



Delay discounting differentiates pre-adolescents at high and low risk for substance use disorders based on family history



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ARTICLE INFO

Article history:

Received 24 January 2014

Received in revised form 10 July 2014

Accepted 10 July 2014

Available online 23 July 2014

Keywords:

Family history of substance use disorders
Risk

Impulsivity

Pre-adolescent

ABSTRACT

Background: Youth with family histories of substance use disorders (FH+) are at increased risk for developing substance use disorders relative to those without such histories (FH−). FH+ individuals show deficits in impulse control that parallel those in individuals with substance use disorders. Elucidating how specific components of impulse control are affected in FH+ pre-adolescents would advance our understanding of how deficits in impulse control relate to risk of substance use disorders.

Method: A total of 386 children (305 FH+, 81 FH−; ages 10–12) with no histories of regular alcohol or other drug use were compared on measures of delay discounting (Kirby), response inhibition (GoStop Impulsivity Paradigm), and response initiation impulsivity (Immediate Memory Task). The independent associations between these three behavioral measures of impulsivity and FH status were analyzed using logistic regression models.

Result: FH+ pre-adolescents performed more impulsively on measures of delay discounting and response inhibition impulsivity, but there were no significant group differences on response initiation impulsivity. When the behavioral impulsivity measures were examined simultaneously, delay discounting was most robustly associated with FH status.

Conclusions: These results identify deficits in impulse control present in FH+ pre-adolescents before the onset of regular substance use, and suggest that increased delay discounting may be an important behavioral phenotype for pre-adolescents at risk for substance use involvement.

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1. Introduction

Across a variety of measures and drug classes, substance use disorders are associated with increased impulsivity (de Wit, 2009; Rogers et al., 2010). However, it is not clear if these deficits result from substance use or are due to pre-existing risk factors that may contribute to problem substance use. To address this question, some researchers have studied individuals with a family history of substance use disorders (FH+), who are at increased risk for developing alcohol and other drug use disorders relative to those without such histories (FH−; Finn et al., 1990; Lieb et al., 2002;

McCaul et al., 1990; Merikangas et al., 1998). This risk has a significant genetic basis (Cloninger et al., 1981; Merikangas, 1990; Reich et al., 1998; Slutske et al., 2002), and influences behavior prior to the onset of substance use. In particular, FH+ youth may display greater impulsivity in childhood, which may in turn increase their likelihood of substance use involvement. A better understanding of impulsivity in FH+ youth would help clarify its association with problem substance use.

Impulsivity is a multifaceted construct and different approaches to assessment yield distinct information about impulsivity (de Wit, 2009; Evenden, 1999; Winstanley et al., 2006). One important distinction in impulsivity assessment is that of personality versus behavioral approaches to measurement, which tend to have little association with one another (Cyders and Coskunpinar, 2011; Dougherty et al., 2003b; Lane et al., 2003; Reynolds et al., 2006). This is not surprising, given that personality approaches focus on subjective report of impulsive traits expressed across situations and time, while behavioral approaches examine momentary impulsive

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performance under particular task demands (any one behavioral task reflecting a narrow, specific impulsive process; Reynolds et al., 2006). Personality measures of impulsivity have been reliably associated with substance use onset and risk; however, there has been less research examining underlying behavioral mechanisms in youth at risk for substance use/misuse (de Wit, 2009). Therefore, the focus of this study is an examination of behavioral impulsivity, using multiple behavioral measures, in children at risk for substance use disorders based on their family history.

It is generally recognized that there are at least three core behavioral impulsivity processes: delay discounting, response initiation impulsivity, and response inhibition impulsivity (Dougherty et al., 2009a, 2005). FH+ adults without substance use disorders show increase in each facet of impulsivity that parallel those seen among individuals with substance use disorders (Acheson et al., 2011b; de Wit, 2009; MacKillop, 2013). For example, delay discounting, or devaluing delayed relative to immediate rewards, is elevated in non-affected FH+ adults as well as individuals with substance use disorders (Acheson et al., 2011b; Kirby and Petry, 2004). Similarly, response initiation impulsivity, or the rapid responding that occurs before complete processing and evaluation of a stimulus, is also elevated both in non-affected FH+ adults and individuals with substance use disorders (Acheson et al., 2011a; Finn et al., 2002; Verdejo-Garcia and Perez-Garcia, 2007). Finally, response inhibition impulsivity, or the failure to inhibit an already-initiated response, is elevated in both populations (Acheson et al., 2011a; Li et al., 2009, 2006; Nigg et al., 2004; Saunders et al., 2008).

Collectively, this research indicates increase in different forms of impulsivity are present in individuals with family histories of substance use disorders, and these deficits parallel those in substance users. However, it is not clear to what extent these processes may be differentially related to FH status, since earlier studies did not typically compare all three measures in the same subjects. As a result, it is not clear which forms of impulsivity are most affected in FH+ subjects and thus may make the greatest contributions to their enhanced risk for developing substance use disorders. Additionally, much of this research has focused on young adults, and typically excluded FH+ individuals with past or present substance use disorders. To improve understanding of the contribution of behavioral impulsivity to the development of substance use disorders, it is necessary to first examine impulsivity among FH+ youth prior to the increase in impulsive and sensation-seeking behavior, including substance use that occurs during adolescence.

To address these issues, we used a battery of behavioral impulsivity measures in pre-adolescents with and without family histories of substance use disorders before the onset of regular substance use. Previous studies of behavioral impulsivity in FH+ individuals have relied on adult samples (Acheson et al., 2011a) or more general measures of cognitive functioning rather than focused assessments of impulsivity (Nigg et al., 2004). This study is the first to comprehensively assess behavioral impulsivity in FH+ youths prior to adolescence. FH+ and FH– children (10 to 12 years old) were tested with laboratory measures that index three distinct forms of behavioral impulsivity: delay discounting, response inhibition, and response initiation impulsivity. We hypothesized that FH+ pre-adolescents would be more impulsive than FH– children across all measures. Additionally, we sought to examine the magnitude of group differences across the different dimensions of impulsivity to determine which measures are most robustly associated with FH status.

2. Method

2.1. Participants

A total of 386 children participated: 305 children with a family history of substance use disorders (FH+; 152 boys, 153 girls) and 81 children with no family history

of substance use disorders (FH–; 35 boys, 46 girls). These children and their parents were enrolled in a longitudinal study assessing impulse control development and substance use during adolescence (Ryan et al., Under review). Family history was established using the Family History Assessment Module (Rice et al., 1995) based on parent report. FH+ participants had at least a biological father with a past or present substance use disorder. FH– participants had no history of substance use disorders among parents or grandparents. Children and their parents were recruited from the community through internet, radio, newspaper, and television advertisements. Exclusion criteria were: regular substance use (defined as substance use at least once per month for 6 consecutive months; Clark et al., 2005), positive urine test at time of screening, low IQ (<70), or physical/developmental disabilities that would interfere with the ability to understand or complete study requirements. Oppositional defiant disorder, conduct disorder, ADHD, dysthymia, or anxiety disorders were not exclusionary for the FH+ group because these disorders are commonly comorbid with substance use involvement and are an expression of the traits that may underlie inherited risk for substance misuse (Iacono et al., 2008). Written informed assent/consent was obtained from children and their parent/guardian before study participation, and the experimental protocol was approved by the Institutional Review Board of The University of Texas Health Science Center at San Antonio.

2.2. Procedure

Potential participants completed a screening visit to determine eligibility and an initial baseline study visit where the impulsivity measures (described below) were completed. Participants provided breath and urine samples to screen for recent substance use upon arrival at the laboratory. No subjects tested positive for alcohol or drug use. Parents and children completed interviews, questionnaires, and behavioral measures separately. The administration of laboratory behavioral measures of impulsivity was counterbalanced, with standardized instructions given before each task. Children and one of their parents were paid approximately \$100 each for completing the on-site screening visit and the initial baseline study visit.

2.3. Measures

2.3.1. Screening measures. Participants provided expired-air samples to screen for recent alcohol use (AlcoTest® 7110 MKIII C, Draeger Safety Inc., Durango, CO) and urine samples to screen for recent drug use (THC, cocaine, benzodiazepines, opiates, and amphetamines; Panel/Dip Drugs of Abuse Testing Device, Redwood Biotech, Santa Rosa, CA). Family history classification was based on information collected from the participating parent using the Family History Assessment Module (Janca et al., 1992; Rice et al., 1995). Psychiatric symptoms and diagnoses were assessed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997). Tests were administered by trained research assistants and results reviewed by a staff psychiatrist who is board-certified in child and adolescent psychiatry. Intelligence was assessed using the Wechsler Abbreviated Scale of Intelligence (WASI; Psychological Corporation, 1999). Family socioeconomic status was measured using the Four Factor Index of Socioeconomic Status (FFISS; Hollingshead, 1975). Child health was assessed during a physical exam that included a measure of pubertal development (Brooks-Gunn et al., 1987; Petersen et al., 1988). Self-reported impulsivity was assessed using the Barratt Impulsiveness Scale (BIS-11; Patton et al., 1995; Stanford et al., 2009).

2.3.2. Delay discounting. The delay discounting procedure has been described previously (Kirby, 2009; Kirby et al., 1999) and consisted of 27 choices between smaller, immediate and larger, delayed amounts of money such as, “Would you prefer (a) \$34 today or (b) \$50 in 30 days?” The magnitude of the delayed choice varied; nine of the choices offered small amounts of delayed money (\$25–\$35), 9 offered medium amounts of delayed money (\$50–\$60), and nine offered large amounts of delayed money (\$75–\$85). Typically, delay discounting increases as reward magnitude increases. Discount rate estimates (k) based on the hyperbolic discounting function of Mazur (1987) were estimated for each participant based on the pattern of choices across the small, medium, and large amount of money. An average value for all items was also calculated. Possible values of k ranged from 0.00016 (choosing all delayed options) to 0.25 (choosing all immediate options).

2.3.3. Immediate memory task (IMT). The IMT (Dougherty et al., 2003a, 2002) is a go/no go task used to measure response initiation impulsivity. In this procedure, a series of 5-digit numbers appear on a computer monitor in black text on a white background. Numbers are randomly generated and appear for 500 ms at a rate of one per second. The children were instructed to respond when the 5-digit number they saw was identical to the one that preceded it. This task yielded two variables of interest: (1) *Correct Detections*, how often children correctly responded to a 5-digit number identical to the preceding number; and (2) *Commission Errors*, how often children responded to a 5-digit number that differed from the preceding number by only one digit (its position and value determined randomly). In this 11 min session, 600 trials were delivered, there were equal numbers of trials where Correct Detections and Commission Errors were possible (i.e., 33% of nonconsecutive trials). The primary dependent measure for this task was the *IMT Ratio* (proportion of Commission Errors relative to Correct Detections).

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