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Abnormal decision-making in generalized anxiety disorder: Aversion of risk or stimulus-reinforcement impairment?

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ABSTRACT

There is preliminary data indicating that patients with generalized anxiety disorder (GAD) show impairment on decision-making tasks requiring the appropriate representation of reinforcement value. The current study aimed to extend this literature using the passive avoidance (PA) learning task, where the participant has to learn to respond to stimuli that engender reward and avoid responding to stimuli that engender punishment. Six stimuli engendering reward and six engendering punishment are presented once per block for 10 blocks of trials. Thirty-nine medication-free patients with GAD and 29 age-, IQ and gender matched healthy comparison individuals performed the task. In addition, indexes of social functioning as assessed by the Global Assessment of Functioning (GAF) scale were obtained to allow for correlational analyzes of potential relations between cognitive and social impairments. The results revealed a Group-by-Error Type-by-Block interaction; patients with GAD committed significantly more commission (passive avoidance) errors than comparison individuals in the later blocks (blocks 7,8, and 9). In addition, the extent of impairment on these blocks was associated with their functional impairment as measured by the GAF scale. These results link GAD with anomalous decision-making and indicate that a potential problem in reinforcement representation may contribute to the severity of expression of their disorder.

1. Introduction

Generalized anxiety disorder (GAD) is associated with significant disability and characterized by excessive, uncontrollable worry (e.g., Whittchen et al., 1994). Occupied by worry, GAD patients may show impaired social, occupational, and role functioning, reflected in high rates of unemployment, divorce, emotional problems, and self-reported interference with daily activities (e.g., Henning et al., 2007; Massion et al., 1993).

The avoidance model of worry explains symptoms of GAD focusing specifically on thought processes. This model asserts that worry is a linguistic activity that inhibits vivid mental imagery and associated somatic and emotional evaluation (e.g., Borkovec et al., 2004). This emphasis on thought shares features with other theories that focus both on thoughts and associated neural processes. Specifically, in such neuroscience-based theories, worry is viewed as a prefrontal-based process that leads to top-down priming of semantic threat representations, which disrupt appropriate processing of current environmental stimuli and lead to impaired decision-making (Blair and Blair, 2012).

Reinforcement-based decision-making involves the selection of response options according to the reinforcement (reward/ punishment) associated with these options. Such decision-making has been receiving more attention with respect to anxiety recently. Several studies have examined reinforcement-based decision-making in individuals reporting heightened anxiety (e.g., Luhman et al., 2011; Maner et al., 2007; Raghunathan and Pham, 1999) though only one study has directly examined this issue in *patients* with GAD (Devido et al., 2009). In this study, the performance of patients with GAD, Generalized Social Phobia (GSP) and healthy controls (HC) was compared on the differential reward/punishment learning task (Devido et al., 2009). This task assesses the individual's ability to learn the value of objects and select between these objects to maximize reward/minimize punishment (Blair et al., 2006). Patients with GAD showed impaired performance on this task compared to both patients with GSP and HCs (Devido et al., 2009). Similarly, work with subclinical participants reporting heightened anxiety or intolerance of uncertainty has, for the most part, reported indications of impaired decision-making; the choices of high anxious individuals result in lower winnings compared to lower anxious individuals (e.g., Luhman et al., 2011; Maner

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et al., 2007; Raghunathan and Pham, 1999). For example, Raghunathan and Pham (1999) asked participants to choose between high-probability, small reward and low-probability, large reward monetary options. Higher anxiety individuals were significantly more likely to choose the high-probability, small reward options relative to individuals reporting low anxiety. Similar results have been found using the balloon analog risk task (BART) (Maner et al., 2007). In this task, participants earn monetary rewards as they "pump up" a balloon but can lose their earnings if the balloon is pumped too many times. Higher anxiety individuals anxious made significantly fewer pumps than individuals reporting low anxiety (Maner et al., 2007). Further, in recent work Luhman et al. used a form of delay discounting task where participants chose between small, low-probability rewards available immediately at the beginning of each trial and large, high-probability rewards only available after some variable delay (Luhman et al., 2011). This study reported that higher levels of intolerance of uncertainty were associated with a tendency to select the immediately available, but less valuable and less probable rewards. However, not all studies report impaired decision-making performance. Undergraduates meeting GAD criteria according to the generalized anxiety disorder questionnaire (GADQ) -IV (GAD analogs) showed superior performance on the Iowa gambling task than undergraduates not meeting criteria (Mueller et al., 2010).

Much of this literature has been interpreted as indicating that anxious individuals make decisions to avoid uncertain or risky consequences (Luhman et al., 2011; Mueller et al., 2010). However, it is worth considering an alternative explanation: individuals with GAD may be impaired in reinforcement-based decision-making. Considerable fMRI data has demonstrated that ventromedial prefrontal cortex (vmPFC), striatum and posterior cingulate cortex are importantly involved in the representation of reinforcement information (Clithero and Rangel, 2014). Lesions to vmPFC in particular have been shown to disrupt decision-making. Interestingly, with respect to impairments seen in patients with GAD, animal work indicates that orbital frontal cortex lesions (the region critically involved in the representation of reinforcement) promotes preference for the smaller and more immediate (as opposed to larger and delayed; c.f. Luhman et al., 2011) and the smaller and more certain (as opposed to larger and more probabilistic; cf. Raghunathan and Pham, 1999) of two reinforcers (Mobbini et al., 2002). Similarly, vmPFC atrophy in patients with frontal variant fronto-temporal dementia is associated with a reduction of pumps on the Balloon Analog Risk Task (Strenziok et al., 2011). As such, it can be hypothesized that GAD involves impaired representation of reinforcement information within ventromedial prefrontal cortex (vmPFC) and associated structures and consequent decision-making impairment. Importantly, this second explanation has advantages over the avoidance hypothesis; it is unclear, for example, why a decision to avoid uncertain or risky consequences should result in increased errors when choosing between two stimuli associated with different levels of reward (cf. Devido et al., 2009).

Given the paucity of evidence on reinforcement-based decision-making in GAD, particularly work involving patients with DSM diagnoses of GAD, the goal of the current study was to examine the performance of patients on the passive avoidance (PA) learning task. The PA task was chosen because it allows a distinction between the vmPFC dependent reinforcement representation account of GAD briefly outlined above and hypotheses based on the suggestion that observed decision-making deficits in GAD reflect anxious individuals making decisions to avoid uncertain or risky consequences (Luhman et al., 2011; Mueller et al., 2010).

In the PA task, participants learn to respond to (approach) stimuli that engender reward and not respond to (passively avoid) stimuli that engender punishment (Finger et al., 2011). Not responding to a stimulus, passively avoiding it, results in neither reward nor punishment. Lesion and functional magnetic resonance imaging (fMRI) work suggest that vmPFC's role in the representation of reinforcement is critical for successful performance on this task (Finger et al., 2011; Schoenbaum and Roesch, 2005). Deficits in reinforcement representation should increase commission errors (responding inappropriately to stimuli that engender punishment); the individual is less able to use the expected value of the stimulus to guide their decision-making. In contrast, if patients with GAD make decisions to avoid uncertain or risky consequences, then these individuals should make significantly more *omission* errors – they will be directly choosing to avoid uncertain or risky consequences by not responding to the stimuli. The current study tests these contrasting predictions.

2. Method

2.1. Patients

Thirty-nine patients with GAD and 29 healthy control individuals participated in the study and were paid for their participation. All patients met criteria for generalized anxiety according to the Structural Clinical Interview for DSM-IV (1994) Axis I disorders (SCID) conducted by a board-certified psychiatrist (First et al., 1997). Thirteen of the 39 patients with GAD were also comorbid for GSP. All other co-occurring anxiety disorders as well as an ongoing diagnosis of major depressive disorder (MDD) were exclusory. All participants were required to be currently medication-free (no regular use of psychotropic medication within two weeks or fluoxetine/benzodiazepine within eight weeks of the study). Healthy comparison participants were in good physical health with no history of any psychiatric illness as confirmed by a physical exam and SCID.

Participants were matched on age, gender, and IQ as assessed by the verbal and matrix reasoning subtests of the Wechsler Abbreviated Scale of Intelligence (WASI) (see Table 1). Groups differed significantly on the Beck Anxiety Inventory (BAI) and the Inventory of Depressive Symptoms (IDS) (see Table 1). All participants provided written informed consent to participate in the study, which was approved by the NIMH Institutional Review Board. Recruitment occurred through NIMH Institutional Review Board (IRB) approved flyers and advertisements and through the NIH outpatient clinical services.

Table 1
Subject characteristics (standard deviations in brackets).

	Patients with GAD ($N=29$)		Healthy Comparison ($N=39$)	
Characteristic	Mean	(SD)	Mean	(SD)
Age (years)	35.8	(10.74)	31.3	(9.92)
IQ[a]	117.3	(13.46)	117.8	(10.60)
GAF	61.0	(4.57)	–	–
BAI	11.5	(7.60)	2.4*	(2.58)
IDS	19.5	(7.75)	5.2*	(4.38)
Gender		12 male	14 male	

Key to Table 1: GAF=Global assessment of functioning; BAI=Beck anxiety inventory; IDS=Inventory of depressive symptoms.

[a] Assessed with the Wechsler abbreviated scale of intelligence (two-subtest form)

* significantly different at $p < 0.001$