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Loss aversion and 5HTT gene variants in adolescent anxiety☆

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ABSTRACT

Loss aversion, a well-documented behavioral phenomenon, characterizes decisions under risk in adult populations. As such, loss aversion may provide a reliable measure of risky behavior. Surprisingly, little is known about loss aversion in adolescents, a group who manifests risk-taking behavior, or in anxiety disorders, which are associated with risk-avoidance. Finally, loss aversion is expected to be modulated by genotype, particularly the serotonin transporter (SERT) gene variant, based on its role in anxiety and impulsivity. This genetic modulation may also differ between anxious and healthy adolescents, given their distinct propensities for risk taking. The present work examines the modulation of loss aversion, an index of risk-taking, and reaction-time to decision, an index of impulsivity, by the serotonin-transporter-gene-linked polymorphisms (5HTTLPR) in healthy and clinically anxious adolescents. Findings show that loss aversion (1) does manifest in adolescents, (2) does not differ between healthy and clinically anxious participants, and (3), when stratified by SERT genotype, identifies a subset of anxious adolescents who are high SERT-expressers, and show excessively low loss-aversion and high impulsivity. This last finding may serve as preliminary evidence for 5HTTLPR as a risk factor for the development of comorbid disorders associated with risk-taking and impulsivity in clinically anxious adolescents.

1. Introduction

Loss aversion is a classical concept in behavioral economics (Kahneman and Tversky, 1979). Indeed, a prominent theoretical account of economic decision-making, Prospect Theory (Kahneman and Tversky, 1979), indicates that people are more sensitive to losses than gains, typically by a factor of two (Novemsky and Kahneman, 2005). Loss aversion is traditionally measured using a series of mixed gambles that vary in magnitude of potential gains and losses. It is computed as the ratio (lambda) of the contribution of loss magnitude to that of gain magnitude to the subject's decision (e.g., Tom et al., 2007). This mathematically modeled, extensively studied behavioral characteristic appears highly reliable in adults. It captures an aspect of risk-avoidance and, its converse, risk-taking, both, of which are particularly relevant to adolescence and anxiety.

Adolescence is a unique time in life, when developmental factors might have opposing effects on loss aversion. On the one hand, adolescents experience a peak in their risk-taking behavior (Spear, 2000), which, at face value, could be associated with low levels of loss aversion (Kahneman and Lovallo, 1993). Thus, adolescence might be expected to signal low levels of loss aversion. On the other hand, adolescence also is a time when anxiety increases, and

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prior research links anxiety to risk avoidance (Lorian and Grisham, 2010; Maner et al., 2007; Mueller et al., 2010), which could be associated with high levels of loss aversion. Taken together, these two sets of contrasting findings raise major questions on the way in which loss aversion manifests in adolescents, in general, as well as in adolescents with *high* levels of anxiety. At present, only one study has compared loss aversion in adolescents and adults, and this study failed to detect differences in the measure of loss aversion, lambda, between these age groups (Barkley-Levenson et al., 2013). No studies have yet assessed the relationship between loss aversion and anxiety at any age.

Finally, anxiety is a heterogeneous set of clinical conditions, showing variable relationships to environmental risks, such as stress or trauma, and genetic factors. Particular interest has arisen concerning the relationship between anxiety and variation in the serotonin transporter (SERT) gene (Bengel et al., 1999; Gonda et al., 2009; Lesch et al., 1996; Sen et al., 2004). Understanding the contribution of genotype to anxiety is important because genetics may moderate relationships between anxiety and its neurobiological correlates (e.g., Pine et al., 2010; Xu et al., 2006). Accordingly, SERT variants could also moderate the relation of anxiety with loss aversion, a relation which, in the future, could be captured at the neural level in follow-up studies using functional neuroimaging tools.

This study tests four hypotheses. We expect that (1) adolescents would exhibit some degree of loss aversion, since loss aversion is a well-established phenomenon across adult populations (Novemsky and Kahneman, 2005); (2) Loss aversion would be higher in clinically anxious compared to healthy adolescents; (3) Loss aversion would be influenced by SERT gene variants. Specifically, we expect that high-expressers (LaLa carriers) would show lower levels of loss aversion based on the role of this gene variant in impulsive-related behaviors (e.g., Beitchman et al., 2003; Curran et al., 2005; Manor et al., 2001; Retz et al., 2008, 2002; Seeger et al., 2001; Zoroglu et al., 2002), relative to low-expressers (S/Lg carriers) who would manifest higher levels of loss aversion based on the role of this gene variant in anxiety and harm avoidance (e.g., Bengel et al., 1999; Gonda et al., 2009; Lesch et al., 1996; Sen et al., 2004). Similarly, we anticipate differences in reaction time to execute a decision involving risky options, such that fast reaction time, indicative of impulsivity, would characterize low loss-averse individuals, whereas long reaction time would characterize high loss-averse individuals. Finally, (4) we expect that genotype would moderate the relationship between anxiety and loss aversion (lambda), emerging in an interaction between diagnosis and genotype.

2. Methods

2.1. Participants

A total of 66 Caucasian adolescents, 27 with an anxiety disorder and 39 healthy comparisons were assessed on the Loss Aversion task, a paradigm of mixed monetary gambles (Tom et al., 2007). Most patients carried more than one anxiety disorder, as delineated in Table 1. In addition, five patients met another non-anxiety comorbid diagnosis (see Table 1).

Table 1
Distribution of diagnoses (a) in the anxious adolescents as a whole and (b) by genotype. As expected based on comorbid anxiety disorders, the total numbers of diagnoses exceed the size of each sample. For example, the high-expresser sample includes 9 subjects, while the total number of diagnoses amount to 11. Two high-expresser subjects had 2 anxiety diagnoses. GAD, Generalized Anxiety Disorder; SocPh, Social Phobia; SAD, Separation Anxiety Disorder.

(a)

	Total		Comorbidity
GAD	16	GAD-only	12
		GAD/SAD/SocPh	2
		GAD/SAD	2
SocPh	7	SocPh-only	4
		Soc-Ph/SAD	1
SAD	11	SAD-only	6

(b)

Patients	GAD	SocPh	SAD
High expressers ($n=9$)	4 (44.4%)	1 (11.1%)	6 (66.7%)
Low expressers ($n=18$)	12 (66.7%)	6 (33.3%)	5 (27.8%)

Participants were recruited through local newspaper advertisements and word of mouth, and the study was approved by the National Institute of Mental Health Institutional Review Board. The group of anxious adolescents was recruited for a treatment study of anxiety, and the comparisons were recruited from the same community. For the participants enrolled in the treatment study of anxiety, the task was completed during an initial research period prior to treatment entry. The parents of all children gave informed consent, and minors gave informed assent.

Inclusion criteria for comparisons comprised (1) age between 8 and 17 years; (2) absence of acute or chronic medical problems; and (3) absence of current or past psychiatric disorders. Inclusion criteria for anxious youths included: (1) primary diagnosis of an anxiety disorder based on a semi-structured diagnostic interview (K-SADS; Kaufman et al., 1997) completed by a trained clinical psychologist; (2) desire for outpatient treatment; (3) age between 8 and 17 years. Exclusion criteria for all participants consisted of (1) current use of any psychoactive substance; (2) current Tourette's syndrome, obsessive-compulsive disorder, PTSD, conduct disorder, exposure to extreme trauma, or suicidal ideation; (3) lifetime history of mania, psychosis, or pervasive developmental disorder; or (4) IQ < 70.

2.2. Assessment tools and genotyping

IQ was measured using the vocabulary and matrix reasoning subscales of the Wechsler Abbreviated Scale of Intelligence (WASI; Weschler, 1999). Socioeconomic status was obtained through parental report and calculated based on Hollingshead's index of social position for education and Hollingshead's categories for employment (Hollingshead, 1975). The parent and child version of the Screen for Child Anxiety Related Emotional Disorders (SCARED; Birmaher et al., 1997; Muris et al., 1999) were collected, and the