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Short communication

Probing implicit learning in obsessive-compulsive disorder: Moderating role of medication on the weather prediction task

Benjamin Kelmendi [a,e], Thomas Adams Jr. [a,e,*], Ewgeni Jakubovski [b], Keith A. Hawkins [a], Vladimir Coric [a,1], Christopher Pittenger [a,b,c,d]

[a] Department of Psychiatry, Yale University, United States
[b] Child Study Center, Yale University, United States
[c] Department of Psychology, Yale University, United States
[d] Interdepartmental Neuroscience Program Yale University, United States
[e] National Center for Post-Traumatic Stress Disorder, VA Connecticut Healthcare System, United States

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ABSTRACT

Deficits in implicit learning, a process by which knowledge is acquired accretively through practice independent of conscious awareness, have been implicated in Obsessive-compulsive disorder (OCD). The weather-prediction task (WPT) was used to assess implicit learning in 26 unmedicated patients with OCD and 23 healthy controls. An additional analysis compared these two groups with 25 medicated patients with OCD. In the comparison of unmedicated patients with healthy controls there was a subtle but statistically significant group-by-block interaction. Patients with OCD showed slower improvement in performance during the middle phase of learning. In a three-group comparison, there was no main effect of group; in post-hoc tests, medicated patients with OCD differed from unmedicated patients and were not different from healthy controls. Unmedicated patients with OCD have a subtle deficit in implicit learning in the WPT. This may be mitigated by pharmacotherapy, although prospective studies would be required to confirm this conclusion.

1. Introduction

Obsessive-compulsive disorder (OCD) is characterized by recurrent, intrusive thoughts (obsessions) and repetitive behaviors (compulsions) that result in significant distress and/or functional impairment. OCD affects approximately one person in 40 worldwide (Ruscio, Stein, Chiu, & Kessler, 2010). Neuropsychological and neuroimaging studies have implicated dysfunction of fronto-striatal circuitry in its pathophysiology, noting hyperactivity of orbitofrontal cortex (OFC) and striatum (right caudate) at baseline and during symptom provocation tasks (Menzies et al., 2008). Fronto-striatal circuitry is implicated in probabilistic classification learning (Knowlton et al., 1996; Squire & Zola, 1996). Studies have suggested that patients with OCD have general difficulties in learning probabilistic association between cues and outcome (Deckersbach et al., 2002; Kathmann, Rupertseder, Hauke, & Zaudig, 2005; Marker, Calamari, Woodard, & Riemann, 2006; Goldman et al., 2008).

Probabilistic classification learning describes a family of implicit learning tasks in which participants learn arbitrary associations between cues and a predicted outcome (Shohamy, Myers, Kalanithi, & Gluck, 2008), knowledge is acquired accretively over multiple repetitions, independent of conscious awareness. Associations are stochastic: rather than directly predicting the outcome, a cue or constellation of cues determines a probability of a given outcome. This makes the associations difficult to learn by an explicit strategy; even an optimal rule-based explicit strategy will not produce the correct result on every trial, due to the stochastic nature of the outcome. In contrast, explicit learning – the conscious acquisition and retrieval of knowledge – is associated with activity in the hippocampus and parahippocampal cortex and the dorsolateral prefrontal cortex (Squire, 2002).

The Weather Prediction Task (WPT) was developed as a probabilistic classification task to probe abnormalities in implicit learning (Knowlton et al., 1996; Knowlton, Squire, & Gluck, 1994; Marsh et al., 2004). On this task, participants learn to categorize a set of visually presented cues that are probabilistically related to one of two outcomes by receiving feedback on the accuracy of their response. Patients with Parkinson's or Huntington's disease, both of which affect integrity of the basal ganglia, show deficits in the WPT (Knowlton et al., 1996; Knowlton, Squire, Swenson,

* Correspondence to: Department of Psychiatry, Yale University, 34 Park Street, W312, New Haven, CT, United States.
E-mail address: thomas.adamsjr@yale.edu (T. Adams Jr.).
[1] Current address: 234 Church Street, Suite 301, New Haven, CT 06510, United States.

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Swerdlow, & Butters, 1996). A more subtle deficit in the WPT has been shown in patients with Tourette syndrome (Keri, Szlobodnyik, Benedek, Janka, & Gadoros, 2002; Marsh et al., 2004). In contrast, amnesic patients with hippocampal damage (Knowlton et al., 1994) or Alzheimer's disease (Eldridge, Masterman, & Knowlton, 2002) show normal learning in the WPT, despite explicit memory impairments. For this reason, the WPT has been used extensively to examine the neurocircuitry to support implicit learning (Price, 2009).

Functional neuroimaging data support dependence of the WPT on intact striatal function (Wilkinson & Jahanshahi, 2007; Wilkinson, Khan, & Jahanshahi, 2009). The striatum (right caudate) is activated during WPT task completion, as are cortical areas that project to it (Aron, Gluck, & Poldrack, 2006; Poldrack, Prabhakaran, Seger, & Gabrieli, 1999; Seger & Cincotta, 2005). Patients with Parkinson's disease, who show impaired implicit learning, show a corresponding decrease in learning-related activation of the striatum (Moody, Bookheimer, Vanek, & Knowlton, 2004). Interestingly, they show enhanced activation of the medial temporal lobe, suggesting that when the implicit learning system is compromised they attempt to compensate by engaging the explicit learning system (Moody et al., 2004). Although the WPT is commonly considered a measure of implicit learning, recent neuropsychological evidence suggests that participants can use explicit strategies to improve performance (Ashby & Maddox, 2005; Price, 2009; Shohamay, Myers, Kalanithi, & Gluck, 2008).

Studies of implicit learning in OCD have produced mixed results. Several studies have shown a modest deficit in putative implicit learning tasks, including a serial reaction time task (SRT), (Deckersbach et al., 2002; Goldman et al., 2008; Kathmann et al., 2005; Marker et al., 2006) an implicit card betting task (Joel et al., 2005), and an implicit learning component in the Tower of Hanoi task (Cavedini, Cisima, Riboldi, & D'Annucci, Bellodi, 2001). However, other studies employing implicit learning tasks, including the WPT (Exner, Zetsche, Lincoln, & Rief, 2014) and pursuit rotor task (Roth, Baribeau, Milovan, O'Connor, & Todorov, 2004), have shown no deficit. In the SRT, patients with OCD showed activation of the medial temporal lobe, while healthy controls showed activation of the inferior striatum (Rauch & Rosen, 1997; Rauch et al., 2007). This finding has been interpreted as suggesting that patients with OCD, much like Parkinson's patients, compensate by engaging the explicit learning system (Joel et al., 2005). Consistent with this interpretation, patients with OCD exhibit a deficit in the SRT when required to perform a concurrent explicit task (Deckersbach et al., 2002).

Inconsistent results in studies of implicit learning in OCD may be partly due to the heterogeneity of the studied populations, including comorbidity and the inclusion of medicated patients. Pharmacotherapy with SRIs reduces symptomatology in a majority of patients with OCD (Jenike, 2004; Soomro, Altman, Rajagopal, & Oakley-Browne, 2008) and reverses hyperactivity in the striatum and interconnected frontal cortical areas (Atmaca, 2013; Saxena & Rauch, 2000). Whether or not SRI pharmacotherapy in OCD mitigates deficits in implicit learning remains an important unresolved question.

We tested implicit learning in OCD using WPT. We expected patients with OCD to show a general deficit in implicit learning relative to healthy controls. We further expected that the performance of the medicated patients on WPT to differ from unmedicated and healthy controls.

2. Methods

2.1. Participants

All participants were recruited using advertisements and provided written informed consent. The study was approved by the Yale University Institutional Review Board. Participants consisted of 26 unmedicated patients with OCD, 25 SRI-medicated patients with OCD, and 23 healthy controls; groups were matched for age and gender (see Table 1). Of the 51 patients with OCD, 22 also met the criteria for major depressive disorder (MDD); 10 of these were medicated. All 25 patients with OCD in the medicated group were on a stable dose (>8 weeks) of an SRI. In addition, one patient was treated with riluzole, one with duloxetine, and two with PRN alprazolam. Diagnoses were established by a doctoral-level clinician and confirmed using the Structured Clinical Interview (SCID) for DSM-IV (First, 1996). Patients were free of comorbid substance abuse or dependence, current Tourette syndrome, psychotic disorders, and neurological disease or major head trauma.

2.2. Materials

Severity of symptoms was assessed using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) (Goodman et al., 1989) and the 25-item Hamilton Depression Scale (HAM-D) (Hamilton, 1960).

The WPT is an implicit learning task that requires participants to predict which of two possible outcomes will occur on each trial, based on a set of visual cues. Participants were told that their job was to decide whether a given set of cues predicted rain or sunshine. They were told that the relationship between cues and outcomes was complex, and that they would initially be guessing but would gradually become better at deciding which cues predicted rain or sunshine.

The full experiment consisted of 100 trials. Each trial consisted of stimulus presentation, decision, and feedback. Stimuli consisted of 1–3 cards displaying four geometric shapes, for a total of 14 possible card combinations. The relationship between the presented cards and the 'correct' decision was probabilistic rather than deterministic (see Table 2). Each individual card was associated with the outcomes according to a fixed probability; the probability associated with each collection of cards (Table 2) was calculated from the probabilities associated with the component cards (Table 3). Due to the probabilistic nature of the task, the 'true' outcome on each trial, on the basis of which feedback was given, did not always correspond to the outcome most likely to be associated with the presented stimuli. For analyses, a correct response was defined as one that corresponded to the outcome most likely to be associated with the presented cues. Mean accuracy,

Table 1
Demographic and clinical characteristics of participants.

Variable	Healthy controls (*M*, *SD*)	Medicated OCD (*M*, *SD*)	Unmedicated OCD (*M*, *SD*)	Test statistic
n	23	25	26	
Age	31.6 (12.16)	37 (12.91)	32.85 (13.48)	$F=1.17$
Gender (M/F)	12/11	11/14	14/12	$\chi^2=0.56$
Y-BOCS		26.44 (5.24)	28.84 (3.68)	$F=3.51$†
HAM-D		23.46 (10.41)	24.90 (9.61)	$F=.22$

Note. All *p*-values >0.10. Y-BOCS = Yale-Brown Obsessive Compulsive Scale; HAM-D = Hamilton Depression Scale. Y-BOCS and HAM-D test statistics for comparisons between medicated and unmedicated OCD patients. All tests were non-significant at the $p<0.05$ level. † denotes trend-level significance ($p<0.10$). YBOCS data were missing from one unmedicated OCD patient, HAM-D data were missing from 6 unmedicated and 3 medicated OCD patients.