Impaired generalization of reward but not loss in obsessive–compulsive disorder

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Background: Generalizing from past experiences can be adaptive by allowing those experiences to guide behavior in new situations. Generalizing too much, however, can be maladaptive. For example, individuals with pathological anxiety are believed to overgeneralize emotional responses from past threats, broadening their scope of fears. Whether individuals with pathological anxiety overgeneralize in other situations remains unclear.

Methods: The present study (N = 57) used a monetary sensory preconditioning paradigm with rewards and losses to address this question in individuals with obsessive–compulsive disorder (OCD) and social anxiety disorder (SAD), comparing them to healthy control subjects (HC). In all groups, we tested direct learning of associations between cues and reward vs. loss outcomes, as well as generalization of learning to novel choice options.

Results: We found no differences between the three groups in the direct learning of stimuli with their outcomes: all subjects demonstrated intact stimulus-response learning by choosing rewarding options and avoiding negative ones. However, OCD subjects were less likely to generalize from rewards than either the SAD or HC groups, and this impairment was not found for losses. Additionally, greater deficits in reward generalization were correlated with severity of threat estimation, as measured by a subscale of the Obsessive Beliefs Questionnaire, both within OCD and across all groups.

Conclusions: These findings suggest that a compromised ability to generalize from rewarding events may impede adaptive behavior in OCD and in those susceptible to high estimation of threat.

KEYWORDS

cognition, decision-making, reinforcement learning, reward generalization, sensory preconditioning

1 INTRODUCTION

A critical feature of adaptive learning is the ability to generalize from past experience to guide future decisions. When deciding among options that have never been directly experienced, generalization allows for similar or associated experiences to influence choice, motivating individuals to seek new experiences related to positive past outcomes and avoid ones related to negative outcomes. In the healthy brain, generalization is supported by the hippocampus as well as the orbitofrontal cortex (Eichenbaum & Cohen, 2004; Gerraty, Davidow, Wimmer, Kahn, & Shohamy, 2014; Jones et al., 2012). One way to test generalization of learned associations is with a "sensory preconditioning" task (Brogden, 1939; Dunsmoor, Murty, Davachi, & Phelps, 2015; Jones et al., 2012; Wimmer & Shohamy, 2012). In humans, fMRI studies with a sensory preconditioning paradigm found that generalization of reward value varies across participants, and this variability is related to hippocampal activity and to connectivity between the hippocampus and the striatum (Wimmer & Shohamy, 2012) as well as between the hippocampus and the ventromedial prefrontal cortex (Gerraty et al., 2014). Here, we used this same paradigm in behavior to investigate how generalizing from past reward experiences to novel situations may be altered in individuals with pathological anxiety, who have previously been shown to overgeneralize to threatening experiences (Dunsmoor & Paz, 2015; Laufer, Israeli, & Paz, 2016; Lissek et al., 2014). In addition, to compare generalization for both positive and negative events, we extended the task to include a monetary loss condition.

Previous laboratory studies of generalization in individuals with pathological anxiety have focused on generalization of threat stimuli (for a review, see Dunsmoor & Paz, 2015). Specifically, those with panic disorder (Lissek et al., 2010), posttraumatic stress disorder (Lissek & Grillon, 2012), and generalized anxiety disorder (Lissek et al., 2014) are more likely to demonstrate a threat response to nonthreatening stimuli that are perceptually similar to the threatening stimulus, although other studies of generalized anxiety disorder have not found such effects (Greenberg, Carlson, Cha, & Mujica-Parodi, 2013; Tinoco-gonzález et al., 2015). Anxiety is thought to increase this generalization through biasing the hippocampus to "pattern complete" the experience of a nonthreatening event into a similar threatening experience, instead of "pattern separating" threatening and nonthreatening episodes into distinct representations (Lissek, 2012). However, it is unclear whether pathological anxiety affects generalization from stimuli other than threats, such as when learning to generalize from rewards and losses. It is also unclear whether anxiety affects generalization based on memory associations rather than perceptual similarity. The present paradigm tests for generalization to relational memories that were formed before conditioning, relying on a reactivation of those previously learned associations during reinforcement learning, and an interaction between striatal learning and hippocampal memory systems.

Two disorders associated with pathological anxiety are obsessive– compulsive disorder (OCD), characterized by intrusive thoughts (obsessions) and repetitive behaviors (compulsions) that are typically associated with anxiety, and social anxiety disorder (SAD), characterized by fear and anxiety in social situations. Patients with these

disorders have been observed clinically to generalize from an anxiety-provoking experience with one threat stimulus (e.g., a potential contaminant in OCD or a specific social situation in SAD) to a broader class of stimuli (Kaczkurkin & Lissek, 2014), but few studies have tested generalization in experimental tasks in these populations. Although generalization to threat has not been studied in a clinical sample with OCD, in an analogue sample of undergraduates with clinically significant OCD symptoms, subjects with greater estimation of threat in the environment evidenced greater perceptual generalization of a conditioned fear stimulus (Kaczkurkin & Lissek, 2014). In SAD, one laboratory study of threat stimulus generalization reported mixed results, with physiological evidence of overgeneralization but no differences in self-reports relative to healthy control subjects (Ahrens et al., 2016).

OCD has, however, been associated with differential learning from gains and losses. Specifically, individuals with OCD have been shown to have increased avoidance learning and loss aversion (Gillan et al., 2014, 2015; Sip, Gonzalez, Taylor, & Stern, 2018) but decreased reward learning in reinforcement learning tasks (Endrass, Kloft, Kaufmann, & Kathmann, 2011). Moreover, another study found that subjects with OCD deploy a goal-directed, “model-based” system when learning about losses, whereas they rely on a habitual, “model-free” system when learning about gains (Voon et al., 2015). It has been speculated that the cycle of obsessions and compulsions in OCD may in a sense hijack the dopaminergic reward system, leading to insensitivity to external rewards and incentives, and preventing the adaptive pursuit of rewards in the environment (Koch et al., 2018). These findings strongly suggest that individuals with

OCD might generalize differentially from reward and losses. SAD has also been associated with deficient goal-directed learning of reward, although loss learning was not assessed (Alvares, Balleine, & Guastella, 2014).

To explore whether individuals with OCD and SAD generalize differently from rewards versus losses, we recruited unmedicated individuals with OCD and SAD as well as healthy comparison (HC) participants and administered a “sensory preconditioning” paradigm. This paradigm assesses stimulus-response learning as well as generalization from monetary rewards, losses, and neutral outcomes and has been used in prior behavioral and imaging studies in healthy individuals (Wimmer & Shohamy, 2012). Based on the literature reviewed above, we predicted that OCD participants would generalize less from rewards than losses compared to HC participants. By including SAD participants, we were able to test whether differential performance on this task compared to HCs is specific to OCD or is transdiagnostic across patients with anxiety. Finally, we were interested in exploring whether task-based generalization was related to individual estimation of threat in the environment (Steketee et al., 2005), based on previous research showing that this measure predicts overgeneralization in fear learning in individuals with obsessive–compulsive traits (Kaczkurkin & Lissek, 2014).

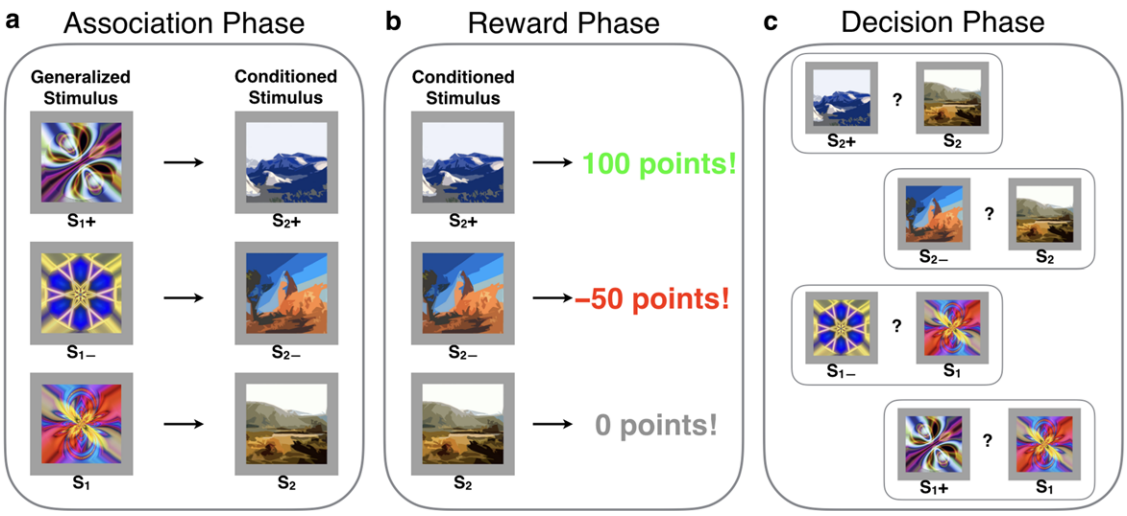

FIGURE 1 Task design. (a) During the association phase, participants were exposed to repeated pairs of stimuli. Each repeated pair included an S1 stimulus (a fractal) followed by an S2 stimulus (an “art piece”) while performing a cover task of detecting whether a displayed image was in an incorrect or correct format. (b) During the reward phase, participants learned through classical conditioning to predict which art piece (S2 stimuli) led to a gain, loss, or neutral outcome. (c) During the decision phase, participants chose between pairs of S1 and S2 stimuli for monetary gain, without feedback.

2 METHODS AND MATERIALS

2.1 Setting

This study was conducted at an outpatient research clinic specializing in the diagnosis and treatment of anxiety disorders and OCD. Procedures were approved by the Institutional Review Board of the New York State Psychiatric Institute (NYSPI), and participants provided written, informed consent.

2.2 Participants

Adults (aged 18–50 years) with a principal diagnosis of OCD, or SAD, and matched HC, were recruited via media and referral. Diagnoses were made by a psychiatrist, and confirmed by another clinician using a semi-structured interview (First, Spitzer, Gibbon, & William, 1996).HC had no lifetime Axis I psychiatric disorders. OCD and SAD participants had no lifetime history of psychotic, bipolar, attention deficit hyperactivity, or primary hoarding disorder, and no other current Axis I disorders (including major depressive disorder) except comorbid specific phobia (*n* =3OCDand *n* = 3 SAD). All participants were free from psychiatric medications at the time of testing (at least 4 weeks for most and 6 weeks for fluoxetine). Menstruating females were tested during the first week of their menstrual cycle and were not pregnant, nursing, postmenopausal, or using hormonal birth control. Fifty-seven subjects consented to this study and completed the sensory preconditioning paradigm (*n* = 19 OCD, *n* = 16 SAD, and *n* = 22 HC). Four were excluded (*n* = 3 OCD and *n* = 1 HC) because they scored under 50% for both gain and loss conditioning, indicating a general deficit in learning and making the generalization results difficult to interpret, yielding a final sample of 53 subjects.

2.3 Clinical assessments

Participants were evaluated by a trained rater using the Yale-Brown Obsessive–Compulsive Scale (Y-BOCS; Goodman et al., 1989) and the Liebowitz Social Anxiety Scale (LSAS; Heimberg et al., 1999). Participants completed the Threat Estimation subscale of the Obsessive Beliefs Questionnaire (OBQ-44; Steketee et al., 2005) as well as the Spielberger State-Trait Anxiety Inventory (STAI; Spielberger & Gorsuch, 1983).

2.4 Task procedure

Subjects participated in a computerized sensory preconditioning paradigm (Brogden, 1939; Wimmer & Shohamy, 2012). The task consisted of three phases, as shown in 1 Phase 1: an association phase, where participants learned to associate pairs of images through repeated exposure to the pairs (denoted as S1 and S2 stimuli: S1 represents the generalized stimulus and S2 represents the conditioned stimulus); Phase 2: a reward phase: where the S2 stimuli were either paired with reward, loss, or a neutral outcome; and Phase 3: a final decision phase, where participants made choices between pairs of S1 and S2 stimuli without any reinforcement. This final phase revealed subjects' tendency to learn and generalize rewards and losses (details below). Subjects were told they were playing a computer game in which their job was to be an art dealer participating in an art auction. In Phase 1, the association phase, participants experienced a "slideshow of paintings" where they were asked to indicate whether a painting was in a correct or an incorrect format (upside down, missing, or a solid color) on their keyboard. Participants were incidentally exposed to pairs of stimuli (S1 stimulus, a fractal, always preceding the S2 stimulus, an "art piece"). There were four pairs of stimuli, each presented 10 times in a pseudo-random order, and intermixed with 14 unrepeated pairs. During Phase 2, the reward phase, the S2 stimuli observed in Phase 1 underwent classical conditioning, such that participants learned which of the four images predicted a reward, a loss or a neutral outcome (the fourth S2 stimulus was not paired with an outcome and did not appear in Phase 2). Here, participants were required to "bid" on paintings (S2 stimuli) in an art auction, and were told bidding on

each painting could lead to a number of points—either a 100 point gain, a 50 point loss, or a 0 point neutral outcome. A 100 point gain and 50 point loss were deemed equivalent given that losses subjectively weigh about twice as much as gains (Kahneman & Tversky, 1979; Tom, Fox, Trepel, & Poldrack, 2007; Tversky & Kahneman, 1992). Participants' goal was to maximize their number of points, as they were told a percentage of the points would be translated to their actual earnings. There was a total of 60 trials, with each S2 stimulus presented 20 times. The gain (S2+) and loss stimulus (S2–) were reinforced 80% of the time (and were paired with a 0 outcome 20% of the time). Subjects received feedback after every bidding decision (regardless of the decision). In Phase 3, the final decision phase, participants chose between two images that they had either previously seen in Phase 1, the association phase, or Phase 2, the reward phase. They were instructed to choose the more valuable image, going with their "gut reaction." There was a total of 30 choice trials, including choices between previously reinforced items (S2 stimuli pairs), and choices that reflected generalization of value to paired associates (S1 stimuli pairs). There were five trial types (six choices within each) including: gain associated stimuli (S+) versus loss associated stimuli (S–), S+ versus S(neutral), S+ versus S(not conditioned), S– versus S(neutral), and S– versus S(not conditioned). The participants did not receive any feedback during the decision phase. We focused on two measures, both obtained in Phase 3. "Direct learning of stimulus-reward associations" was measured by preference for the S2 stimulus leading to reward, and avoidance of the S2 stimulus leading to loss (from Phase 2). "Generalization" was measured by preference for the S1 stimulus from Phase 1 that had been paired with the rewarded S2 image, and avoidance of the S1 associate

that had been paired with the S2 image predicting loss. We examined each of these measures separately for rewards and losses.

2.5 Statistical analysis

2.5.1 Demographic and clinical characteristics

We conducted analyses of variance (ANOVAs) testing for group differences in our demographic and clinical measures for continuous variables, and chi-square for categorical variables (see Table 1). If significant, we next conducted a Tukey's post hoc test for multiple comparisons to analyze pair comparisons.

TABLE 1 Demographic and clinical characteristics

	Healthy comparisons ($n = 21$) Mean ± *SD*	Obsessive–compulsive disorder ($n = 16$) Mean ± *SD*	Social anxiety disorder ($n = 16$) Mean ± *SD*
Age (years)	27.6 ± 5.7	30.0 ± 4.7	28.5 ± 6.8
Gender (F)	13 (62%)	9 (56%)	9 (56%)
Years of education	15.7 ± 2.2	15.7 ± 1.9	14.9 ± 1.4
Estimated IQ (NAART)	109.6 ± 8.7	110.9 ± 5.0	109.6 ± 9.3
OBQ-threat estimation	9.5 ± 4.9	20.2 ± 12.0	16.25 ± 9.8
Y-BOCS-total	0.3 ± 1.3	25.5 ± 4.2	1.1 ± 2.0
LSAS, total	9.6 ± 5.6	19.1 ± 13.2	74.3 ± 21.3
STAI-trait	26.4 ± 4.6	40.3 ± 10.7	47.5 ± 10.7

LSAS, Liebowitz Social Anxiety Scale; NAART, North American Adult Reading Test; OBQ, Obsessive Beliefs Questionnaire; STAI, State Trait Anxiety Inventory; Y-BOCS, Yale-Brown Obsessive–Compulsive Scale.

2.5.2 Conditioning

To determine how well subjects learned to associate the images (S2 stimuli) with their outcomes, we calculated the proportion of choices from Phase 3 for the rewarding image (S2+, a measure of reward conditioning), and the proportion of choices away from the loss image (S2–, a measure of loss conditioning). We then ran three ANOVAs

testing for group differences (1) for overall conditioning (combining reward and loss conditioning), (2) for reward conditioning, and (3) loss f conditioning separately.

2.5.3 Generalization

To determine whether subjects generalized the gain and loss events to their associated images (S1 stimuli), we calculated the proportion of choices from Phase 3 for the S1 stimulus paired with S2+ (S1+, a measure of reward generalization), and did not choose the S1 stimulus paired with S2– (S1–, a measure of loss generalization). We then ran three ANOVAs (and if significant, subsequent Tukey's post hoc tests) testing for group differences (1) for overall generalization (combining reward and loss generalization), (2) for reward generalization, and (3) loss generalization separately. We assessed whether group scores were below chance using a one-sample *t*-test. To compare reward and loss generalization to each other (without contamination), we used the proportion of S1+ over the neutral S1 as our measure of reward generalization, and the proportion of S1– over the neutral S1 as our measure of loss generalization, and subtracted these two measures to quantify the asymmetry between loss and reward generalization.

2.5.4 Threat estimation

We used subjects' total threat estimation scores from the OBQ, and conducted separate regression analyses (both within the OCD group and across groups) testing for whether threat estimation predicted (1) reward generalization and (2) loss generalization. We also explored whether these effects (slopes) were different from each other by

assessing the interaction between threat estimation and generalization type (reward or loss) in predicting generalization.

3 RESULTS

3.1 Sample

Demographic and clinical characteristics of the 53 participants are shown in Table 1. All were unmedicated at the time of testing. There were no group differences in age ($F(2,50) = 0.73$, $P = 0.49$), gender ($X2[2, N = 53] = 0.17$, $P = 0.92$), years of education ($F(2,50) = 0.93$, $P = 0.40$), or estimated IQ(National Adult Reading Test; $F(2,50) = 0.15$, $P = 0.87$; see Table 1). As expected, there were group differences in OCD severity (Y-BOCS; $F(2,50) = 458$, $P < 0.001$), with OCD participants scoring higher than SAD participants and HCs (OCDHC: $P < 0.001$; SAD-OCD: $P < 0.001$; SAD-HC: $P = 0.64$). There were also group differences in OBQ threat estimation score (OBQ; $F(2,50) = 6.68$, $P < 0.01$), with OCD participants scoring higher than HCs (OCD-HC: $P < 0.01$) but not higher than SAD participants (OCDSAD: $P = 0.44$; SAD-HC: $P = 0.07$). Similarly as expected, there were differences in the severity of social anxiety (LSAS; $F(2,50) = 101.2$, $P < 0.001$) with SAD participants scoring higher than OCD participants and HCs (SAD-HC: $P < 0.001$; SAD-OCD: $P < 0.001$; OCD-HC: $P=0.12$). Both patient groups also scored higher than HCs on degree of trait anxiety (State Trait Anxiety Inventory; $F(2,50) = 27.91$, $P < 0.001$; SAD-HC: $P < 0.001$; OCD-HC: $P < 0.001$; OCD-SAD: $P = 0.40$). Finally, 83% (44 of 53) had never been on psychotropic medication. Of the nine

who had been exposed (*n* = 5 SAD and *n* = 4 OCD), none had been on psychotropic medication for at least a year.

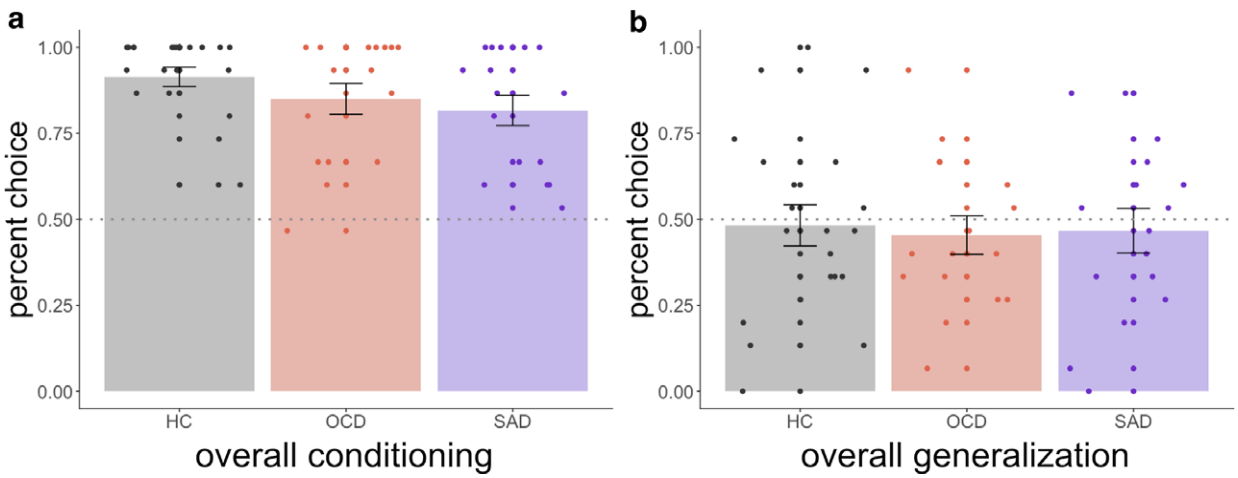

FIGURE 2 Learning plots in healthy comparison (HC) subjects, and obsessive–compulsive disorder (OCD) and social anxiety disorder (SAD) patients. (a) The bars represent choice preference for the gain stimulus (S2+), over both the neutral (S2) and the loss stimulus (S2–). There were no differences in overall conditioning across groups. (b) The bars represent choice preference towards the stimulus associated with the gain stimulus (S1+) and away from the stimulus associated with neutral (S1) and loss stimuli (S1–). There were no differences in overall generalization across groups.

3.2 Conditioning

There were no significant group differences in overall conditioning ($F(2,50) = 1.80$, $P = 0.18$; see Figure 2a), nor, when analyzed separately, for reward conditioning ($F(2,50) = 0.52$, $P = 0.60$) or loss conditioning ($F(2,50) = 1.21$, $P = 0.31$). Each group had conditioning scores above chance (OCD: $t[15] = 7.79$, $P < 0.001$; SAD: $t[15] = 7.18$, $P < 0.001$; HC: $t[20] = 14.78$, $P < 0.001$) demonstrating intact first-order learning.

3.3 Generalization

While there were no overall group differences for generalization ($F(2,50) = 0.06$, $P = 0.94$; see Figure 2b), nor for loss generalization ($F(2,50) = 1.80$, $P = 0.18$; Figure 3b), there were significant group differences in reward generalization ($F(2,50) = 4.05$, $P = 0.02$; Figure 3a). Specifically, OCD participants generalized significantly less from gain than HCs ($P = 0.04$) and the SAD group ($P = 0.05$). Comparing each group's performance to chance, we found that the OCD group generalized to gain at a rate below chance ($t[15] = –3.87$, $P < 0.01$), unlike the HCs ($t[20] = 0.62$, $P = 0.54$) and SAD group ($t[15]) = 0.66$, $P = 0.52$), whose overall group performance was no significantly different from chance. This suggests that not only did OCD participants fail to show a bias toward the rewarded associate, but instead avoided choosing that image altogether. This was reflected in group differences in the asymmetry between reward and loss generalization ($F(2,50) = 4.54$, $P = 0.01$; Figure 3c), with OCD participants generalizing more from losses than gains ($t[15] = 3.43$, $P < 0.01$). This asymmetry in OCD was greater than HC ($P = 0.05$) and SAD ($P = 0.02$) groups.

3.4 Threat estimation and anxiety

Both within OCD participants and across groups, greater threat estimation was related to impaired reward generalization (OCD participants: $t[14]=–2.32$, $P=0.04$, $\beta=–0.01$; total population: $t[51]=–2.56$, $P = 0.01$, $\beta = –0.01$; Figure 3d). Threat estimation, however, was not related to loss generalization ($t = 0.40$, $P = 0.69$, $\beta = 0.002$; Figure 3e) and there was a significant difference in the slopes between the loss and reward conditions ($t[51] = –2.05$, $P = 0.04$, $\beta = –0.02$). There was not a relationship between state or trait anxiety measures (STAI) and generalization scores.

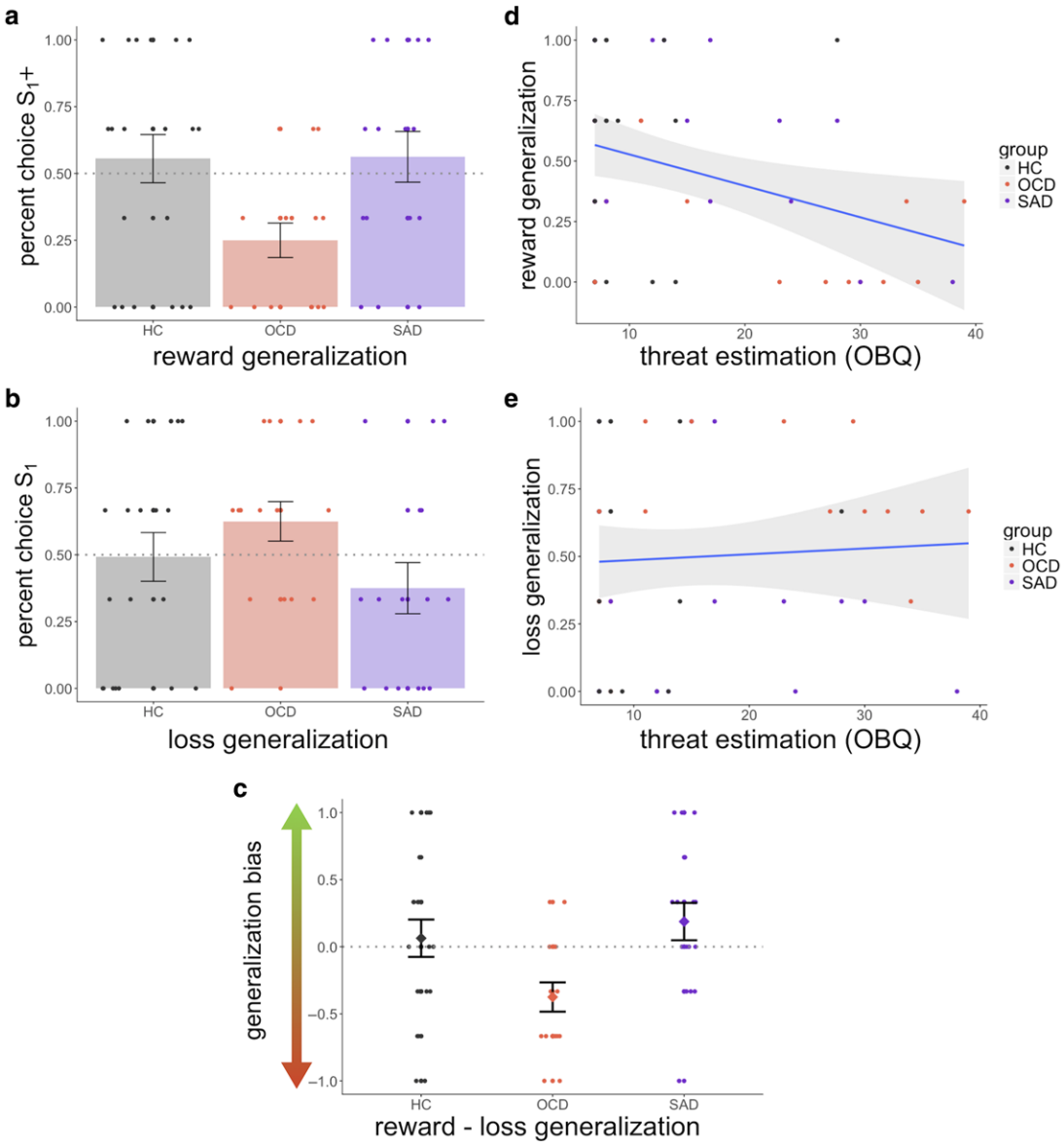

FIGURE 3 Generalization plots for healthy comparison (HC) subjects, and obsessive–compulsive disorder (OCD) and social anxiety disorder (SAD) patients. (a) Choice preference for the stimulus associated with the gain stimulus (S1+) versus the stimulus associated with the neutral stimulus (S1). The OCD patients chose the S1+ stimulus significantly less than HC and SAD patients. (b) Choice preference for the stimulus associated with the neutral stimulus (S1) versus the stimulus associated with the loss stimulus (S1–). There were no differences in loss generalization across groups. (c) The difference between positive (vs. neutral) generalization and loss (vs. neutral) generalization for each group. The OCD group generalized significantly less from gain

stimuli than from loss stimuli, and less than HCs and SAD patients. (d) Reward (vs. neutral) generalization as a function of scores from the obsessive beliefs questionnaire (OBQ) threat estimation subscale. Higher threat estimation predicted worse reward generalization across groups. (e) Loss (vs. neutral) generalization as a function of threat estimation scores. Threat estimation did not predict loss generalization. Shaded regions in (d) and (e) represent 95% confidence intervals.

4 DISCUSSION

Generalizing from past experiences supports decisions for choices that have never been directly experienced. The present study examined reward and loss generalization in a sample of OCD, SAD, and HC subjects using a sensory preconditioning paradigm. This paradigm allowed us to detect the extent to which subjects were leveraging past experiences to guide behavior. We found no differences between groups in the direct learning of associations between cues and outcomes: all subjects learned to seek rewards and avoid loss, demonstrating intact stimulus-response learning. However, OCD subjects were less likely to generalize from rewards than SAD and HC groups. This impairment was not found for loss generalization. Finally, this deficit in reward generalization was correlated with the threat estimation dimension of the OBQ within OCD and across all groups.

The finding that OCD subjects were less likely to generalize from rewards but showed no impairment in loss generalization is consistent with prior studies suggesting that OCD patients have abnormalities in reward processing, although these other studies examined different aspects of reward processing than generalization (e.g., Kaufmann et

al., 2013). Our finding that OCD subjects were less likely to generalize to rewards is consistent with a recent study showing that OCD patients have a more flexible, “model-based” representation when learning about losses, and an inflexible, or “model-free” representation when learning about rewards (Voon et al., 2015). Model-based learning is linked to the use of relational and associative memory (Doll, Shohamy, & Daw, 2015), supported by the hippocampus (Shohamy & Wagner, 2008), whereas model-free learning, linked to habitual and procedural learning, is not thought to depend on hippocampal functioning. Our results moreover show that OCD individuals are choosing the generalized reward stimulus below chance. Previous fMRI studies using this paradigm with healthy participants (Gerraty et al., 2014; Wimmer& Shohamy, 2012) have shown that individual variability in reward generalization is related to functional connectivity between the hippocampus and reward systems, suggesting possible alterations in connectivity in these networks in OCD. Given that the hippocampus is important for sensory preconditioning in the healthy brain and hippocampal abnormalities have been reported in OCD (Milad et al., 2013), our findings suggest need for further study of the possibility that hippocampal abnormalities contribute to the pattern of behavioral performance in reward-based decision-making in OCD. Previous studies have not directly investigated a trade-off between reward and loss generalization in OCD. In our sample, we did not find impaired loss learning or abnormal loss generalization in either OCD or SAD. The literature on OCD and loss learning is mixed. Some studies have found excessive loss learning and deficient reward learning in behavior and in the brain (Endrass et al., 2011; Kaufmann et al., 2013). For example, loss learning in OCD has been related to “hyperactivation” of

neural areas linked to motivational salience (Kaufmann et al., 2013) and reward processing (Jung et al., 2011).Conversely, gain learning in OCD is associated with “hypoactivation” of neural circuits associated with reward learning, including the nucleus accumbens (Figee et al., 2011; Jung et al., 2013; Kaufmann et al., 2013). For the SAD group, the lack of impaired reward generalization in in this study is consistent with suggestions that aberrant reward processing in SAD may be specific to social reward cues (Richey et al., 2017). Our data did reveal a relationship between threat overestimation, a common feature of pathological anxiety and previously related to generalization in individuals with obsessive–compulsive traits (Lissek et al., 2014), and reward generalization, with greater threat estimation related to greater impairment in reward generalization. We did not find that state or trait anxiety modulated generalization, suggesting that this relationship is specific to threat estimation and not anxiety symptoms per se. Moreover, this association was selective to reward generalization and did not exist for loss generalization, suggesting that reward and threat may not be completely dissociable systems. For example, a greater preoccupation with avoiding threat coupled with an overestimation of the likelihood and severity of threat in the environment may possibly compromise reward generalization, thus hindering the adaptive seeking of rewarding events. Alternatively, impaired reward processing could prevent pleasurable events from acting as a buffer to stress (e.g., Ulrich-Lai et al., 2010) furthering the negative impact of stressful experiences. Finally, it has been suggested that reward and threat share common neurobiological substrates (Leknes & Tracey, 2008), which implies that a deficit in one system entails dysfunction

in the other. This potential interaction between threat estimation and reward seeking may be a productive area for future investigation.

Strengths of this study included well-characterized unmedicated samples, with minimal comorbidity in the OCD and SAD groups. We used an established paradigm, which, in healthy participants, has shown that reward-based generalization is supported by the hippocampus and by interactions between the hippocampus and the striatum (Wimmer & Shohamy, 2012), and that individual differences in generalization are related to connectivity within these circuits (Gerraty et al., 2014) allowing us to behaviorally detect the degree to which participants are relying on amore habitual versus a more flexible learning system. Nevertheless, our sample is relatively small, and these findings will require replication. Moreover, this paradigm was limited to assessment of monetary rewards and losses. These secondary reinforcers may not engage identical mechanisms, nor to the same extent, as primary reinforcers. In the case of aversive events, learning about shocks is supported by regions distinct from monetary losses, such as the amygdala (Delgado, Jou, & Phelps, 2011), perhaps explaining why our monetary loss condition did not replicate previous findings of excessive fear learning in OCD, which typically use primary reinforcers like shock (e.g., Gillan et al., 2015). It will additionally be of interest to test generalization for disorder-specific types of rewards and losses (e.g., social in SAD) and its association with alternative measures of threat sensitivity. Our findings together with prior studies describing deficits in reward processing in OCD suggest reward learning as a novel therapeutic target in OCD. For example, it might be fruitful to enhance an individual's capacity to generalize to rewards

in the environment, especially in the face of potential threat. Beyond OCD, such an approach might benefit others with pathological anxiety and high threat estimation. Our findings also suggest that the interplay among reward processing, threat estimation, and habit-like behavior is complex and warrants careful study in both healthy control and clinical populations using validated paradigms that can tap all three domains in the same subjects.

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CONFLICTS OF INTEREST

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