Archival Report

Biological Psychiatry

The Genetics of Impulsivity: Evidence for the Heritability of Delay Discounting

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ABSTRACT

BACKGROUND: Delay discounting (DD), a decline in the subjective value of reward with increasing delay until its receipt, is an established behavioral model of impulsive choice, a key component of a broader impulsivity construct. Greater DD, i.e., a tendency to choose smaller immediate over larger delayed rewards, has been implicated as a potential intermediate phenotype (endophenotype) for addictive disorders and comorbid externalizing psychopathology, particularly in adolescence. However, genetic and environmental origins of DD remain unclear. Accordingly, the goal of the present study was to assess heritability of DD, an important aspect of its utility as an endophenotype.

METHODS: A commonly used computerized procedure involving choice between varying amounts of money available immediately and a standard amount of $100 presented at variable delays was administered to a population-based sample of twins aged 16 and 18 (n = 560, including 134 monozygotic and 142 dizygotic pairs). DD was quantified using area under the discounting curve and the k coefficient estimated by fitting a hyperbolic model to individual data. Heritability was assessed using linear structural equation modeling of twin data.

RESULTS: The genetic analysis revealed significant heritability of both DD measures (area under the discounting curve: 46% and 62%; k: 35% and 55% at age 16 and 18, respectively).

CONCLUSIONS: The present study provides evidence for heritability of both model-based and model-free DD measures and suggests that DD is a promising intermediate phenotype for genetic dissection of impulsivity and externalizing spectrum disorders.

Keywords: Decision making, Delay discounting, Endophenotype, Heritability, Reward, Twins

http://dx.doi.org/10.1016/j.biopsych.2014.10.022

In their everyday lives, humans face numerous decisions where choices have immediate or remote consequences: go to a party today or stay home and prepare for an exam? Enjoy a nice dessert now or skip it in favor of losing weight in the longer run? Spend money on vacation or put it away for buying a house or retirement? In all of the above examples, decisions involve a choice between smaller-sooner and larger-later rewards. The subjective value of rewards tends to decline with increasing delay to its receipt, a phenomenon known in behavioral economics as delay discounting (DD). As the temporal distance to larger reward increases, its subjective value decreases until it reaches the subjective value of a smaller but immediate reward (indifference point). In more general terms, when the consequences of one's decision are delayed, they are less effective in controlling ongoing behavior (1). Individuals may differ in the degree to which they discount delayed rewards, i.e., how rapidly the value of reward diminishes with increasing time to its delivery.

DD is a ubiquitous phenomenon extensively studied in many living species, including pigeons, mice, rats, and humans. Experimental approaches measuring delay discounting were originally developed in animal studies of operant behavior, where animals chose between, e.g., one pellet of food available immediately and two pellets of food delivered after a certain delay (2,3). In human studies, choice paradigms typically involve hypothetical or real monetary rewards [reviewed in (1)]. Importantly, DD measures obtained from hypothetical choices correlate strongly with measures obtained from real rewards (4–7).

Studies using repeated measurements of DD in the same individuals have shown that DD measures represent a stable, trait-like characteristic, with estimates of test-retest reliability of DD measures ranging from .55 to .90 (8–14).

Extensive studies in animal models and recent human neuroimaging studies have provided insight into the neural substrates of DD. Animal studies suggest that the choice between immediate and delayed reward critically depends on the orbitofrontal cortex and the core of the nucleus accumbens [reviewed in (15)]. Human data implicate the left dorsolateral prefrontal cortex, left insula, inferior frontal gyrus, frontal pole, and the anterior cingulate cortex as key regions associated with the tendency to choose larger-later rewards (16,17), while increased ventral striatal activity has been implicated in preference for immediate rewards (18).

Delay discounting is considered a behavioral model of impulsivity and can be empirically measured using laboratory choice paradigms (19). Substantial evidence indicates that higher propensity to impulsive choice is associated with psychopathology, most notably addictive disorders, but also with other disorders in which impulsivity is a core behavioral

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ISSN: 0006-3223

dysfunction, such as externalizing spectrum disorders. In animal studies, preference for smaller-sooner rewards predicted increased susceptibility to substance dependence including alcohol preference and cocaine self-administration (20,21). Human studies have provided strong evidence for higher rates of DD in individuals with substance use disorders, as is summarized in a recent meta-analysis (22) and several reviews (1,23–29). Although it remains to be determined whether high DD is a pre-existing risk factor or a consequence of substance abuse, some evidence suggests that heightened DD predates substance use and abuse (30). Furthermore, steeper DD has been shown to predict relapse in smoking cessation trials (31,32). Indeed, the conceptual relevance of DD to substance abuse is quite straightforward, since the hallmark of the latter is a strong preference for the immediate rewarding effects of drugs and disregard for delayed adverse consequences of one's decisions. Finally, substantial evidence points to an association between DD and other unhealthy behaviors such as overeating, obesity, risky sex, and overall poorer health [reviewed in (33,34)] as well as pathological gambling, compulsive shopping, and financial mismanagement [reviewed in (27)].

It has also been suggested that DD may serve as an intermediate phenotype, or endophenotype, in genetic studies of addictive disorders and other externalizing psychopathology in which impulsivity is implicated as a core underlying dysfunction (23,24,35,36). Efforts to identify genes conferring risk for addictive disorders have yielded very modest results so far, which can be attributed largely to the complexity of the phenotype. Shifting the focus of psychiatric genetic research from complex diagnostic phenotypes to relatively discrete and homogenous component processes contributing to liability might aid in elucidating the neurobiological and genetic underpinnings of addiction and psychopathology, resolve possible genetic heterogeneity, and clarify the mechanisms of comorbidity. Furthermore, intermediate phenotypes might be helpful in the functional characterization of genetic risk variants being identified in large-scale association studies of psychiatric disorders and thus contribute to bridging the gap between genes and complex phenotypes with which they are associated. Finally, a validation of DD as an intermediate biobehavioral phenotype is directly relevant to the goals of the National Institute of Mental Health sponsored Research Domain Criteria initiative, the goal of which is to explicate fundamental biobehavioral dimensions that cut across current heterogeneous disorder categories to improve the existing classification of psychiatric disorders based on better knowledge of the underlying pathophysiology (37,38).

Taken together, evidence for the validity of DD as a behavioral model of impulsivity, its test-retest reliability, increasing knowledge of its neural substrates, and evidence for its robust relationship with the externalizing spectrum disorders cited above strongly support the role of DD as an endophenotype for a spectrum of disorders characterized by relative insensitivity to delayed outcomes.

A key requirement for such an intermediate phenotype is its significant heritability. Yet, current knowledge of the relative contribution of genetic factors to interindividual variation of DD is very limited. Animal studies have demonstrated significant strain differences in DD in rats (39,40). Furthermore, mice selectively bred for alcohol preference show increased DD rates (41,42). However, little is known about the heritability of DD in humans. Our recent study of adolescent twins aged 12 to 14 showed significant genetic influences on DD in humans using a single-choice delay gratification paradigm in which participants were offered a choice between a real amount of $7 available immediately and $10 available in 7 days (35). The heritability of individual differences in the ability to delay gratification was estimated at 30% at age 12 and at 51% at age 14.

However, most clinical studies of DD utilize a different paradigm that provides a quantitative measure of the rate of discounting of hypothetical monetary rewards as a function of their delay. To obtain an individual discounting function, choice options, including both amounts and delay duration, are varied systematically to obtain a point of indifference between smaller immediate and larger delayed rewards at each of the delays. This laboratory procedure has been a standard in DD research, and most of the evidence for association with psychopathology cited above was obtained using this method (1). However, little is known about heritability of this DD measure. Furthermore, generalization of data obtained in younger adolescents to the older age is problematic due to the possibility of significant changes in heritability in the course of development.

Accordingly, the aim of the present study was to estimate the heritability of DD, i.e., the extent to which observed interindividual variability in the rate of discounting of delayed rewards is determined by genetic factors.

METHODS AND MATERIALS

Sample

Participants were adolescent twins (134 monozygotic [MZ] and 142 dizygotic [DZ] pairs, $n = 560$, 50.7% female participants, including 84% Caucasian, 12% Black, and 4% other minorities). One hundred eighty-three participants were first tested at mean age (±SD) of 16.6 ± .26 years, with 126 of them (34 MZ and 28 DZ pairs) retested at a mean age of 18.5 ± .21 years. An additional 377 participants were first tested at mean age of 18.7 ± .37 years. All participants were recruited from the local population using the state birth records database; therefore, the sample is largely representative of the general population with respect to the distribution of socioeconomic status (9-point Hollingshead Index Occupational Status Scale score for parents: M = 5.6 ± 1.9) and general intelligence (Raven's Standard Progressive Matrices: median score 47, corresponding to 50th percentile, IQ = 100 according to US norms). Zygosity was determined using a set of 160 DNA markers, an interview administered to the twins' parents, and ratings by research assistants of twins' physical similarity. Subjects with a history of serious head trauma or health conditions precluding a laboratory visit or the ability to perform the experimental tasks (e.g., severe visual impairment or mental retardation) were excluded. The study was approved by Washington University Institutional Review Board, and written informed assent and consent were obtained from adolescent participants and their parents, respectively, after complete description of the study to the subjects and their parents.