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A Developmental Perspective on Neuroeconomic Mechanisms of Contingency Management

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Abstract

This paper provides a developmental overview of relevant theory and research on delay discounting and neuroeconomics, and their implications for CM approaches to treatment. Recent advances in neuroscience, and in particular the neuroscience of decision making, have the potential to inform treatment development for adolescent substance use in general, and contingency management (CM) treatments in particular. CM utilizes abstinence-based reinforcement to enhance motivation to engage in treatment and engender abstinence. CM interventions may be informed by research on delay discounting, a type of decision making that reflects how individuals value immediate vs. delayed rewards. Delay discounting reliably distinguishes substance abusers from non abusers and is a significant predictor of individual differences in response to substance use treatments. Delay discounting is also of high potential importance in the development of substance use problems in adolescence. Discounting may also be important in predicting response to CM, as CM attempts to directly influence this decision making process, shifting the preference from the immediate rewards of use to delayed rewards for choosing not to use. Multiple neural processes underlie decision making, and those processes have implications for adolescent substance abuse. There are significant neurodevelopmental processes that differentiate adolescents from adults. These processes are implicated in delay discounting, suggesting that adolescence may reflect a period of plasticity in temporal decision making. Understanding the neural mechanisms of delay discounting has led to promising working memory interventions directly targeting the executive functions that underlie individual choices. These interventions may be particularly helpful in combination with CM interventions that offer immediate rewards for brief periods of abstinence, and may show particular benefit in adolescence due to the heightened neural plasticity of systems that underlie temporal discounting in adolescence.

Keywords

adolescent substance abuse; contingency management; neuroeconomics

An emerging literature indicates that adolescents (i.e., youth ages 12–18) in treatment for substance abuse have better outcomes than those not in treatment, and suggests that multiple types of behavioral interventions hold promise (Waldron & Turner, 2008). Treatments with

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empirical support from well-designed, randomized clinical trials include individual and family based approaches. However, even with the most potent interventions tested to date, reductions in substance use observed have been modest, and robust effects on abstinence rates have been difficult to demonstrate. For example, the largest published clinical trial included adolescents aged 12 to 18 who endorsed at least 1 criterion for cannabis abuse or dependence and had used cannabis in the previous 90 days (Dennis et al., 2004). Although reductions in drug use were promising compared with that observed in prior treatment studies, approximately two-thirds of the youth continued to experience significant substance-related symptoms. That is, many never achieve abstinence or substantial reductions in cannabis use, and many of those who are initially successful relapse. These findings indicate a strong need for continued exploration and development of more potent adolescent treatment interventions (Compton & Pringle, 2004). Moreover, few studies have attempted to isolate active components of multi-faceted treatments and little is known about mechanisms of action for the positive effects observed across studies (Waldron & Turner, 2008).

One candidate for enhancing outcomes with a strong probability of success is contingency-management based interventions (CM). CM interventions are based on extensive basic science and clinical research evidence demonstrating that drug use and abuse are sensitive to systematically applied environmental consequences, i.e., reinforcement and punishment contingencies (Higgins, Heil, & Lussier, 2004). CM approaches have become one of the most thoroughly researched and effective behavioral procedures to increase drug abstinence and other treatment targets across *adult* substance-dependence disorders (Higgins, Silverman, & Heil, 2008; Petry & Simic, 2002; Stitzer, 2006). CM interventions, as of yet, have received only minimal attention in the adolescent treatment literature (Henggeler et al., 2006; Krishnan-Sarin et al., 2006; Reynolds, Dallery, Shroff, Patak, & Leraas, 2008; Stanger, Budney, Kamon, & Thostensen, 2009).

CM interventions for substance use attempt to alter decision making about substance use. Typically, financial incentives (non drug reinforcers) are offered for choosing not to use drugs. A primary model of decision making that has been used to explain substance use behavior is intertemporal decision making, and this model is generally studied within the discipline of behavior economics. Intertemporal decision making refers to choices between two alternatives that occur at different points in time. There is a general tendency for rewards to lose value the farther away they are in the future on the temporal horizon. This phenomenon is referred to as delay discounting. Delay discounting is hypothesized to be particularly relevant to substance use because substance use can be characterized as a choice between the reliable and immediate rewards of consumption and the delayed rewards of abstinence. Delay discounting is likely to have great relevance for CM interventions because CM attempts to directly influence this decision making process, shifting the preference from the immediate rewards of use to delayed rewards for choosing not to use. The science of delay discounting and decision making has the potential to inform modifications to increase the efficacy of contingency management interventions. Delay discounting may serve as a moderator of contingency management and/or other substance abuse treatment modalities, with high vs. low discounters showing greater or smaller magnitude improvements in different types of treatment. If delay discounting is a significant moderator of treatment effects, it may be possible to tailor future treatments to the pretreatment level of delay discounting (i.e., assigning those above or below cutoff scores to different levels of care or types of treatment). Changes in delay discounting may also be a mechanism by which contingency management and other effective substance abuse treatments result in reduced substance use or abstinence. Further, the repeated experience of forgoing immediate drug rewards and choosing delayed nondrug rewards may strengthen executive cognitive control,

reduce subjective reward value of drug use, or increase subjective reward value of delayed choice.

Our thesis is that recent advances in neuroscience, and in particular the neuroscience of decision making, can inform treatment development for adolescent substance use in general, and contingency management treatments in particular. This paper attempts to support this thesis by providing a developmental overview of relevant theory and research on delay discounting and neuroeconomics, and their implications for CM approaches to treatment. In the sections below, the relevance of delay discounting in research on substance use is outlined. Neuroeconomics, which integrates methods of behavioral economics and other decision-making approaches with cognitive neuroscience paradigms, is also described. The behavioral and neural development of temporal decision making is discussed. Normal developmental processes that result in dramatic changes in decision making in adolescence have implications for the onset of substance use and potentially for the development of substance use problems and interventions to target those problems. Substance use itself may impact decision making, even among adolescents at an early stage of use. Multiple neural processes underlie decision making, and those processes have implications for problematic substance use and adolescent risk behavior. CM principles are also outlined, and ways CM interventions may be informed by research on how individuals make decisions about immediate vs. delayed rewards are highlighted. Finally, hypotheses are presented concerning the ways in which decision making and its underlying neural processes might moderate the efficacy of CM for adolescent substance use and might also be a mechanism by which CM results in abstinence or reductions in use.

Operationalizing Delay Discounting

Delay discounting is assessed in behavioral tasks in which participants are asked to choose between a series of immediate and delayed rewards. Assessment methods include questionnaires (Kirby & Petry, 2004; Kirby, Petry, & Bickel, 1999), computerized tasks involving hypothetical rewards (Baker, Johnson, & Bickel, 2003; Johnson & Bickel, 2002), and experiential tasks involving delays in seconds (Reynolds & Fields, 2011). As an example, we have used a computerized choice program with adolescent substance abusers (Stanger et al., in press). Participants completed this task four times in a single session, twice for hypothetical monetary rewards as the reinforcer with magnitudes of $100 and $1,000; and twice for amounts of marijuana subjectively equivalent to $100 and $1,000 as the reinforcer. Adolescents chose between smaller immediate rewards (e.g., $50 right now) and larger delayed rewards (e.g., $100 in 1 month). The larger delayed reward was either $100 or $1,000 (or the amount of marijuana equivalent to these dollar amounts for delay discounting of marijuana). The smaller immediate reward was determined using an adjusting amount algorithm (Du, Green, & Myerson, 2002). Thus, the smaller immediate reward amount varied on each trial. The delay periods were 1 day, 1 week, 1 month, and 6 months. The starting value of the smaller, sooner (adjusting) reward was always 50% of the larger, delayed reward. On subsequent trials, the smaller sooner reward adjusted up or down by 50% depending on the subject's choice (smaller, sooner choices resulted in decreases; larger, delayed choices resulted in increases).

Across different types of tasks, choices of immediate rewards over future rewards and choices of future rewards over immediate rewards can be used to calculate participants' delay discounting rate (Mazur, 1987). Delay discounting is generally estimated using Mazur's (1987) equation: $V_d = V/(1 + kD)$, where V_d represents the discounted value at D delay in days, V is the undiscounted amount, and k is the estimated discounting parameter. High values of k indicate greater discounting (i.e., impulsive decisions) and low values of k indicate less discounting (i.e., reflective decisions). V_d was derived by calculating

individuals' indifference point, which is the value of the immediate reward that is subjectively equivalent to that of the delayed reward. Indifference points were calculated for each magnitude and commodity at each delay and fit to the hyperbolic model of delay discounting rate (*k*). Area-under-the-curve (AUC) can also be used to quantify delay discounting (Myerson, Green, & Warusawitharana, 2001).

Developmental Changes in Delay Discounting

Delay discounting in adolescence and adulthood is likely linked to the earlier developmental construct of delay of gratification. In laboratory tasks assessing this construct, preschool and school aged children are presented with small reinforcers they can have immediately, and larger reinforcers they can have if they wait (Mischel, Zeiss, & Ebbesen, 1972). The measure of delay of gratification is the amount of time the child can wait for a larger reward. Using variations of this task, research has reliably shown an increasing tendency to wait for a larger reinforcer as children get older (Miller, Weinstein, & Karniol, 1978; Yates, Lippett, & Yates, 1981). Individual differences in the ability to delay gratification evident as early as the preschool period have long term predictive utility. Preschool children who score higher on this measure of willingness to delay gratification show better school and standardized-test performance, more social responsibility and social competence in adolescence, and lesser tendencies toward frustration and aggression later in life (Mischel, Shoda, & Rodriguez, 1989). Individual differences in ability to delay appear stable into the 20s and 30s, with low delayers showing greater ventral striatal activation and high delayers showing greater prefrontal cortex activation when required to suppress responses to alluring cues (Casey et al., 2011). These findings suggest the potential for early identification of a risk factor that may be important in the development of substance use, and a potentially important target for prevention. There is new prevention research targeting executive function in the preschool period (e.g., Diamond, Barnett, Thomas, & Munro, 2007), and improvements in executive function in this early period may have important effects on later substance use. However, even if early intervention can reduce later delay discounting and substance use, there will remain a need for effective substance use interventions across the lifespan.

In terms of the specific development of delay discounting, this task has been studied in children ages 9 and older. There are no true longitudinal studies of the development of delay discounting, but a recent cross sectional study comparing delay discounting from ages 10 to 30 showed a significant decrease with age, but greater changes prior to than after age 16, with youth ages 13 and under showing significantly higher rates of discounting than those 16 and older (Steinberg et al., 2009). Thus the period of mid adolescence (ages 14–16) appears to be the time of greatest change in delay discounting. This pattern of change is somewhat distinct from the developmental trajectories of planning ahead (an executive function) which improves in relatively stable and constant fashion across adolescence and early adulthood and from reward seeking/sensation seeking, which reaches its peak in mid adolescence, and declines into adulthood (Steinberg, 2010). The plasticity of delay discounting in mid-adolescence suggests that adolescence might be a unique and ideal time to attempt to reduce delay discounting. Interventions like contingency management that attempt to shift preferences to delayed rewards might be most effective during this developmental period. This maturational pattern also suggests that delay discounting might be an informative individual difference variable with similar relations to substance abuse across the developmental period from mid-adolescence into adulthood.

Neural Mechanisms in Decision Making: Neuroeconomics

Neuroeconomic approaches can contribute to the understanding of neural mechanisms that underlie delay discounting behavior, and thereby may offer additional clues to better direct prevention or treatment approaches. Neuroeconomics integrates the behavioral methods of behavioral economics and other decision-making approaches with cognitive neuroscience paradigms (Glimcher, Camerer, Poldrack, & Fehr, 2008). Several fMRI studies have revealed a relatively consistent profile of brain regions that appear to underlie temporal discounting preferences (Bickel, Pitcock, Yi, & Angtuaco, 2009; Boettiger et al., 2007; McClure, Ericson, Laibson, Loewenstein, & Cohen, 2007; McClure, Laibson, Loewenstein, & Cohen, 2004; Monterosso et al., 2007). A meta-analysis of delay discounting in healthy adults (Carter, Meyer, & Huettel, 2010) identified 25 regions of significant activation in the cerebral cortex during delay discounting tasks. Three primary regions of robust activation include value-related regions (ventral striatum), value consideration regions (medial prefrontal cortex), and future forecasting regions (posterior cingulate). These regions are consistent with the valuation network proposed by Peters & Buchel (2011), who also propose two additional related networks important in delay discounting. They hypothesize that reduced activity in a cognitive control network, involving activation of the anterior cingulate associated with decision conflict (difficult decisions among options of similar value) and reduced top-down regulation of the medial prefrontal cortex by the dorsolateral prefrontal cortex are related to higher delay discounting. In addition, they further suggest that activity in the medial temporal lobe (hippocampus and amygdala) reflects prospection and episodic imagery, which may be related to lower delay discounting.

The hypothesized interaction among these regions that support delay discounting has been described in competing neurobehavioral decision systems theory (Bechara, 2005; Jentsch & Taylor, 1999). This theory posits that choices between immediate and delayed reinforcers are related to the regulatory balance of activation in two neural systems. The evolutionarily older impulsive system, which consists of portions of the limbic and paralimbic areas, is primarily involved in the valuation of immediate rewards. In contrast, the more recently developed executive system, which consists of portions of the prefrontal cortices, is involved in the consideration of the future and the selection of delayed rewards. The balance (or imbalance) in activation and connectivity between these systems is hypothesized to underlie individual delay discounting rates (Bickel et al., 2007).

Neural Manipulation of Delay Discounting

Repetitive transcranial magnetic stimulation (rTCMS) over the right DLPFC (Camus et al., 2009) and the left lateral PFC (Figner et al., 2010), a procedure that can interfere with processing in the targeted brain area, has been shown to impair the “top down” components of delay discounting. An example of “bottom up” influences on discounting is a study involving administration of the dopamine precursor l-dopa to healthy adult volunteers resulting in increased discounting (Pine, Shiner, Seymour, & Dolan, 2010). Transcrianial direct current stimulation (tDCS) of the right DLPFC decreased risk taking in a gambling task (Fecteau et al., 2007). Similarly, continuous theta burst stimulation of the right DLPFC resulted in improvements in delay discounting (Cho et al., 2010). These studies support the critical role of the DLPFC in delay discounting.

Development and Neuroeconomics

Perhaps due to the underdevelopment of brain systems that are related to optimal decision making, adolescents may be particularly vulnerable to deficits in making decisions related to substance use (Casey, Jones, & Hare, 2008). Developmental neurobiology suggests that brain systems implicated in delay discounting develop at different rates. The limbic and

paralimbic “bottom up” brain regions that function with respect to primary reinforcers mature first (Blakemore & Choudhury, 2006; Giedd et al., 1999); the “top down” frontal and prefrontal cortex, which regulate executive function and decision making, mature at a later period than other brain regions (Blakemore & Choudhury, 2006; Giedd, et al., 1999; Gogtay et al., 2004; Passler, Isaac, & Hynd, 1985). This asymmetric development has been theorized to be related to the well-known observation that children and adolescents make riskier choices than adults (Green, Fry, & Myerson, 1994; Green, Myerson, & Ostaszewski, 1999; Steinberg, et al., 2009), and adolescence can represent a risk factor for the development of problems associated with sensation seeking (Colder & Stice, 1998; Romer, Duckworth, Sznitman, & Park, 2010; Vitaro, Brendgen, Ladouceur, & Tremblay, 2001). Further, the combination of heightened neural response to reward and motivational cues and delayed behavioral and cortical control has been hypothesized to contribute to adolescent preferences for immediate rewards (Casey, Jones, & Somerville, 2011). Further, adolescents show differential recruitment of limbic regions relative to cognitive control regions in the context of affective stimuli including reward (Richards, Plate, & Ernst, 2011).

However, it is important to consider that the well documented neural changes in adolescence may have greater explanatory power for the *timing and onset of experimental substance use* (a normative behavior) than for the *development of substance use problems* or response to substance use treatment. The nature of deviations from normal development that might explain frequent and problematic use in adolescence is much less well understood. There are multiple studies documenting neural structural and activation differences between adolescent substance users and controls (e.g., Abdullaev, Posner, Nunnally, & Dishion, 2010; Crowley et al., 2010; Lopez-Larson et al., 2011). There is also longitudinal evidence that alcohol use in adolescence may negatively impact both memory and attention (Tapert, Granholm, Leedy, & Brown, 2002), and evidence of neural activation differences between substance users even at the earliest stages of tobacco use and demographically matched same age peers (e.g., Rubinstein et al., 2011). However, it will be most informative in terms of treatment development to identify the predictive utility of individual neural differences among youth (and adults) who display problem use and/or who meet diagnostic criteria in order to account for good vs. poor treatment response and ultimately improve treatment outcomes.

There are relatively few studies of neural mechanisms of delay discounting in adolescence. One study assessed discounting and neural function in a sample of males ages 12–31 (Christakou, Brammer, & Rubia, 2011). Age dependent changes in activation associated with age dependent changes in discounting were observed, including increases in activity in ventromedial (VM) PFC, and decreases in activity in ventral striatum (VS), anterior cingulate cortex (ACC), and the temporal lobe. In addition, using these regions as regions of interest, all regions showed strengthening in their activation coupling with increased age and with decreased discounting, suggesting that developing connectivity between the VMPFC and VS systems may be the mechanism by which discounting decreases with age. Adolescent discounting differed from that of adults most in choices at longer delays, and this behavioral phenomenon was consistent with developmental increases in connectivity between lateral prefrontal and inferior parietal areas predicting improvements in delay discounting. These results highlight the development of coordinated processing between top down and bottom up neural systems in the development of delay discounting.

Developmental increases in ventral PFC white matter organization are also related to developmental improvements (reductions) in delay discounting, with stronger age effects in youth ages 13–16 than 17–23 years (Olson et al., 2009). However, there are age-independent associations between white matter development and delay discounting as well (Olson, et al., 2009). Similarly, Herting et al. (2010) reported that white matter microstructure

abnormalities mediate the relations between family substance use history and behavioral differences on a discounting task among alcohol naïve youth ages 11–15. These results suggest that in addition to a normal neural development process that influences developmental differences in delay discounting, there may be individual neural and behavioral differences evident in early adolescence that confer risk independent of developmental changes in adolescence. We are testing such individual differences in an ongoing study of adolescent substance users participating in two randomized trials comparing CBT+CM to CBT only (Stanger & Ryan, 2011). At treatment intake and again at the end of treatment, participants complete a delay discounting task optimized for fMRI. We plan to identify neural networks correlated with individual differences in delay discounting and test whether activity in those networks accounts for individual differences in treatment outcome.

In one of the only examples to date of an attempt to influence neural responses among adolescent substance users, Chung et al. (2011) compared the responses of substance (primarily marijuana) using and control adolescents on an anti-saccade (AS) response inhibition task. On some trials, adolescents were told that they could earn incentives for "correct" performance. Control and substance using teens did not show activation differences in regions related to reward processing (e.g., ventral striatum, orbitofrontal cortex), however the substance using teens showed greater activations in prefrontal cognitive control regions on trials when rewards were available. This ability to increase neural cognitive control when rewards are available, suggests that adolescent (and potentially adult) substance users could show greater cognitive control when offered reward-based interventions targeting their substance use. However, it will be important to replicate these results with a larger sample, compare results directly between adolescents and adults, and use an incentive condition that provides clear information about the magnitude of reward available on each trial and feedback on each trial regarding correct performance. Results of a similar AS study comparing adolescents and adults further suggest that the use of rewards facilitates cognitive control among adolescents to a greater extent than for adults (Jazbec et al., 2006), suggesting that adolescents' neural functions might be more influenced by rewards than adults. Thus, CM treatment approaches that offer consistent and tangible rewards might be particularly effective in adolescence, and the mechanism for such enhanced effects might be enhanced neural function in cognitive control or executive regions.

Delay Discounting and Adult Substance Use

Delay discounting of both real and hypothetical reinforcers has been reliably found to discriminate adult substance using from non substance using populations for opiates, cocaine, alcohol, and tobacco (Baker, et al., 2003; Bickel, Odum, & Madden, 1999; Coffey, Gudleski, Saladin, & Brady, 2003; Heil, Johnson, Higgins, & Bickel, 2006; Kirby, et al., 1999; Madden, Petry, Badger, & Bickel, 1997; Mitchell, Fields, D'Esposito, & Boettiger, 2005; Petry, 2001). Higher delay discounting among substance users (reflecting a stronger preference for immediate, small rewards) may explain, in part, why they are more likely to choose the immediate gratification resulting from substance use. Discounting rate has also demonstrated relations with addiction severity and substance use frequency in several cross sectional studies (Bickel, et al., 1999; Vuchinich & Simpson, 1998). Further, smoking frequency correlated with discounting rate among heavy smokers (Johnson, Bickel, & Baker, 2007). Thus, the current rate of substance use seems to be related to an individual's rate of discounting.

Delay Discounting and Adolescent Substance Abuse

Research in adolescence has also addressed the role of delay discounting and substance use, in particular whether increased delay discounting appears to be the cause or the effect of substance use. In general, higher delay discounting appears to influence the onset of substance use. For example, Audrain-McGovern et al. (2009) found that delay discounting predicted the development of early onset tobacco use in a longitudinal study. Consistent with delay discounting serving as a potential marker of substance use risk, Reynolds et al. (2009) reported that children of smoking parents showed higher discounting rates than children of nonsmokers. More recently, Reynolds and Fields (2011) reported that youth who had smoked no more than 3 cigarettes had higher discounting rates than never smokers, and rates similar to daily smokers. These results are consistent with delay discounting as a risk factor for substance use.

Discounting may also be a mechanism by which environmental influences lead to substance use behavior. For example, Fields et al. (2009) reported that individual differences in delay discounting accounted for relations between stress and smoking status among adolescents. Consistent with these results, Wills et al. (2011) reported that good behavioral self control (including low delay discounting) moderates the influence of poor behavioral regulation on substance use problems in adolescence.

Consistent with data showing that delay discounting reaches “adult” levels by mid adolescence, studies show that relations between delay discounting and adolescent substance abuse are similar to those found among adult substance abusers. For example, similar to adults, delay discounting rates are associated with level of tobacco use among adolescent smokers (Audrain-McGovern et al., 2004). Among adolescents, delay discounting rates were higher for daily smokers compared to never-smokers (Reynolds, Patak, & Shroff, 2007), and heavy drinkers showed higher delay discounting than light drinkers (Field, Christiansen, Cole, & Goudie, 2007).

Together, these results suggest an important and complex role for delay discounting in the onset of substance use and the development of problem use in adolescence. If delay discounting shows greater plasticity in adolescence than other developmental periods, it is likely that negative environmental influences (e.g., stress or exposure to substance using peers) might more readily result in a greater preference for immediate rewards during this period, including the immediate positive effects of substance use. However, this same plasticity might be beneficial in treating adolescent substance abuse, if interventions successfully target and alter temporal decision making.

Delay Discounting and Substance Abuse Treatment Outcome

Consistent with the conceptualization of delay discounting as an individual difference variable that conveys information about substance use severity and potential treatment outcome, several recent studies have tested relations between delay discounting and treatment outcome. Results have been mixed. Some adult studies have failed to find significant relations between measures of discounting and treatment outcome (e.g., Landes, Christensen, & Bickel, in press; Passetti, Clark, Mehta, Joyce, & King, 2008), although one such study reported an overall decrease in delay discounting during a 12 week outpatient treatment (Landes, et al., in press). However, others have reported worse outcomes for high discounters. For example, Mueller et al. (2009) reported that delay discounting predicted time to relapse to smoking in a laboratory study. In addition, Yoon et al. (2007) reported that discounting of $1,000 of money predicted smoking status at 24 weeks postpartum among women who discontinued smoking during pregnancy, after controlling age, educational level, and history of depressive symptoms. Two other studies reported a similar relation

between delay discounting and relapse to tobacco smoking (MacKillop & Kahler, 2009; Sheffer et al., in press). Recently, delay discounting was reported to predict continuous weeks of cocaine abstinence achieved, even after adjusting for treatment condition (high vs. low magnitude CM) (Washio et al., 2011).

There have been two studies testing delay discounting as a predictor of adolescent substance use treatment outcome. Among adolescent smokers, steeper rates of delay discounting predicted less success in a CM smoking cessation treatment program (Krishnan-Sarin et al., 2007). We have tested discounting as a predictor of treatment outcome among adolescent marijuana abusers (Stanger, et al., in press). Teens (N=165; 88% male; mean age=15.8) enrolled in a clinical trial comparing three 14 week treatments: (1) Cognitive Behavior Therapy (CBT) only (Sampl & Kadden, 2001; Webb, Scudder, Kaminer, & Kadden, 2002), (2) CBT + CM (clinic- and parent-based incentives for abstinence), or (3) CBT + CM + a Family Management Curriculum (Dishion & Kavanagh, 2003). The CM schedule used escalating rewards for abstinence, with a reset procedure for substance use, with total potential earnings over 14 weeks of $590 (Stanger, et al., 2009). Delay discounting rates at treatment onset were concurrently related to demographic variables (SES, race). Delay discounting of money predicted during treatment abstinence outcomes over and above the effects of type of treatment received. However, discounting did not predict treatment outcome once race, SES and frequency of marijuana use were controlled. A similar pattern of relations between DD, substance use status and other socioeconomic variables was reported by Fields et al. (2009), with adolescent smokers showing higher discounting than nonsmokers, but not when controlling for IQ and income level. These results suggest complex relations between decision making and other variables that influence response to treatment. Decision making shares variance in common with these other variables, and this shared variance is related to treatment outcomes. However, among this set of variables, decision making is unique in that it is potentially modifiable, and thus a potential mechanism by which CM or other treatments may influence substance use outcomes.

Neuroeconomics and Substance Use

Despite major advances in understanding delay discounting via neuroeconomics among adults, this area of study remains a new domain with much variability in methods across studies limiting the ability to generalize and directly compare studies. Further, only a small number of investigators have applied neuroeconomics to addiction research, with none among adolescents. Comparing alcohol-dependent individuals to control participants, Boettiger et al. (2007) found significant relations between number of “now” choices and neural activity across alcoholic and control adults, and also differences between alcoholics and controls in these same regions, suggesting that individual differences in neural activation when making decisions about rewards across time are related to substance abuse. Similarly, Claus et al. (2011) found that, among adults with alcohol use disorders, those with more severe alcohol problems had greater activity in several regions, including the insula, when choosing delayed rewards. These results suggest that consideration of delayed rewards may increase negative feelings and internal conflict to a greater extent among those with more severe substance use disorders.

These findings are complemented by two fMRI studies comparing delay discounting among stimulant-dependent individuals to control participants. Monterosso et al. (2007) found that stimulant-dependent individuals exhibited less prefrontal and parietal cortex activity compared to controls when making easy choices. Hoffman et al. (2008) identified similar patterns of reduced activity among adult methamphetamine users in the dorsolateral prefrontal cortex (DLPFC), the precuneus of the parietal cortex, and ventral striatum. Similarly, a study comparing neural activation in adolescent recent onset smokers and

nonsmokers during a monetary incentive delay task showed hypoactivation in the ventral striatum during reward anticipation (Peters et al., 2011) that are likely independent of long term exposure to drug (nicotine). These studies provide an initial suggestion of meaningful discounting-related differences in cortical regions responsible for inhibition and consideration of future circumstances and are consistent with competing neurobehavioral decision systems theory. Interventions to modify delay discounting and its underlying neural mechanisms might better enable substance users to choose delayed abstinence-related rewards.

Delay Discounting Summary

Decision making as reflected in delay discounting appears important in the onset and worsening of substance use in adults and adolescents. Further, delay discounting might be a useful and informative substance use endophenotype that generalizes across various forms of substance abuse, and a potentially informative marker of individual differences that could predict treatment response and/or improve as a result of treatment. However, longitudinal studies are needed to clarify the extent to which delay discounting changes across stages of substance use at the level of the individual. Neural processes implicated in delay discounting include valuation, cognitive control, and prospection, with task performance influenced by activity in diverse brain regions. Bottom up (e.g., limbic and paralimbic) and top down (e.g., frontal and prefrontal) networks appear to interact when individuals make temporal decisions about rewards. Developmental differences in the maturation of regions in these networks may make teens both more vulnerable to impulsive decision making and substance use and more responsive to interventions targeting these systems.

CM Conceptualization and Basic Principles

CM applications are derived from an operant framework of substance abuse, which posits that substance use is initiated and maintained, in part, by the pharmacological actions of the substance in conjunction with reinforcement derived from a substance using lifestyle. Typically, CM interventions are used to engender therapeutic change within a comprehensive treatment program in a substance abuse treatment clinic. CM programs attempt to modify the substance user's environment such that (a) drug abstinence is carefully monitored, and (b) reinforcing events (e.g., tangible rewards or incentives) occur when abstinence is achieved, and (c) punishing events (e.g., suspension of employment or school, loss of privileges) occur when abstinence is not achieved.

CM interventions involve multiple elements: a *target behavior*, the *monitoring* of the target behavior, the *schedule* used to deliver consequences, the *magnitude* of the consequence, and the *type of consequence* (Petry, 2011; Sulzer-Azaroff & Meyer, 1991). The most common *target behavior* has been drug abstinence. However, some CM programs have targeted reductions in use or successive approximations toward abstinence (Correia, Sigmon, Silverman, Bigelow, & Stitzer, 2005; Lamb, Kirby, Morral, Galbicka, & Iguchi, 2010; Lamb, Morral, Galbicka, Kirby, & Iguchi, 2005; Preston, Umbricht, Wong, & Epstein, 2001). *Effective monitoring* of the targeted behavior is essential, because consequences (reinforcement or punishment) must be applied systematically. With substance abusers, this typically involves biochemical verification of drug abstinence, usually via urinalysis testing. The *schedule* of reinforcement or punishment refers to the temporal relation between the target behavior and the delivery of the consequence. Two schedules that have demonstrated efficacy across multiple substance abuse treatment studies are a fixed schedule with escalating rewards and a reset contingency (typically referred to as abstinence-based vouchers or incentives) (Higgins, et al., 2004) and an intermittent schedule of rewards using the fishbowl method (Petry et al., 2005). Multiple studies have demonstrated that greater

magnitude schedules of reinforcement have resulted in better outcomes than lower magnitude (Lussier, Heil, Mongeon, Badger, & Higgins, 2006; Washio, et al., 2011). CM interventions have ranged from brief experimental manipulations to interventions lasting over a year (Prendergast, Podus, Finney, Greenwell, & Roll, 2006). Use of relatively low magnitude reinforcers and variable or intermittent schedules can engender abstinence (Petry & Martin, 2002). However, larger magnitude incentives have been shown to be more cost effective than lower magnitude incentives (Olmstead, Sindelar, Easton, & Carroll, 2007; Sindelar, Elbel, & Petry, 2007). The *type of reinforcers* or punishers used have ranged from cash, choice of gift cards, on-site retail items, increased chance to receive prizes, desirable clinic privileges, employment or housing opportunities, and refunds on treatment service fees (Higgins, et al., 2008).

Importantly, in abstinence-based CM programs, rewards are contingent on providing a drug free urine sample. Providing a drug free urine sample requires a period of abstinence that ranges from days to weeks, depending on the drug used and the frequency of use. Thus, although optimal CM programs strive to provide rewards in close temporal proximity to abstinence choices, there is by definition a delay ranging from days to weeks between individual decisions to be abstinent (forgo the immediate rewards of drug use) and the receipt of rewards. Thus, the degree to which individuals vary in their preference for immediate vs. delayed rewards is likely to influence their behavior in CM programs. That said, the rewards offered in CM programs are still provided much sooner than the much more delayed naturalistic rewards available for abstinence, potentially benefitting those who prefer immediate rewards. However, there is likely to be a delay threshold for the highest discounters, making it more difficult for them to choose the briefly delayed rewards available in CM programs. Also, CM may alter decision making about drug use, for example, by shifting an individual's preference from immediate to more delayed rewards. Increased preference for delayed rewards may result either from a reduction in the subjective reward value of drug use or from an increase in the subjective reward value of the delayed reward. In addition, the repeated experience of choosing a delayed reward for abstinence over the immediate reward of drug use may strengthen executive cognitive control.

CM for Adolescent Substance Abuse

Despite the clear and robust data supporting CM for adult substance use treatment outcomes with a mean effect size of d=.42 (Prendergast, et al., 2006), there are few studies testing CM for adolescent drug use. Henggeler et al. (2006) tested whether a home and clinic abstinence-based incentive intervention would enhance outcomes in adolescents participating in Drug Court. The CM procedure did not enhance outcomes when added to Drug Court and a comprehensive family based therapy (MST). However, the Drug Court procedures had some overlap with CM as they involved incentives and consequences based on urine drug testing results. Godley et al. (2008) described a CM intervention for adolescent substance users during continuing care provided after residential treatment. The intervention involved weekly sessions for 12 weeks and used a fishbowl reinforcement program to reinforce participation in personal goal related activities and abstinence, with youth completing 64% of the activities they specified. To date, they have reported only on the completion of activities by youth in the CM conditions as an index of the feasibility of identifying, verifying, and increasing prosocial, goal-oriented activities.

Several studies have used CM to target adolescent tobacco use. Brief laboratory studies have demonstrated the potential use of CM for adolescent smoking (Corby, Roll, Ledgerwood, & Schuster, 2000; Roll, 2005). In a larger randomized trial, Krishnan-Sarin et al. (2006) found that youth participating in a school based tobacco cessation program who received a 4-week abstinence-based incentive intervention with maximum earnings of about $300 plus CBT

had greater rates of tobacco abstinence than youth who received CBT alone. In a second trial, Cavallo et al (2007) found similar high abstinence rates for the same CM intervention plus either of two methods of CBT delivery (standard weekly vs. more frequent brief sessions), however, high relapse rates suggested the need for longer duration interventions. Another CM program for adolescent smoking, a web-based 30 day intervention, was tested using a reversal design with 4 youth (Reynolds, et al., 2008). All four participants achieved abstinence, and three of the four participants met abstinence criteria when incentives were thinned and during a return to baseline phase. Although larger and longer term studies need to be conducted, this promising method appears feasible and could extend the reach of CM.

In an effort to enhance outcomes for adolescent substance abuse we created a developmentally-appropriate outpatient CM-based intervention (Kamon, Budney, & Stanger, 2005; Stanger, et al., 2009). This model utilizes an abstinence-based CM (voucher program) to enhance motivation to engage in treatment and engender marijuana and other drug abstinence. Moreover, parents are taught to use rewards and consequences at home contingent on urine drug tests results to further motivate initiation and maintenance of drug abstinence and to better manage other related behavior problems. In addition to these CM components, adolescents receive individual therapy (MET/CBT) to enhance motivation and provide coping skills training focused on achieving and maintaining abstinence (Sampl & Kadden, 2001; Webb, Scudder, Kaminer, & Kadden, 2001).

We completed an initial two-group randomized trial comparing MET/CBT+CM to CBT +parent drug education (PDE; an attention control condition) (Stanger, et al., 2009). As hypothesized, CM enhanced continuous abstinence outcomes, engendering more weeks of continuous marijuana abstinence during treatment (d=.48, medium effect). Those in the CM group were also more likely to achieve ≥8 weeks of continuous abstinence (53% vs. 30%, p=.06) and ≥10 weeks of continuous abstinence (50% vs. 19%, p=.006). We are currently replicating and extending these findings in a subsequent randomized trial.

Delay Discounting and Neural Moderation of Response to CM

Although delay discounting and its neural mechanisms may form a risk endophenotype that influences the development of adolescent substance use disorders and that impacts individual decisions to use substances among such youth, there are clearly individual differences among substance users along these dimensions. There is evidence (reviewed above) of main effects of individual delay discounting on treatment outcome. However, individual variability may also moderate response to particular treatments, including CM (Potenza, Sofuoglu, Carroll, & Rounsaville, 2011). Moderation would be reflected in an interaction between type of treatment and delay discounting, such that greater or smaller effects of particular treatments might be found for high vs. low discounters. This type of moderation has not been tested to date, as studies have tested only main effects of delay discounting on treatment outcome, and most have involved only CM interventions. Moreover, youth with high discounting may have overall worse outcomes than youth with low discounting (a main effect) and youth with high discounting might differentially benefit from CM (an interaction effect). In order to test moderation, outcomes for high and low discounters receiving different interventions must be compared. In the case of CM which seeks to influence choices or decisions about substance use, and in particular increase choices in favor of delay, some CM interventions may improve outcomes for youth who show high discounting of the future, but have less impact on youth with low discounting. This hypothesis is partially consistent with the results of the Washio et al. (2011) study in which high (but not low) magnitude CM was observed to compensate for the negative effects of high discounting. That is high discounters showed improved outcomes under high magnitude but not low magnitude CM, suggesting that under certain conditions, they would

shift their preference from immediate drug rewards to delayed money rewards. However, high magnitude CM was not more effective for low discounters, potentially because of a ceiling effect (low discounters shifted their preference from immediate drug rewards when any money rewards were available at delays of days). In terms of neural mechanisms, this type of interaction might result in larger increases in activation in top down executive regions among high discounters receiving CM relative to those in other treatments, reflecting a normalization of function relative to low discounters.

Alternatively, substance using adolescents who show less discounting of delayed rewards (a greater ability to delay gratification) may show better outcomes in CM interventions compared to non-CM interventions than high discounting substance abusing youth. Adolescent substance abusers with more "intact" or mature discounting should be more likely to choose the financial rewards offered at brief delays (periods of days) over drug use than those who value delayed rewards less (discount delayed rewards more). Thus they would be expected to have higher rates of abstinence when treated with CM compared to control conditions or non CM treatments. Higher discounting youth might be expected to show little improvement when treated with CM involving delayed rewards, even at relatively brief delays. This hypothesis is consistent with research showing that youth with better neurocognitive (executive) skills showed better response to a substance abuse prevention curriculum (Fishbein et al., 2006). It is also consistent with research showing that high adult discounters were more likely make frequent, suboptimal redemptions of voucher earnings in a CM intervention targeting opiate and cocaine use added to buprenorphine maintenance (Bickel et al., 2010). Moderation effects that favor low discounters might be reflected in youth who show greater relative activation in executive regions or networks (evidence of better top down control) while engaged in discounting tasks showing better CM outcomes than those with less relative executive activation. Youth with weaker neurocognitive (executive) function might require direct neurocognitive intervention to boost the efficacy of interventions such as CM.

Improvement in Delay Discounting and Neural Mechanisms to Improve Response to CM

In addition to discounting as a behavioral and neuroeconomic moderator of CM effects, changes in delay discounting might also be a mechanism or mediator of CM effects on treatment outcomes among adolescents. Thus, exposure to CM might produce improvements or normalization in delay discounting, and these changes might result in better treatment outcomes. Further, exposure to CM might produce activation or connectivity changes in one or more neural networks involved in temporal decision-making. Such changes might be direct or indirect through effects of abstinence from substance use, which may also affect brain structure and function. For example, CM could impact a variety of neural processes related to making behavioral choices including executive (top down) and motivational and emotional (bottom up) processes. CM provides rewards for choosing abstinence. Although delayed, rewards are much more immediate and consistent than the existing environmental rewards for choosing abstinence. Teens are asked to choose a financial reward delayed by a period of days instead of choosing drug use, which is immediately rewarding. The repeated experience of making this delayed choice may strengthen executive control or it may reduce the subjective reward value of drug use or increase the subjective reward value of the delayed choice. There are no studies to date assessing neurocognitive mediators of adolescent substance abuse treatment outcomes. However, there are a few examples indicating that improvement in neurocognitive skills mediate the effects of behavioral interventions in preschool (Bierman et al., 2008) and childhood (Riggs, Greenberg, Kusche, & Pentz, 2006). The use of experimental methods including neuroimaging to identify intervention effects on these mechanisms should provide clues as to how to improve the

effectiveness of CM or how to target other systems through other interventions to improve outcomes.

Specific neural mechanisms can be explored through pre and post treatment administration and neuroimaging of behavioral decision making tasks. One approach that might be particularly informative in identifying the effects of CM on discounting is the use of cross commodity discounting tasks in which preference for immediate substances of abuse is assessed relative to preference for delayed money (Bickel, Landes, et al., 2011), for example choosing between 1oz of marijuana now vs. $100 in one week. Cross commodity discounting tasks may represent a closer analog to CM interventions where patients are offered monetary incentives at brief delays to compete with the immediate rewards resulting from drug use than the single commodity delay discounting tasks that have been utilized to date. This hypothesis is supported by Yoon et al. (2009) showing that choices of delayed money over immediate cigarettes increased in adults receiving a CM treatment for smoking relative to those in the control condition. No change was observed in single commodity money discounting. Further, performance on the cross commodity task predicted laboratory smoking behavior.

Of considerable importance is to test whether neural changes associated with a positive response to CM are uniquely associated with CM or reflect a mechanism of action common to effective substance abuse interventions in general. The literature on neural changes associated with the treatment of other mental health disorders finds evidence for both patterns. For example, studies of behavioral and medication treatments for anxiety disorders generally find common neural changes associated with positive treatment response across treatment modalities (Linden, 2007; Porto et al., 2009). However, similar studies for depression generally find divergent and even opposite neural changes associate with positive treatment response to psychological vs. medication treatments (Linden, 2007).

An interesting possibility is whether interventions that reduce delay discounting would enhance the response to CM. For example, individual differences in delay discounting among healthy adults have been found to be significantly related to activity in the left anterior prefrontal cortex while performing a working memory task (Shamosh et al., 2008). This relation between working memory and discounting in substance users was supported by a recent study by Bickel, Yi, et al., 2011 showing that working memory training resulted in reductions in delay discounting among adult stimulant abusers. Similarly, Houben et al. (2011) showed working memory training (25 sessions over at least 25 days) led to significant reductions in alcohol intake among problem drinkers. Further, changes in working memory accounted for the intervention effects, with additional evidence of moderation of those relations by stronger implicit preferences for alcohol. Relations between changes in working memory (improvements in executive function) were most beneficial for those with the greatest implicit preference for alcohol. These results suggest that interventions targeting working memory might enhance CM treatment response, particularly among those most at risk of poor outcomes (high discounters).

Another method to reduce delay discounting was developed by Peters and Buchel (2010). They demonstrated that providing cues to healthy adults about real future events planned for the day of reward delivery significantly reduced delay discounting, with stronger effects observed the more vividly subjects imagined the events. Reduced delay discounting was also associated with upregulation of neural value signals in the prefrontal cortex. Similarly, Radu et al. (2011) showed that reframing immediate choices as “something now but nothing later” and delayed choices as “nothing now but more later” in order to make the “hidden zeros” in delay discounting choices explicit (as described by Magen, Dweck, & Gross, 2008) reduced delayed discounting. These experimental manipulations could be integrated into contingency

management procedures (e.g., linking future reward availability dates with personal events) to decrease impulsive substance use choices in favor of delayed incentives for abstinence.

Conclusion

Delay discounting, a type of decision making that reflects how individuals value immediate vs. delayed rewards, reliably distinguishes substance abusers from non abusers and is a significant predictor of individual differences in response to substance use treatments. Discounting may also be important in predicting response to CM, as CM attempts to directly influence this decision making process, shifting the preference from the immediate rewards of use to delayed rewards for choosing not to use. The plasticity of delay discounting in mid-adolescence suggests that adolescence might be a unique and ideal time to attempt to reduce delay discounting. Interventions like contingency management that attempt to shift preferences to delayed rewards might be most effective during this developmental period. Delay discounting might also be an informative individual difference variable among substance using adults and adolescents, however, research supporting this hypothesis is currently limited. Neuroeconomic approaches can contribute to the understanding of neural mechanisms that underlie delay discounting behavior, and thereby may offer additional clues to better direct prevention or treatment approaches. Delay discounting involves interaction among multiple cortical regions, including “top down” cognitive control regions (e.g., dorsolateral prefrontal cortex) and valuation regions (e.g., medial prefrontal cortex and ventral striatum). Asymmetric development in these regions in adolescence may account for development differences in substance use and delay discounting behaviors, and individual differences present in adolescence may account for individual differences in substance use treatment outcome generally and CM in particular. Further, the plasticity in delay discounting in adolescence might be beneficial in treating adolescent substance abuse, if interventions successfully target and alter temporal decision making. Research with adults suggests that substance users show discounting-related differences in cortical activation consistent with competing neurobehavioral decision systems theory. Interventions to modify delay discounting and its underlying neural mechanisms including those targeting working memory and using future event focused imagery might better enable high discounting substance users to choose delayed abstinence-related rewards available in CM.

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