Anxiety and Gender Influence Reward-Related Processes in Children and Adolescents

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Abstract

Objective: This study examined the effects of pediatric anxiety and its interaction with gender on reward processes. Based on the purported greater sensitivity to risk in females than males and the propensity for risk aversion in anxiety, clinical anxiety and female gender were hypothesized to act synergistically in reducing reward sensitivity and increasing risk aversion in a pediatric population.

Methods: This hypothesis was tested in two separate experiments using two independent samples. Both experiments compared clinically anxious with typically developing (TD) youth, 8–18 years. Experiment 1 used a decision-making task, the Wheel of Fortune task (WOF), to examine risk taking as a function of varying levels of risk and reward in 36 anxious and 61 TD youths. Experiment 2 used an incentive delay task, the Piñata task, to examine sensitivity to reward and motivation to work for a reward in 38 anxious and 30 TD youth. Percent bet, reaction time, and accuracy were analyzed as a function of gender and diagnostic group.

Results: As hypothesized, anxiety was associated with reduced risk taking and sensitivity to reward. However, contrary to prediction, this effect was seen in males and not in females. These findings are consistent across both experiments. In experiment 1 (WOF), betting rate (i.e., risk taking) was significantly lower in anxious than in TD males ($F[1;53] = 7.07$, $p = 0.01$), whereas anxious females did not differ from TD females ($F[1;42] = 1.2$, $p = 0.28$). In experiment 2 (Piñata), anxiety impaired performance accuracy in males ($F[1;36] = 8.39$; $p < 0.01$) but not females ($F[1;28] = 0.6$; $p = 0.445$).

Conclusions: Anxiety affected reward function differently in males and females. Contrary to hypothesis, anxious females behaved similarly to TD females on both tasks. However, anxious males were significantly more risk averse and less accurate than TD males. These findings suggest that therapeutic interventions for anxiety, which use manipulations of reward processes, should consider gender for optimal outcome.

Introduction

CHILDHOOD AND ADOLESCENCE ARE CRITICAL PERIODS for the development of anxiety symptoms (Beesdo et al. 2009). Pediatric anxiety disorders are the most prevalent psychiatric disorders in this age group (Beesdo et al. 2009) and predict adult psychopathology, notably anxiety disorders and depression (Silk et al. 2012; Ginsburg et al. 2014). Although behavioral research on anxiety has focused for the most part on attention bias and threat learning (Britton et al. 2011; Cisler and Koster 2012; Shechner et al. 2012, 2014), other processes, such as reward processes, are beginning to be examined (Jazbec et al. 2005; Hardin et al. 2007a; Bar-Haim et al. 2009; DeVido et al. 2009; Paulus and Yu 2012; Silk et al. 2012). The present study addresses reward processes in the context of pediatric anxiety. Reward processes determine motivated behavior. Several aspects of motivated behavior have been associated with anxiety and include risk aversion, intolerance of uncertainty, and altered sensitivity to incentives. In addition, gender has been shown to modulate both risk aversion and sensitivity to

incentives, and may interact with anxiety on incentive-related responses. Risk aversion, intolerance of uncertainty, sensitivity to incentives, and gender, are briefly reviewed in relation to reward processes in anxiety.

Anxiety has been characterized by decision-making bias (e.g., risk aversion) (Maner and Schmidt 2006; Maner et al. 2007; Lorian and Grisham 2010, 2011; Lorian et al. 2012a,b) and deviant responses to incentives (i.e., reward or punishment) (Hardin et al. 2007a; DeVido et al. 2009; Hardin et al. 2009; Goschke 2014). Risk aversion refers to individual differences in the motivation to act in the face of uncertainty (Tversky and Kahneman 1974). In the laboratory, risk aversion is often assessed via betting tasks, and is measured as the individual's willingness to accept a bargain when presented with bets of various outcome values and levels of risk. Risk aversion is influenced by individual differences in sensitivity to incentives (subjective values placed on rewards/punishments) and costs of uncertainty. For example, anxious individuals might avoid placing bets, because they are less motivated by reward or more deterred by potential punishment, compared with unanxious

individuals. Alternatively, they might appreciate the value of the reward, but avoid taking an action in the context of uncertainty, a behavior referred to as intolerance to uncertainty.

Even though risk aversion is held as a hallmark of motivated behavior in anxiety (Maner and Schmidt 2006; Maner et al. 2007; Carleton 2012; Carleton et al. 2012; Giorgetta et al. 2012), formal investigations of this pattern of risk-related decision making in anxiety have revealed inconsistent results. For example, studies using gambling tasks, such as the Iowa Gambling Task (IGT) and its modified versions (Bechara et al. 1994), reported that young adults with high trait-anxiety (Werner et al. 2009), generalized anxiety disorder (GAD), or panic disorder (Maner et al. 2007; Giorgetta et al. 2012) were more risk averse than their unanxious counterparts. However, other studies were inconsistent with these findings. Specifically, adults characterized as high worriers did not differ from non-worriers on risk avoidance (Drost et al. 2014). Additional complexity emerged in a study of a nonclinical sample of adolescents performing a risk-related decision-making task (Lejuez et al. 2002). In this study, it was the interaction between social stress and social anxiety that determined decision making; that is, adolescents with high social anxiety made more risky decisions under social stress than no stress, whereas adolescents with low social anxiety were not influenced in their pattern of risk-related decision-making by social stress (Reynolds et al. 2013). These discrepant findings suggest that the factors mediating the interactions of anxiety with risk avoidance are complex. The mediating factors might include differences in sample characteristics (e.g., clinical vs. subclinical anxiety, age, gender), the context in which the tasks were administered (e.g., social, stressful context), or the type of incentive (e.g., reward vs. punishment), as well as other variations in task design. The present study aimed to address these discrepancies by 1) taking into account gender differences, and 2) examining risk aversion and sensitivity to incentives in two independent tasks and two independent samples.

Sensitivity to incentives is another aspect of decision making that is affected by anxiety. Here, we define "sensitivity to incentives" as the influence of incentives on cognitive performance (Bonner and Sprinkle 2002). Accordingly, larger incentives typically promote better cognitive performance. The more sensitive an individual is to incentives, the greater is the improvement in that individual's performance for a given incentive. This incentive-dependent improvement in cognitive performance might be caused, in part, by increased motivation in the presence of higher potential reward. It is of note that improved attention in the presence of a larger reward could also contribute to performance improvement.

Accumulating evidence suggests that anxiety alters the influence of incentives on cognitive performance. In two earlier behavioral studies, we reported that incentives were less effective at improving cognitive performance in anxious than in typically developing (TD) adolescents (Jazbec et al. 2005; Hardin et al. 2007b). Taken together, this research not only predicts decreased sensitivity to rewards at the behavioral level in anxious versus unanxious individuals, but also suggests variability in this pattern, perhaps related to task parameters and/or sample characteristics, such as gender.

Gender has emerged as an important modulator of both risk-related decision making and anxiety. Studies suggest that female gender, similarly to anxiety, is associated with increased risk aversion (Larkin and Pines 2003), decreased sensation seeking (Cross et al. 2011), decreased sensitivity to rewards (Li et al. 2007; Cross et al. 2011), and increased sensitivity to punishment (Moeller and Robinson 2010; Cross et al. 2011). In addition, female gender represents one of the main risk factors for developing an anxiety disorder in

one's lifetime (Bekker MH and Mens-Verhulst 2007). Therefore, literature suggests the likelihood of significant interactions among gender, anxiety, and risk aversion and/or incentive sensitivity. To our knowledge, no studies have yet investigated the nature of these interactions in clinically anxious pediatric populations.

The present work addresses these questions in two separate experiments, using two independent samples of clinically anxious and TD children and adolescents. In Experiment 1 (Wheel of Fortune [WOF] task), we examined risk aversion (percent bet) as a function of the estimated value of the bet and the level of risk. In this task, we predicted less willingness to bet (e.g., increased risk aversion) in anxious than in TD youths. We also predicted that female participants would demonstrate greater risk aversion than males. Finally, we expected a synergistic effect of anxiety and female gender on betting behavior, yielding the highest degree of risk avoidance in anxious females. Experiment 2 (Piñata task) focused specifically on reward sensitivity using a reaction-time task that examined motivation to earn reward as a function of reward magnitude. We expected lower sensitivity to rewards in anxious than in TD youth, as indexed by lower accuracy and longer reaction time. We also expected females versus males to show a pattern similar to the anxious versus TD group, resulting in the most deviant behavior in anxious female participants.

Experiment 1 – Risk-Related Decision Making: WOF Task

Methods

Participants. Participants were recruited through local newspaper advertisements and word of mouth. The study was approved by the National Institute of Mental Health Institutional Review Board. All participants provided informed assent and participant's guardians provided informed consent.

Inclusion criteria for TD youth included: 1) Being between 8 and 18 years of age, 2) absence of acute or chronic medical problems, and 3) absence of current or past psychiatric disorders. Inclusion criteria for anxious youth included: 1) Primary diagnosis of an anxiety disorder based on a semistructured diagnostic interview (Kiddie-Schedule for Affective Disorders and Schizophrenia [K-SADS]) (Kaufman et al. 1997), 2) desire for outpatient treatment, and 3) being between 8 and 18 years of age. Additional self-report anxiety data were collected with the Screen for Child Anxiety Related Emotional Disorders (SCARED) (Birmaher et al. 1997). Because our ultimate goal was to understand biological correlates that are relevant to treatment, we used desire for outpatient treatment as part of the inclusion criteria for anxious youth, to ensure that the sample population is relevant to treatment.

Exclusion criteria for all participants included: 1) Current use of any psychoactive substance; 2) current Tourette's syndrome, obsessive-compulsive disorder, posttraumatic stress disorder, conduct disorder, exposure to extreme trauma, or suicidal ideation; 3) lifetime history of mania, psychosis, or pervasive developmental disorder; and 4) intelligence quotient (IQ) <70, as measured by the Wechsler Abbreviated Scale of Intelligence (WASI) (Clements 1965; Axelrod 2002). Socioeconomic status (SES) (Haro et al. 2006) was obtained through parental report, and calculated on the basis of the Hollingshead's index of social position for education and employment (Hollingshead 1970). All diagnoses were determined via a K-SADS semistructured interview with the child and the parent (Kaufman et al. 1997). Interviews were conducted by senior clinicians who specialized in pediatric psychiatric interviews, and demonstrated excellent interrater reliability ($\kappa > 0.75$).

TABLE 1. SAMPLE CHARACTERISTICS

<i>WOF task sample characteristics</i>						
	<i>TD</i>		<i>Anxious</i>		<i>Diagnostic group diff</i>	<i>Sex diff</i>
	<i>Male</i>	<i>Female</i>	<i>Male</i>	<i>Female</i>		
<i>n</i>	35	26	19	19		
<i>Age</i>	12.53 (0.5)	12.77 (0.49)	12.12 (0.54)	11.75 (0.54)	$F(1,98)=1.8; p=0.18$	$F(1,98)=0.02; p=0.9$
<i>IQ</i>	114.61 (2.3)	111.46 (2.2)	113.47 (2.4)	114.42 (3.1)	$F(1,96)=0.119; p=0.73$	$F(1,96)=0.181; p=0.7$
<i>SES</i>	41.44 (4.04)	45.88 (4.4)	40.31 (4.9)	35.23 (4.14)	$F(1,80)=1.6; p=0.2$	$F(1,80)=0.01; p=0.95$
<i>SCAREDpc</i>	6.48 (0.77)	7.59 (1.11)	32.81 (1.5)	33.7 (3.02)	$F(1,96)=188.7; p<0.001$	$F(1,96)=0.002; p=0.97$
<i>Piñata task sample characteristics</i>						
	<i>TD</i>		<i>Anxious</i>		<i>Diagnostic group diff</i>	<i>Sex diff</i>
	<i>Male</i>	<i>Female</i>	<i>Male</i>	<i>Female</i>		
<i>n</i>	16	14	22	16		
<i>Age</i>	12.3 (0.5)	11.96 (0.76)	12.18 (0.52)	12.08 (0.75)	$F(1,67)=0; p=0.9$	$F(1,67)=0.12; p=0.74$
<i>IQ</i>	114.00 (2.8)	114.21 (3.2)	109.00 (2.7)	110.25 (2.7)	$F(1,67)=2.4; p=0.128$	$F(1,67)=0.06; p=0.8$
<i>SES</i>	49.8 (7.2)	34.91 (4.8)	37.41 (3.4)	44.80 (7.05)	$F(1,60)=0.05; p=0.8$	$F(1,60)=0.43; p=0.5$
<i>SCAREDpc</i>	7.5 (1.6)	6.45 (2.4)	32.81 (1.5)	32.58 (2.4)	$F(1,63)=168; p<0.01$	$F(1,63)=0.12; p=0.75$

Subject groups did not differ on age, IQ, and SES. Anxious and TD groups differed significantly on anxiety symptom scores. Within each diagnostic group there were no gender differences in anxiety symptom scores. Means and standard deviations are reported for age, IQ, SES and SCAREDpc.

WOF, Wheel of Fortune; TD, typically developing; IQ, intelligence quotient; SES, socioeconomic status; SCAREDpc, Screen for Child Anxiety Related Emotional Disorders, pediatric anxiety rating scale, child and parent responses are averaged.

Interrater reliability is established in a three step process. In a first step, each expert clinician is trained through a series of didactic classes and interviews performed with another senior clinician. This is then followed by an independent rating by the interviewer and another expert of a series of 20 tapes, where a minimal threshold of $\kappa > 0.70$ must be met for this set of standard interviews. In the second step, each interview performed by the clinician is taped on an ongoing basis, and a randomly selected sample of 10% is reviewed by another expert clinician. Finally, each case is seen by two clinicians in two visits, separated by at least a week, and these clinicians derive independent diagnoses. Potential reasons for discrepancies are discussed in the group.

Additional anxiety and depression self-reports were collected using the State Trait Anxiety Inventory (STAI) (Spielberger and Vagg 1984), and the Children's Depression Inventory (CDI) (Kovacs 1985), respectively.

Anxious and TD participants were matched on age, SES, and IQ. The final sample included 99 participants (mean age 12.3 years), 61 TD (35 males) and 38 anxious subjects (19 males). The lowest IQ in this sample was 88. Demographics are listed in Table 1. Diagnoses are reported in Table 2.

WOF task. The WOF task (Roy et al. 2011) was designed to measure decision making under conditions of uncertainty. Participants were asked to decide between betting and passing. By betting, participants took the risk of losing points, in order to have a chance at gaining points. By passing, participants selected the safe option, which offered no risk of loss, but also no chance of gain. The task consisted of the presentation of wheels, each divided into two sections of different colors (pink and yellow) (Fig. 1A). The colors designated gain or loss conditions (e.g., pink for gain, and yellow for loss). This rule was maintained throughout the task for a given participant. In the present study, half of the participants

played the task with pink as the winning condition, and half with yellow as the winning condition.

Each section of the wheels also contained a number. This number represented the number of points that could be won or lost if the participant chose to bet. The task included six types of wheels, which differed from one another on the level of risk (probability of winning/probability of losing: 100/0, 0/100, 40/60, or 60/40) and the overall value (i.e., expected value [EV]: +12 or -12). Two wheels were no-risk (100/0 and 0/100), and four wheels were risky. There were two high-risk wheels (40/60 with positive EV [EV+] and 40/60 with negative EV [EV-]) and two low-risk wheels (60/40 with EV+, 60/40 with EV-). Each of the risky wheels was presented 22 times, and each of the no-risk wheels was presented 8 times.

The order of wheels was randomized across the whole task. EVs were not discussed with the participants. However, the participants were told that the points printed on each section of the wheels represented dollar values that could be won or lost. Participants were asked to bet (press "1") or pass (press "2") on every wheel presented. The wheel then spun. An arrow on the outside of the wheel indicated which section had been "landed" on. Participants

TABLE 2. DIAGNOSES IN THE WHEEL OF FORTUNE AND PIÑATA TASK ANXIOUS GROUPS

<i>Diagnosis</i>	<i>WOF task</i>	<i>Piñata task</i>
GAD	22	27
Social phobia	13	23
SAD	13	10
MDD	5	1

GAD, generalized anxiety disorder; SAD, separation anxiety disorder; MDD, major depressive disorder; WOF, Wheel of Fortune.

FIG. 1. Wheel of Fortune Task (WOF) and Piñata tasks. **(A)** On the WOF task, subjects were presented with six wheels that varied in the win and loss probabilities. Subjects were given an opportunity to bet or pass. Wheels 1 and 2 were no-risk comparison. Wheels 3–6 had fixed win amount but varied in win probability and loss probability and loss amount. Expected value (EV) was fixed as 12 and –12. **(B)** Piñata task is composed of four stages: Cue, anticipation, motor response, and feedback. During the cue stage, subjects saw a piñata containing a number of stars (0, 1, 2, or 4). In the anticipation stage, the piñata disappeared and subjects waited for its reappearance. In the response stage, the piñata returned and subjects had an opportunity to make a response by pressing a button as fast as possible to hit the piñata. In the outcome stage, the piñata appeared either broken (successful hit) with the stars falling into a basket (reward) or flying in the sky (unsuccessful hit).

gained points if they bet and the arrow landed on the “win” section of the wheel. They lost points if the arrow landed on the “lose” section. Choosing to pass resulted in neither a gain nor loss of points. The decision-making period was 3 seconds. If participants did not indicate a choice in the allotted time, the trial was assigned its loss value. This strategy was used to encourage participants to make a choice rather than default.

Task rules were explained to the participants and they were trained on the task to make sure that they correctly understood the rules. However, the probabilities were not explained to them, because we were interested in the implicit strategy of the decision making. In addition, participants were told that they could earn money depending upon their performance on the WOF, whereas in fact, every participant earned \$5. The measures of the risk-taking performance on the WOF included 1) percent bet and 2) reaction time (RT).

Data analysis. Only valid trials (RTs >200 ms) were analyzed. Risky trials were analyzed separately from no-risk trials. A linear mixed model analysis using SPSS was applied to percent bet and RT. Percent bet was analyzed as a function of level of risk (risk-level: 40%, 60%), EV of the trial (EV: +12, –12), diagnostic group (anxious, TD), and gender (male, female). The analysis of reaction time tested the influence of two additional factors, trial order and

decision type (bet vs. pass). Trial order defined the position of the trial in the task for each type of stimulus (e.g., “1” was the first trial to be presented and “22” the last one). This factor was used to control for the observation that reaction time consistently decreased as the trials progressed and participants became more familiar with the task. Significant effects were set at $p < 0.05$.

For the no-risk trials, we expected participants to always bet on the 100% win probability and always pass on the 100% lose probability. Accordingly, for the entire sample, participants bet incorrectly only 18 times (out of the 1568 no-risk trials). These incorrect no-risk trials were filtered out of the analysis, as they indicated attention lapses. In addition, decision type and percent bet did not vary in the no-risk trials (all bets in 100/0, and passes in 0/100 trials). Therefore, percent bet was not analyzed in no-risk trials. However, RT for no-risk trials was examined separately using a three way (diagnosis, gender, and risk-level) linear mixed model.

Results

WOF task: Analysis of percent bet on risky trials. Betting rate (percent bet), a measure of risk-related behavior, was analyzed as a function of diagnosis, gender, the estimated value of the bet (+12=high EV, –12=low EV), and the level of risk (40/60=high risk, 60/40=low risk). We hypothesized that anxious females would

be least likely to bet (i.e., most risk avoidant) on the highest risk bets; that is, high risk wheels with low EV. In addition, we predicted that 1) percent bet would be lower in anxious than TD youth, 2) percent bet would be lower in females than males, and 3) percent bet would be higher on low risk trials and on higher EV trials.

The four way (risk-level, EV, diagnosis, gender) linear mixed model analysis of percent bet revealed two significant interactions. First, there was a three way interaction (risk-level by diagnosis by gender: $F[1, 285] = 9.015$; $p = 0.003$). Second, there was a two way (diagnosis by gender: $F[1, 53] = 7.07$, $p = 0.01$) interaction. Finally, there was a main effect of EV ($F[1, 285] = 21.9$; $p < 0.01$) and a main effect of risk-level ($F[1, 285] = 137.9$; $p < 0.01$).

The three way interaction was decomposed by risk-level. Accordingly, a two way (diagnosis by gender) ANOVA was conducted for high and low risk levels separately (Fig. 2).

For the low-risk trials, the gender by diagnosis interaction was not significant.

For the high-risk trials, the gender by diagnosis interaction was significant ($F[1, 95] = 8.72$; $p < 0.01$). Post-hoc analysis of this interaction revealed that anxious males bet significantly less than TD males ($F[1, 53] = 7.3$; $p < 0.01$). In addition, these anxious males bet significantly less than anxious females ($F[1, 36] = 4.3$; $p = 0.05$). Percent bet did not differ between anxious females and TD females. However, on visual inspection of Figure 2, anxious females, relative to TD females, might have been somewhat more likely to bet under high-risk conditions. Finally, within the TD group, percent bet did not differ between males and females, although Figure 2 evidences lower percent bet in TD females than TD males.

The overall two way (diagnosis by gender) interaction showed that anxious males bet less than TD males ($F[1, 53] = 7.07$, $p = 0.01$), whereas anxious females did not differ from TD females

($F[1, 42] = 1.2$, $p = 0.28$). However, this two way interaction was subsumed under the three way interaction reported.

The main effects were that as expected and by task design, youth bet more frequently on the low-risk than high-risk trials (main effect of risk level), and on the positive than on the negative EV trials (main effect of EV), similarly to previously reported findings in healthy adults (Roy et al. 2011). As reported earlier and on visual inspection of Figure 3A, percent bet appeared to be more sensitive to the risk level than to the EV.

WOF task: Analysis of RT on risky trials. RT was analyzed as a function of diagnosis, gender, decision-type (bet vs. pass), the estimated value of the bet (+12 = high EV, -12 = low EV), and the level of risk (40/60 = high risk, 60/40 = low risk).

Faster RT was expected to characterize responses to less conflictual trials; that is, low risk and high EV trials. In addition, we expected slower RT to bet in anxious subjects and in females, because of purportedly enhanced behavioral inhibition in these groups, resulting in the slowest RT in anxious females.

The five way (risk level, EV, decision type, diagnosis, gender) mixed model analysis revealed the following significant effects: 1) A four way (gender by diagnosis by decision type by EV) interaction, 2) main effect of risk level, and 3) main effect of decision type.

The four way interaction ($F[1, 7376.8] = 4.75$; $p = 0.029$) is depicted in Figure 4. Post-hoc tests revealed that this interaction was mainly driven by TD males, who, in the negative EV trials (EV = -12), showed exaggerated sensitivity to their decision (i.e., slower to pass and faster to bet) relative to the other three groups (see Fig. 4).

The main effects were that as expected, all subjects responded significantly faster to the low risk trials than to the high risk trials, as

FIG. 2 Effect of gender, diagnostic group, and risk-level on percent bet in Wheel of Fortune (WOF) task. On high risk level wheels, anxious males were significantly less likely to bet than typically developing (TD) males ($F[1, 53] = 7.3$; $p < 0.01$). There was no statistically significant diagnostic group difference for females. In the TD group, there was no statistically significant effect of gender. In the anxiety group, females were significantly more likely to bet than males ($F[1, 36] = 4.3$; $p = 0.05$). On low risk level wheels, there were no group or gender effects on percent bet.

FIG. 3. Effects of risk-level and expected value (EV) on percent bet and reaction time (RT) in Wheel of Fortune (WOF) task. **(A)** Percent bet was influenced by risk level ($F[1, 285]=137.9$; $p<0.01$) and EV ($F[1,285]=21.9$; $p<0.01$) of the wheel. As predicted, youth bet more frequently on the low risk level than on the high risk level trials and on the positive than on the negative EV trials. **(B)** RT was significantly influenced by risk level, but not EV. Subjects responded significantly faster to low risk level trials ($F[1, 7396]=24.7$; $p<0.01$).

evidenced by the significant main effect of risk level ($F[1, 7396]=24.7$; $p<0.01$) (Fig. 3). The model also revealed the expected main effect of decision type (faster RT to bet than to pass ($F[1, 7446]=97.8$; $p<0.01$). Unlike percent bet, RT was not influenced by EV.

WOF task: Analysis of RT on no-risk trials. The three way (EV by diagnosis by gender) mixed model analysis revealed no interactions. However, a significant main effect of diagnosis ($F[1, 93.1]=4.6$; $p=0.03$) showed that RT was slower in anxious than in TD participants. Additionally, a main effect of EV ($F[1, 1349]=42.8$; $p<0.01$) indicated shorter RT to positive than negative EV trials.

WOF task: Discussion

The WOF task assessed risk-related decision making by manipulating probability and magnitude of incentives. Findings are twofold. First, they validate the task in a pediatric population, and

second, they provide evidence for a differential effect of anxiety on decision making as a function of gender.

First, the experiment replicated in a pediatric sample the findings obtained in a previous study with adults using the same task (Roy et al. 2011). Regarding the risky trials, as previously reported and expected, the most appealing trials; that is, the low risk-level and high EV trials, generated the highest betting rate and fastest RT (Fig. 3). In addition, betting behavior was modulated by risk level more strongly than by EV. This finding was previously reported (Roy et al. 2011) and may reflect a generally greater sensitivity to reward probability than to reward magnitude. Similarly to prior reports, we found that all subjects were faster to bet than to pass on all trials (Britton et al 2012). This finding suggests that, in general, approach behavior, indexed here by the decision to bet, tends to be less conflictual and more motivating or arousing than avoidance behavior, indexed by the decision to pass.

Second, anxiety affected betting behavior, but this effect was significantly modulated by gender and risk-level. The effects of anxiety were observed only in males and only in the high-risk condition. Specifically, percent bet did not significantly differ among groups in low risk level trials (Fig. 2). However, in high risk level trials, group differences emerged. Contrary to our hypothesis, anxiety increased risk avoidance in males but not in females. Anxious males chose to pass (were more risk avoidant) significantly more frequently than did TD males, whereas anxious females did not differ from TD females. In other words, anxious males were more sensitive to making a risky decision than TD males, as if they anticipated more losses or were less motivated to seek gains.

The null finding in females can be interpreted in three ways. First, it may reflect the similarities between anxiety and female gender, resulting in reduced range of outcomes in females. In contrast, the range of outcomes may be larger for males, allowing for differences to be observed. Second, the absence of an anxiety effect in females might reflect a ceiling effect. Anxiety might not be able to potentiate the already relatively elevated level of risk avoidance that is purportedly typical of females, relative to males (Powell and Ansic 1997; Larkin and Pines 2003). These interpretations are not supported by the data, which did not show significantly higher risk avoidance in TD females than in TD males. In addition, on visual examination, Figure 2 suggests that anxious females might be somewhat less risk avoidant than TD females, although this comparison was not significant. Finally, anxious females were significantly less risk avoidant than anxious males. Therefore, these data support the third possibility that anxiety affects risk-related decision making differently in females than in males; that is, qualitatively and not just to a lesser degree.

Similarly to percent bet, anxiety modulated RT, and this effect was significantly influenced by gender and by the value of the trial (EV). It emerged only in males, and only in the low-value (EV-) trials. In these trials, TD males were most extreme in their RT to betting (faster RT) versus passing (slower RT). This suggests that the change in the level of arousal/motivation associated with betting versus passing was reduced in anxious males, which could be framed as reflecting a relatively weaker motivation (slower) to approach and a relatively stronger motivation (faster) to avoid.

In sum, anxiety was associated with altered risk-related decision making only in males. These findings are novel in the context of a risk-taking task in pediatric anxiety. However, they are consistent with prior findings in young adults, on a different decision-making task, the IGT (Bechara et al. 1994). On this task, the male patients with GAD were the most extreme group (versus TD males and females) at avoiding the risk of high losses (Mueller et al. 2010).

FIG. 4. Effects of expected value (EV), diagnostic group, gender, and decision-type on reaction time (RT) in the Wheel of Fortune (WOF) task. For RT, the five way (risk-level, EV, decision type, diagnosis, gender) mixed model analysis revealed a four way gender by diagnosis by decision-type by EV interaction ($F[1, 7376.8]=4.75$; $p=0.029$). Post-hoc tests indicated that this interaction was mainly driven by typically developing (TD) males, who, in the negative EV trials ($EV=-12$), showed exaggerated sensitivity to decision type (i.e., slower to pass and faster to bet) relative to the other three groups.

The WOF task pitted probabilistic losses against probabilistic gains, making it difficult to dissociate the effects of gains versus losses on patterns of decision making. The second experiment was designed to selectively examine responses to gains (positive incentives). Based on findings of Experiment 1, we expected TD males to be more sensitive to incentives than any of the other groups.

Experiment 2 – Sensitivity to Reward: The Piñata Task

Methods

Participants. Participant recruitment and inclusion and exclusion conditions were the same as those used for Experiment 1. The sample, independent from the Experiment 1 sample, consisted of 68 youth, 30 TD (16 males) and 38 anxious subjects (22 males). The average age of the participants was 12.12 years. The TD and anxiety groups were similar on age, IQ, and SES. The lowest IQ in this sample was 90. More detailed demographics are listed in Table 1B and diagnoses are detailed in Table 2.

Piñata task. The Piñata task is a pediatric version of the Monetary Incentive Delay task (MID) (Knutson et al. 2000). The task was designed to be visually appealing to children, and it has been previously validated for use in children as young as 8–9 years old (Helfinstein et al. 2013). Whereas the MID task uses white geometrical shapes as cues, the piñata task uses colored pictures of animals, similar to those of piñata games (Fig. 1B).

Similarly to the MID task, each trial of the Piñata task consisted of four stages: Cue, anticipation, motor response, and feedback. In the cue stage, subjects were shown a piñata containing a certain number of stars (0, 1, 2, or 4) to indicate the magnitude of the potential reward (larger reward with more stars). In the anticipation stage, the piñata disappeared, and subjects waited for its re-

appearance to make a response. In the response stage, the piñata returned, and subjects had an opportunity to press a button as fast as possible to hit the piñata. Successful hit was operationalized as pressing the button within the target period, while the target was on the screen. In the outcome stage, the piñata appeared either broken (successful hit) with the stars falling into a basket (reward), or flying into the sky (unsuccessful hit) (Fig. 1B). Subjects were told to press the button as quickly as possible to break the piñata and earn the stars. They were also told that the number of stars they earned during the task would determine the size of the monetary reward (up to \$15) that they would receive at the end of the task.

The task timing followed standards established for the most commonly employed versions of the MID task (Knutson et al. 2000). The cue appeared for 1500 ms, followed by a cue-free anticipatory period that varied between 1000 and 2000 ms. The target appeared for variable periods of time, followed by a delay period. The duration of the target period and delay period amounted to a total of 1500 ms. Finally, the feedback appeared for 1500 ms.

Task difficulty was initially calibrated to each individual participant in order to equalize the level of difficulty among participants. The calibration was done once, using an initial 22 trial practice run, during which target duration varied between 250 and 300 ms. For subjects with accuracy rates between 55% and 80%, the target duration was left unchanged (250 and 300 ms). For subjects with better performance (> 80% accuracy), target duration was set to 200–250 ms, and for subjects with worse performance (< 55% accuracy), it was set to 300–350 ms.

Once target duration level was determined, subjects performed six runs of 22 trials each, for a total of 132 trials. Trials were divided evenly among the four incentive levels: 0 star, 1 star, 2 stars, and 4 stars, for a total of 33 trials at each incentive level. Trial types were fully randomized across the task. The total duration of the task was 15 minutes.

Data analysis. To examine the influence of clinical anxiety and gender on behavioral responses to reward cues, a $4 \times 2 \times 2$ (star value $\times$ diagnosis $\times$ gender) repeated measures ANOVA (rANOVA) was conducted on accuracy (the proportion of successful trials divided by all valid trials) and RT (RT to correct trials). We limited RT analysis to correct trials in order to filter out outliers caused by failure to pay attention to the task. Post-hoc analyses followed significant interactions.

Results

Piñata task focused specifically on reward sensitivity by probing motivation to earn a reward as a function of reward magnitude, diagnosis, and gender. We expected lower sensitivity to rewards in anxious versus TD youth, as indexed by lower accuracy and longer reaction time as well as a lesser improvement in cognitive performance with increasing rewards. We also expected females vs. males to show a pattern similar to the anxious vs. TD group, resulting in the most deviant behavior in the anxious female participants.

Piñata task: Analysis of accuracy of performance. The three way (diagnosis, gender, star value) rANOVA on accuracy revealed a significant two way diagnosis by gender interaction ($F[1;64] = 5.6; p = 0.021$). To be comprehensive, we examined this interaction in two ways. First, we decomposed the interaction by gender and examined the effect of diagnosis in males and females separately. Next, we decomposed this interaction by diagnosis, and looked at the effect of gender in the anxious and TD youth separately.

When decomposed by gender, accuracy was significantly affected by anxiety in males, but not in females. Specifically, anxious males performed significantly less accurately than TD males ($F[1;36] = 8.39; p < 0.01$), whereas anxious females did not differ in accuracy from TD females.

When decomposed by diagnosis, gender differences in accuracy were found in the TD group ($F[1, 28] = 13; p < 0.01$), but not in the anxiety group ($F[1, 36] = 0.28; p = 0.6$). In the TD group, females performed less accurately than males.

Finally, two main effects, star value and gender, emerged. As expected, the main effect of star value ($F[3;192] = 4.14; p < 0.01$) indicated better accuracy with larger rewards (Fig. 5). The main effect of gender showed that males were more accurate than females ($F[1;64] = 9.4; p < 0.01$). However, this effect was subsumed under the diagnosis by gender interaction (Fig. 6), which suggested that this main effect was mainly driven by the better performance of TD males.

Piñata task: Analysis of RT. The three way (diagnosis by gender by star value). rANOVA failed to reveal any significant effects on RT. It is of note that there was a trend for a main effect of diagnosis ($F[1;64] = 3.4; p = 0.07$), suggesting that anxious participants were slower than TD participants. An additional trend for gender ($F[1;64] = 3.9; p = 0.05$) suggested that males were faster than females.

Piñata: Discussion

Experiment 2 examined reward sensitivity on an incentive delay task probing accuracy and speed of performance as a function of reward magnitude. Based on prior research, we predicted lower sensitivity to rewards (star value) in the anxious youth than in the TD youth, indexed by a decreased accuracy and longer reaction

FIG. 5. Effect of star value on accuracy of response in the Piñata task. Accuracy of responses improved with increasing reward (increasing star-value) ($F[3;192] = 4.14; p < 0.01$).

time, and by a lesser improvement in performance as a function of increased rewards. We also expected females to perform worse than males, resulting in the most deviant behavioral pattern in anxious female participants.

Our findings differed from these predictions. With respect to accuracy, as predicted, gender significantly influenced the effect of diagnosis on performance. However, the most deviant behavioral patterns were found in the anxious males, not in females. Males with anxiety were significantly less accurate than TD males,

FIG. 6. Effect of gender and anxiety on accuracy of response in the Piñata task. Anxiety and gender interacted to affect accuracy in Piñata task ($F[1;64] = 5.6; p = 0.021$). Post-hoc tests showed that anxious males were less accurate than typically developing (TD) males ($F[1;36] = 8.39; p < 0.01$), but anxious females were as accurate as same-gender TD controls ($F[1;28] = 0.6; p = 0.445$). In addition, TD males performed significantly better than TD females ($F[1, 28] = 13; p < 0.01$). No gender differences were found in the anxious population ($F[1, 36] = 0.28; p = 0.6$).

whereas accuracy did not differ between anxious and TD females (Fig. 9). In addition, TD males were more accurate than all females. This finding echoed the results of Experiment 1, in which gender similarly modulated the effect of anxiety on the WOF task performance. The finding that TD males were the most accurate group in the Piñata task could be the result of enhanced sensitivity to incentives in TD male group, which translated into high motivation to win. This strong motivation to win might be dampened by anxiety in males. Alternatively, anxious males might be hypersensitive to reward, which could raise their arousal to a level that becomes disruptive to the task performance. Arousal has been shown to affect cognitive performance along an inverted U curve, such that performance improves with arousal up to an optimum point, after which individuals become overwhelmed, resulting in performance impairment (Baldi and Bucherelli 2005; Salehi et al. 2010). Therefore, it is conceivable that anxious males become overly aroused, passing the optimum point and exhibiting impaired performance. Unfortunately, we did not measure the level of arousal during task performance, which precluded us from testing this hypothesis. However, future research will include measures of arousal.

With respect to RT, only trends emerged for the main effects of diagnosis and gender. Anxious youth tended to be slower to respond than TD youth ($F[1;64] = 3.4$; $p = 0.07$).

The second trend indicated that males were faster than females, and this was true for both TD and anxious participants. This gender effect on RT might reflect gender differences in motor function (e.g., motor efficiency [Iverson et al. 2014]), environmental influences, such as higher prevalence of video gaming in males (Desai et al. 2010), or a combination of both.

Discussion (General)

This work compared clinically anxious youth with TD youth on two reward tasks: A decision-making task to probe risk-related decisions, and an incentive-delay task to probe sensitivity to incentives. Based on prior studies of risk and reward, we predicted greater risk avoidance and lower reward sensitivity in anxious than TD participants, and also in females than males. Because enhanced risk avoidance is expected to be amplified in both anxious subjects and females, we expected the findings in anxious subjects to be potentiated in females.

Findings on the risk-related decision-making task (WOF) showed the expected interaction of diagnosis by gender, but the interpretation of this interaction departed from predictions. Contrary to our hypothesis, males were the group that presented the most variability in their risk taking, being more affected by anxiety (See Fig. 2), and more sensitive to risk-related decisions (see Fig. 4). In our study TD females were not significantly less likely to bet than TD males. In addition, anxiety did not increase risk aversion in females. Interestingly, examination of Figure 2 suggests that anxious females might be slightly less risk averse than TD females, even though this comparison was not statistically significant. However, anxious females were significantly less risk averse than anxious males. These observations suggest that anxiety affects male and female risk-related decision making differently. The unexpected greater susceptibility of males to anxiety on the risk-related decision-making task was echoed on the Piñata task, in which anxious males' accuracy, but not anxious females' accuracy, was impaired (see Fig. 6) in comparison with TD same-gender controls.

This gender effect was present in two independent populations, even though severity of anxiety did not differ between females and males as measured by SCARED scores (see Table 1).

The null effect of gender on risk aversion in TD youth stands in contrast to existing literature, which supports higher risk aversion in females than males (Van Leijenhorst et al. 2008). Several possible reasons can be considered. First, the study sample consists of young subjects (12 years old). If increased risk aversion in females is caused by developmental changes associated with puberty, gender differences would not become apparent until later in adolescence. However, a prior study in healthy volunteers between 8 and 30 years of age showed that females were consistently more risk averse than males on a gambling task, independently of age (Van Leijenhorst et al. 2008). These findings argue against the influence of puberty on gender differences in risk aversion. In addition, they indicate that gender-related differences in decision making are established early in life, prior to the age of 8. Therefore, the second and more likely reason for the lack of significant gender differences in TD youth in the present work is likely to be a too-small sample size. This interpretation is supported by the examination of Figure 2, in which the mean percent bet is lower for TD females than for TD males, suggesting typically higher risk avoidance in females than in males. However, this difference was not significant.

Although both experiments support the unique association between anxiety and reward-related behavior in males (decreased risk taking and impaired incentive-related performance), the sensitivity to incentive level in the Piñata task did not differ between diagnosis or gender groups. Although overall performance accuracy improved with incentive level, the effect of stars was small, and no interaction of diagnosis or gender with star value emerged in the full model analysis. This might reflect the relatively small overall effect of the incentive sizes, which might have been insufficiently different from one another to pull out differences in behavior. Therefore, future work should use a larger range of incentive values.

Finally, both experiments revealed that reaction time (to execute a decision or to hit a target) was slower in the anxious group than in the TD group. This consistent effect on RT across samples supports the predictions of the attentional control theory (ACT) of anxiety (Eysenck et al. 2007; Derakshan et al. 2009a,b; Berggren and Derakshan 2013), according to which anxiety impairs the quality of performance (efficiency, indexed by RT) more readily than the level of performance (efficacy, indexed by accuracy). This theory, formulated for anxiety in adults, seems to be applicable to the pediatric population.

Some limitations need to be considered. Overall, the studies would have benefitted from larger sample sizes, providing stronger statistical power to detect group differences, particularly across the incentive levels of the Piñata task. In addition, the relatively small sample size prevented us from examining the unique contributions of different types of anxiety disorders. The relatively high IQ of our sample population might limit the generalizability of the results to the pediatric population at large. Another limitation of this study concerns sensitivity to losses, which was not tested in the Piñata task. This Piñata task was designed to be child friendly, simple, and short. The next version should include loss trials (avoiding losses), and, as mentioned, a greater range of incentive levels.

Conclusions

These preliminary findings highlight the role of gender in the effect of clinical anxiety on reward-related behavior, such that males are more strongly affected than females. Anxious males were significantly less likely to bet under high-risk conditions than TD

males, suggesting increased risk avoidance in anxious males. In addition, anxious males performed significantly less accurately on the incentive delay task, suggesting altered reward sensitivity. In females, no diagnostic differences on these reward-related measures emerged.

The importance of gender differences in psychopathology is being increasingly recognized. In fact, the Institute of Medicine urged an exploration of the functional impact of brain gender differences (Institute of Medicine 2001, 2011). Studying gender differences in anxiety in adolescence is particularly pertinent because not only do anxiety disorders often emerge in adolescence, but also rates of anxiety disorders shift to a 2:1 female predominance in adolescence from an equal prevalence across genders in childhood (Beesdo et al. 2009; Ordaz and Luna 2012). Additionally, in adolescents, gender was shown to modulate the association between symptoms of anxiety and functional impairment. A large longitudinal study of adolescents showed that anxious males were significantly more functionally impaired than anxious females in such areas as academic performance, self-esteem, sense of subjective well-being, and frequency of socializing with friends (Derdikman-Eiron et al. 2012). Therefore, understanding gender differences within a developmental framework can shed light on susceptibility, prevalence, course, and progression of anxiety.

Clinical Significance

The findings of gender-specific alteration of the reward system in anxious males may have direct implications for clinical treatment, suggesting a need for tailoring approach to gender. For example, psychotherapy for anxiety might involve a component aimed at increasing reward-related behaviors particularly for males. Despite evidence for gender differences in prevalence, and severity of anxiety disorders, research on gender-specific treatment is lacking (for review, see Bekker and van Mens-Verhulst 2007). Our work highlights a specific dimension of psychological functioning that is affected by anxiety in a gender-specific way, which, if confirmed, could contribute to the development of personalized treatments. In addition, this study provides *a priori* hypotheses for future work in pediatric anxiety, including the examination of different anxiety disorders (e.g., GAD vs. social phobia), and further extension into adult anxiety.

Disclosures

No competing financial interests exist.

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