Implicit Sequence Learning in Obsessive-Compulsive Disorder: Further Support for the Fronto-Striatal Dysfunction Model

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Background: *Obsessive-compulsive disorder (OCD) is conceived as a disease that implicates dysfunctions in fronto-striatal brain systems. According to this model, performance deficits observed in patients with lesions in these brain areas are hypothesized to be present also in OCD patients. Implicit procedural learning, which refers to the acquisition of motor or nonmotor skills by practice, is one candidate function to test this prediction.*

Methods: *The serial reaction time task was used to assess implicit sequence learning of 33 patients with a diagnosis of OCD and 27 healthy control participants. In addition, explicit (i.e., conscious) knowledge of the sequence was determined. A subgroup of 24 patients was reassessed after intensive cognitive-behavioral psychotherapy.*

Results: *Implicit sequence learning was significantly reduced in the OCD group by 41%, while explicit learning and verbal abilities were unaffected. The deficit remained stable across time, although symptoms remitted substantially. Depressive symptoms did not account for the finding. Partial explicit knowledge of the sequence was not a predictor of the amount of implicit learning.*

Conclusions: *Reduced implicit learning appears to be a dissociable trait of OCD patients. The results confirm previous findings and add supportive evidence for the fronto-striatal dysfunction model of OCD.*

Key Words: Obsessive-compulsive disorder, procedural learning, serial reaction time task, neuropsychology, fronto-striatal dysfunction, follow-up

Obsessive-compulsive disorder (OCD) is a pathological condition characterized by repetitive unwanted intrusive thoughts and ritualistic behaviors aimed at reducing feelings of tension, anxiety, and uncertainty. Psychodynamic (Freud 1955) as well as cognitive-behavioral models (Salkovskis 1999) have explained the disease in psychological terms by implicating adverse conditions in the individual's developmental history. More recently, the neuropsychological underpinnings of the disorder also have come into the focus of research. Results, although somewhat inconsistent so far, point to a variety of cognitive deficits that may be linked to dysfunctions in certain brain regions (Greisberg and McKay 2003; Kuelz et al 2004). Further support of a neuropsychological model of OCD comes from neurological diseases with pathological alterations of the basal ganglia, like Huntington's disease, Sydenham's chorea, Tourette's disorder, or focal basal ganglia lesions. The prevalence of concomitant obsessive-compulsive features in the course of these diseases has been shown to be elevated (Swedo et al 1989; Robertson 1989; Tomer et al 1993; Marder et al 2000; Chacko et al 2000). Moreover, functional brain imaging studies have revealed increased brain activity of OCD patients in the orbitofrontal cortex and the caudate nucleus during rest as well as during symptom provocation (Baxter et al 1987; Breiter et al 1996; Kwon et al 2003), thereby identifying possible disease-related brain circuits.

Based on this and further evidence, a model that implicates disturbed fronto-striatal brain systems in the pathogenesis of the disorder has been developed (Baxter et al 1987; Saxena et al 1998; Rauch and Savage 2000). Specifically, a circuit connecting the orbitofrontal cortex, the ventromedial caudate nucleus, additional substructures of the basal ganglia, and the thalamus, which projects back to orbitofrontal neurons, is supposed to be in a hyperactive state because of an imbalance of positive and negative feedback loops in this network. The imbalance is assumed to set a bias toward executing well-prepared, phylogenetically adaptive behaviors, whereas the ability to switch to new behaviors is weakened.

The basal ganglia, in interaction with cortical and cerebellar structures, play an important role in the nonconscious acquisition of skills, a phenomenon termed procedural learning. This has been demonstrated in neuroimaging studies (Rauch et al 1995; Peigneux et al 2000; Grafton et al 1995; Martis et al 2004), as well as in clinical studies using behavioral measures. Patients with Huntington's disease were shown to be impaired in implicit (i.e., unintended and unconscious) sequence learning (Willingham and Koroshetz 1993; Knopman and Nissen 1991). Parkinson's disease also appears to have a negative impact on the acquisition of procedural skills (Jackson et al 1995; Werheid et al 2003a). In another test of the basal ganglia hypothesis of procedural learning, Vakil et al (2000) found deficits in implicit sequence learning in a group of brain-damaged patients with lesions restricted to the basal ganglia.

These studies adopted the serial reaction time task (SRTT) as a test of implicit procedural learning performance (Nissen and Bullemer 1987). The task makes relatively little cognitive demand on the test participants in that it simply requires them to press keys spatially corresponding to the locus of single stimuli that successively appear at one of four locations. An important argument for the use of the SRTT is that participants with disrupted episodic memory (e.g., patients with Korsakoff's syndrome) are capable of implicitly learning the sequence of stimulus and response locations. That means they decrease their reaction times during repeating sequences relative to random sequences, although they are not aware of the regularity. Therefore, it can be assumed that the task assesses processes dissociable from the type of higher level learning that influences declarative memory.

As yet, only a few studies have addressed implicit procedural learning in patients suffering from OCD. Disrupted performance

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in the SRTT was shown when the patients were concurrently engaged in an explicit memory task (Deckersbach et al 2002). Using positron emission tomography, Rauch et al (1997) found reduced activation of basal ganglia in OCD patients compared with healthy control subjects when performing a variant of the SRTT. Reaction times were not increased in this study, however. The present study aims at extending those findings. We tested the hypothesis derived from the fronto-striatal dysfunction model of OCD that patients suffering from OCD have impaired implicit sequence learning performance in the SRTT as compared with healthy control participants. A single task design was adopted using the classical 10-item sequence SRTT version. To examine the stability of performance levels across time and psychopathological states, a subgroup of patients was retested following behavioral psychotherapy. In addition, the relationship of implicit procedural learning performance to symptom severity was explored cross-sectionally.

Methods and Materials

Participants

Forty-one patients with a diagnosis of obsessive-compulsive disorder and 36 healthy control subjects participated in this experiment. The OCD patients were recruited from consecutive admissions to the Psychosomatic Hospital at Windach, Germany. They were diagnosed according to the criteria of the DSM-IV by consensus of a psychiatrist and an experienced clinical psychologist. These clinicians were not involved in conducting the experiments or in data analysis. Diagnoses were established on the basis of a structured interview (Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version [SCID-CV]) (First et al 1996), extended clinical interviews, medical examination, information obtained from relatives and/or partners, and review of medical charts from previous hospitalizations, if available. Patients with a comorbid diagnosis of schizophrenia, substance abuse, or Tourette syndrome were not included. The included patients reported no history of head trauma or neurological disease.

Nonclinical control participants were recruited through local advertisements. They had no experience with the experimental task used here. In a personal interview (Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Non-Patient Edition [SCID-I/NP]) (First et al 2002), they reported to be free of past and present signs of psychiatric diseases and assured of not abusing alcohol and drugs. Control participants had scores of less than 10 on both the Beck Depression Inventory (BDI) (Beck et al 1961) and the Maudsley Obsessive Compulsive Inventory (MOCI) (Hodgson and Rachman 1977). They reported no intake of psychotropic medication for at least 4 weeks prior to examination. Groups were matched for age and verbal intelligence as measured by their scaled scores on the Vocabulary subtest of the German version of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) (Wechsler 1981). All participants had normal or corrected-to-normal vision.

After completing the experimental task, eight patients and nine healthy control participants were excluded from further analysis because they showed explicit knowledge of the learned sequence (see Data Analysis). The remaining 33 OCD patients and 27 healthy control participants continued to be comparable regarding the matching variables. Group characteristics of this analysis sample are presented in Table 1. Handedness was determined using the Edinburgh Handedness Inventory (EHI) (Oldfield 1971). Thirty patients (91%) were right-handed. Among the control participants, 21 (78%) were right-handed. Proportions of right-handers were not statistically different between patient and control groups ($\chi^2 = 2.1$, $p > .10$).

Table 1. Demographic and Psychopathological Characteristics of Study Groups

	Obsessive-Compulsive Disorder Patients	Healthy Control Subjects
N	33	27
Gender (Male/Female)	14/19	9/18
Age	35.6 (9.2)	38.6 (10.8)
Vocabulary[a]	11.9 (2.8)	11.8 (2.6)
Age at Illness Onset	18.6 (11.0)	—
Y-BOCS Total Score	20.4 (7.1)	—
HRSD-17 Items	7.4 (6.7)	—
MOCI	15.9 (5.4)	4.7 (3.3)
BDI	17.6 (11.5)	2.7 (2.9)

SD in parentheses, if applicable.

Y-BOCS, Yale-Brown Obsessive Compulsive Scale; HRSD-17, Hamilton Rating Scale for Depression, 17-item version; MOCI, Maudsley Obsessive Compulsive Inventory; BDI, Beck Depression Inventory.

[a]Scaled scores obtained in the subtest Vocabulary from the German version of the Wechsler Adult Intelligence Scale-Revised.

Study patients were initially tested in the acute state of illness, about 1 to 2 weeks after admission but before entering the exposure and response prevention program.

Follow-up tests were done after completion of the inpatient treatment phase, i.e., between 4 and 8 weeks after the initial test session. Twenty-four of the original 33 OCD patients participated in a retest session. Control participants were tested once only.

To assess psychopathology, patient behaviors were rated with the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) (Goodman et al 1989) and with the 17-item Hamilton Rating Scale for Depression (HRSD-17) (Hamilton 1960) at the days of the experimental sessions. These assessments were made by the responsible therapists who had been trained in using these instruments. They were blind to task performance. In addition, patients self-rated their symptoms on the MOCI and on the BDI at the same time. Eight OCD patients out of 33 presented current signs of a comorbid major depression (all of them receiving HRSD-17 ratings of 12 or larger). In any case, the depressive symptoms exacerbated after the onset of the obsessive-compulsive symptoms and were therefore considered by the clinicians to be secondary to the OCD.

Nine patients received antidepressive and antiobsessive medication, i.e., individual dosages of selective serotonin reuptake inhibitors (SSRIs); one patient received antipsychotic medication due to therapy-refractory obsessional symptoms; two patients were medicated with benzodiazepines only; one received thyroid hormones; and two patients were medicated with a combination of an SSRI and a benzodiazepine. Eighteen OCD patients were free of any psychotropic medication.

All participants were volunteers who had given written informed consent after having received a complete description of the study. The study protocol was approved by the local ethics committee of the Medical Faculty of the Ludwig Maximilians University of Munich, Germany.

Task and Procedure

Serial Reaction Time Task. A variant of the SRTT (Nissen and Bullemer 1987) was adopted to measure procedural learning performance. Stimuli were presented on the screen of a notebook computer. Four boxes (2 cm × 2 cm) arranged in a single