many of the reviewed studies had small sample sizes and may not have been powered to detect interaction effects. Thus, a null finding may not mean that the two treatments do not differ in efficacy among highly impulsive individuals, but simply that the study was underpowered to detect an effect. A significant interaction effect provides insight into which treatment may be more promising; however, this commonplace approach for comparing treatments requires large sample sizes and numerous studies. Further, very few studies compared the same combination of treatments for the same SUD. Thus, replication attempts

were non-existent. The current approach is slow and unlikely to yield fruitful results in an efficient manner.

The number of eligible studies which included pharmacological treatments was also small (n=6). A number of additional pharmacological treatments for alcohol use disorder show promise for individuals high in impulsivity; however, these medications were not compared to other active treatments and therefore not included in the present study. For example, Voronin and colleagues (2008) found that aripiprazole, an atypical antipsychotic and partial dopamine agonist, was effective at reducing alcoholic drinks per day in an 8-day follow-up period among non-treatment seeking alcoholics, with individuals who reported low self-control on the BIS-11 showing greater response to aripiprazole. Similarly, Joos and colleagues (2013) examined the efficacy of modafinil, a cognitive enhancer, in treatment of alcohol use disorders. They found that modafinil effectively reduced heavy drinking days and increased percentage of abstinent days among individuals with poor baseline response inhibition. In contrast, those with better baseline response inhibition had worse outcomes with modafinil. Lastly, evidence suggests that topiramate, an anticonvulsant medication and GABA-ergic agonist, may be effective in reducing alcohol consumption among alcohol-dependent males, and this effect may be partially mediated by reductions in impulsive responding (Rubio et al., 2009). Because each of these studies provided evidence that the high-risk group (high impulsivity) had superior outcomes than the low-risk group, we can assume that the treatment is more effective for individuals high in impulsivity. However, we do not know how these interventions compare to other interventions for the high-risk population of interest. Comparing these medications' efficacy among highly impulsive individuals is a promising area for future research.

3.3. Limitations of Personalized Approach

Despite potential advantages of successful treatment matching criteria, there are a number of limitations to the patient-treatment matching approach. First, a number of genetic, psychosocial, and environmental factors (in addition to impulsivity and sensation seeking) may influence cumulative risk for both SUD and poor treatment outcome. Thus, it is difficult for researchers and clinicians to measure all phenomena that explain variation in treatment response.

Second, treatment can differ in form or modality (e.g., group, individual, tele-health, online program, medication), duration, dosage, setting (e.g., inpatient, residential, outpatient), clinician characteristics (e.g., one or more clinicians, gender, personality, training), and theoretical treatment orientation/treatment content (e.g., cognitive-behavioral, twelve-step), making it particularly difficult to match patients to psychosocial treatments.

Third, many clinics, physicians, and therapists do not have the training and/or the resources to offer an extensive menu of treatment options and the "best" treatment option for one individual may not be available in close proximity to his or her residence.

Finally, some may argue that matching individuals to treatment is a less worthwhile use of resources than developing new treatments that are accessible to a wider population of individuals in need, increasing dissemination efforts or increasing utilization of existing

services. Indeed, it has been estimated that among individuals in the United States who meet DSM-IV-TR criteria for alcohol and other drug dependence, 27.9% and 37.9%, respectively, have ever received treatment for their disorder (Cohen et al., 2007; Compton et al., 2007). Likewise, it has been estimated that 31.7% of U.S. adult smokers receive NRT, medication, or counseling for smoking cessation annually (Centers for Disease Control and Prevention, 2011). However, improved rates of treatment success may increase consumers' confidence in pursuing treatment.

3.4. Conclusions

In sum, future research should strive to 1) use standardized constructs and instruments across clinical trials for pooling of data, 2) continually improve measurement of SUD risk categories (i.e., ASPIRE model), 3) design/modify treatments with regard to SUD risk categories and their specific treatment needs, and 4) use multivariate approaches and classification techniques to assign individuals to treatment, then replicate the assignment rules with an independent sample. These recommendations apply to precision medicine efforts based on both genetic and non-genetic factors. A shift toward precision medicine will require shifts in researchers' approaches to construct measurement in clinical trials.

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Highlights

- Impulsivity is related to maintenance of substance use disorder (SUD).
- Few studies compare relative efficacy of SUD treatments based on impulsivity.
- More research on contingency management for this population is warranted.
- A methodological shift is essential for identifying personalized SUD treatments.
- Treatment assignment tools should be empirically developed and disseminated.

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Table 1

Treatment Matching Effects for Impulsivity and Novelty/Sensation Seeking

Reference	Sample	Substance(s)	Dispositional Measurement(s)	Treatments	Findings
Batra et al., 2010	N=268 adult smokers (Mean age=46.4; sex unknown; 96% German nationality)	Tobacco	**Novelty-seeking/hyperactive profile** derived from multiple measures as outlined in Batra et al. (2008)	1- Standard Treatment: Nicotine patch *or* gum + behavioral intervention/relapse prevention 2- Modified Treatment for Hyperactive/Novelty Seeking profile: Nicotine patch and gum + Bupropion + additional behavioral treatment modules focusing on impulse control, structuring daily routine, and conflict resolution	High novelty seeking/hyperactivity profile did not show better response to the modified treatment as compared to standard treatment. High risk group: Modified treatment=standard treatment
Bentzley et al., 2016	N= 115 adolescents with cannabis use disorder	Cannabis	**Impulsivity**- Barratt Impulsiveness Scale-Version 11 (BIS-11; Patton et al., 1995)	1- Contingency Management + Placebo 2- Contingency Management + N-Acetylcysteine	Though individuals with high impulsivity had reduced odds of abstinence throughout the trial, there was no evidence of a treatment by impulsivity interaction. High and low risk groups: CM + N-Acetylcysteine> CM + Placebo
Feldstein Ewing et al., 2009	N=67 college student moderate-heavy drinkers (Mean age=21; 68% male, 87% White)	Alcohol	**Novelty/Sensation Seeking**- Tridimensional Personality Questionnaire (TPQ)-Novelty-Seeking subscale (Cloninger, 1987); Zuckerman's IMPSS (Zuckerman and Kuhlman, 2000)	1- Motivational Enhancement Therapy (MET; 1-session) 2- Alcohol education control	Low sensation seeking, as measured by IMPSS, was associated with increased motivation and "taking steps" to change alcohol use at 30-day follow-up for the MET group only. For high sensation seeking individuals, motivation and steps taken were greatest for those in the alcohol education control group. Low novelty seeking, as measured by the TPQ, was related to "taking steps" in the MET group; High novelty seeking was related to "taking steps" in the alcohol education group. Novelty seeking was unrelated to motivation at 30-day follow-up. High risk group: Alcohol education>MET Low risk group: MET>Alcohol education
Helmus et al., 2001	N=68 heroin dependent cocaine users (Mean age=41.4; 64.7% male, 72.1% Black)- 49 randomized to 1 of 3 behavioral treatment conditions	Heroin/ Cocaine	**Novelty/Sensation Seeking**- Tridimensional Personality Questionnaire (TPQ)-Novelty-Seeking subscale (Cloninger, 1987)	1- Buprenorphine + behavioral therapy + Voucher-based reinforcement therapy 2- Buprenorphine + behavioral therapy + Reduced value voucher-based reinforcement therapy 3- Buprenorphine + behavioral therapy +	Across treatment conditions, high novelty seeking was associated with treatment non-retention; however, individuals high in novelty seeking were at lower risk for drop-out during the first 6 weeks of treatment. The interaction between treatment condition and novelty seeking was non-significant; however, small cell sizes may limit ability to test interaction effects. High and low risk groups: All voucher-based reinforcement treatments equal (with regard to treatment *retention*)

Reference	Sample	Substance(s)	Dispositional Measurement(s)	Treatments	Findings
				Non-contingent voucher-based reinforcement (yoked control)	
Helstrom et al., 2007	N=81 adjudicated adolescents (Mean age=16; 58% male, 79% White)	Tobacco	**Novelty/Sensation Seeking**- Zuckerman's IMPSS (Zuckerman and Kuhlman, 2000)	1- Motivational Enhancement Therapy (MET; 1-session) 2- Tobacco education control	Low sensation seeking was related to reduced number of cigarettes per day at 6-month follow-up for those in the MET condition; High sensation seeking was related to reduced number of cigarettes per day at 6-month follow-up for those in the education control condition. Though no baseline differences exist between MET and education group with regards to sensation seeking, there appears to be an interaction such that high sensation seeking heavy smokers were more likely to be assigned to the control condition and that low sensation seeking heavy smokers were more likely to be assigned to the MET condition. It is unclear how this impacted the results. High risk group: Tobacco education>MET Low risk group: MET>Tobacco education
Kravitz, Fawcett, McGuire, Kravitz, and Whitney, 1999	N=170 alcohol-dependent men (Mean age= 39.6; 100% male, predominantly White)	Alcohol	**Novelty/Sensation Seeking**- Tridimensional Personality Questionnaire (TPQ)- Novelty-Seeking subscale (Cloninger, 1987)	1– 6 months of Lithium 2– 6 months of Buspirone 3– 6 months of Placebo	Across all conditions, novelty seeking was lower among those retained in treatment and higher in those who dropped out of treatment. This effect remained after controlling for age, age of alcohol dependence onset, and other demographic variables. However, there was not a significant novelty seeking by treatment type interaction. High and low risk groups: Lithium=Buspirone=Placebo (with regard to treatment *retention*)
Morean et al., 2015	N=64 high school smokers (Mean age=16.36; 53.1% female, 90.6% White)	Tobacco	**Impulsivity**- Barratt Impulsiveness Scale (BIS-11; Patton et al., 1995)- Two factors based on current sample- Behavioral Impulsivity and Impaired Self-Regulation	1- Cognitive-Behavioral Therapy (CBT) 2- Contingency Management (CM) 3- CBT + CM	The interaction between treatment condition and impulsivity was not a significant predictor of abstinence when all treatment conditions were considered. Thus, the authors collapsed groups into CM versus no-CM. The CM group was significantly more effective for individuals high in behavioral impulsivity than the no-CM (i.e., CBT only) group. However, low behavioral impulsivity adolescents did equally well in CM vs. no-CM treatments. High risk group: CM (with or without CBT) > CBT only Low risk group: CM + CBT = CBT only = CM only
Schmitz et al., 2009	N=75 cocaine-dependent adults (Mean age=39.0; 86.0% male, 73% Black)	Cocaine	**Impulsivity**- Barratt Impulsiveness Scale (BIS-11; Patton et al., 1995), Iowa Gambling Task, Developed Impulsive "Profile"	1- Citalopram (12 week trial) + Weekly CBT and CM 2- Placebo + Weekly CBT and CM	BIS non-planning was related to *increased* abstinence across conditions; but there was not a significant impulsivity by treatment interaction. Authors interpret finding to suggest that CBT + CM combination particularly effective for participants higher in impulsivity. High and low risk groups: Citalopram + CBT + CM>Placebo + CBT + CM
Washio et al., 2011	N=36 cocaine-	Cocaine	**Delay Discounting**-	1- CM with low-	Within low-magnitude voucher condition, high DD

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Reference	Sample	Substance(s)	Dispositional Measurement(s)	Treatments	Findings
	dependent adults (Mean age= 33.9; 61% male, race/ethnicity not reported)		Computerized Delay Discounting Task (Johnson and Bickel, 2002)	magnitude vouchers 2- CM with high-magnitude vouchers	scores related to non-abstinence. DD unrelated to abstinence in high-magnitude voucher condition. High risk group: CM with high-magnitude vouchers> CM with low-magnitude vouchers Low risk group: High-magnitude vouchers=low-magnitude vouchers