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# Transcranial sonography in obsessive–compulsive disorder

Paraskevi Mavrogiorgou [a,1], Fabio Nalato [a,1], Saskia Meves [b], Stefanie Luksnat [a], Christine Norra [a], Ralf Gold [b], Georg Juckel [a,*], Christos Krogias [b]

[a] Dept. of Psychiatry, Ruhr University Bochum, LWL-Universitätsklinikum, Alexandrinenstr. 1, 44791 Bochum, Germany
[b] Dept. of Neurology, Ruhr University Bochum, St. Josef-Hospital, Gudrunstr. 56, 44791 Bochum, Germany

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ABSTRACT

There is convergent evidence that basal ganglia structures are involved in the pathogenesis of obsessive–compulsive disorder (OCD). It has been also assumed that OCD is caused by a central serotonergic dysfunction. Transcranial sonography (TCS) has become a reliable, sensitive and non-invasive diagnostic tool concerning the evaluation of extrapyramidal movement disorders. This study used TCS to examine the alterations in different parenchymal regions, especially concerning serotonergic brainstem raphe nuclei as well as basal ganglia in OCD. Thirty-one OCD patients were compared with 31 matched healthy controls. Echogenecities were investigated according to the examination protocol for extrapyramidal disorders using a Siemens Sonoline® Elegra system. Obsessive–compulsive disorder patients showed reduced echogenity of the serotonergic brainstem raphe nuclei (32.3%) compared with healthy controls (16.1%). In nine OCD-patients (31%), but only in 2 control subjects (6.2%), a hyperechogenicity of the caudate nucleus was found. Patients with OCD significantly more often reveal a hypoechogenic brainstem raphe possibly reflecting altered serotonergic neurons there and a hyperechogenicity of caudate nucleus indicating structural or molecular cell changes. Further research is warranted to examine, whether TCS is useful in order to classify OCD and its subtypes.



## 1. Objectives of the study

Obsessive–compulsive disorder (OCD) is a common psychiatric disorder, which affects 1–3% of the population (Fullana et al., 2010; Kessler et al., 2012). Patients with OCD are suffering from recurrent, unwanted thoughts (obsessions) and repetitive, ritualistic behaviour (compulsions), often being intended to neutralize tension and anxiety induced by the obsessions. In the last two decades, efficacious pharmacological and psychotherapeutic treatments for OCD have been validated and well established (Eddy et al., 2004; Fineberg et al., 2013). Cognitive behavioral therapy (Otte, 2011; Ougrin, 2011) and several pharmacological agents, especially serotonin reuptake inhibitors (SSRI) (Soomro et al., 2008; Stein et al., 2012) improve OCD symptoms in up to 70% of patients (Stein, 2002). However, about 40–60% of OCD patients do not show a sufficient response to adequate treatment (Pallanti &, Quercioli, 2006). This high rate of non-responders as well as current neurobiological findings show that OCD is a pathogenetic and phenotypic highly heterogeneous disorder and is possibly composed of many different subtypes (Mataix-Cols et al., 2005; Hoexter et al., 2009).

Several research studies provided growing evidence for a neurobiological basis of OCD (Karch &, Pogarell, 2011). Neurochemical and neuroimaging studies have shown that various neurotransmitters are implicated in the pathophysiology of this disorder including dopamine (Denys et al., 2004; Kim et al., 2007), serotonin (Barr et al., 1992; Westenberg et al., 2007) or glutamate (Carlsson, 2000; Pittenger et al., 2006). The neurochemical model of OCD is postulated as a central serotonergic dysfunction, which has also been implicated based on the efficacy of SSRIs in OCD.

Furthermore, in addition to neurotranmitter dysfunction in OCD, it has been assumed that OCD is caused by abnormal activity in cortico-striato-thalamo-cortical (CSTC) circuits including the orbitofrontal cortex, the striatum within basal ganglia and the thalamus (Baxter et al., 1987; Chamberlain et al., 2006). In particular, it was postulated that obsessive–compulsive symptoms may be represented by increased activity in the orbitofrontal cortex (OFC) as a consequence of diminished inhibitoric effects of the striatum on the thalamus.

There is convergent evidence that basal ganglia, a group of nuclei, which include the striatum (caudate and putamen), the

* Corresponding author. Department of Psychiatry, Ruhr University Bochum, LWL-University Hospital, Alexandrinenstr. 1, 44791 Bochum, Germany. Tel.: +49 234 5077 1100; fax: +49 234 5077 1109.
*E-mail address:* JuckelGWK@aol.com (G. Juckel).
[1] Both authors equally contributed.

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globus pallidus, the subthalamus, and the substantia nigra are implicated in OCD pathogenesis (Saxena et al., 1998; Piras et al., 2013). In particular, the caudate nucleus plays an important role in procedural learning and may contribute to abnormal processing of behavioural sequences generated by frontal subcortical circuits that have been hypothesized to exist in OCD (Saxena &, Rauch, 2000). Multiple imaging studies have shown functional and structural abnormalities in these regions among patients with OCD, but these results are inconsistent (Holzschneider &, Mulert, 2011). However, it remains unclear whether neurotransmitters, especially serotonin, are involved in the abnormalities of CSTC circuit in OCD.

Transcranial sonography (TCS) is a noninvasive and inexpensive method, which depicts the echogenity (intensity of reflected ultrasound waves) in different parenchymal regions of the brain. TCS has become a reliable and sensitive diagnostic tool in the evaluation of extrapyramidal movement disorders, especially in the differentiation of parkinsonian syndromes. In particular, hyperechogenicity of the substantia nigra is a highly characteristic finding for idiopathic Parkinson's disease (Becker et al., 1995a; Walter et al., 2003; Berg et al., 2008). It is assumed that this echo signal alteration is based on increased amounts of iron, bound to proteins other than ferritin (Berg et al., 2002). Furthermore, alterations of serotonergic brainstem raphe (BR) nuclei have been observed by TCS in major depression as well as in depressed Parkinson's or Huntington's disease patients (Becker et al., 1995b; Berg et al., 1999; Walter et al., 2007a,b; Krogias et al., 2011a). Although there was no significant difference in the presentation of BR signals between bipolar patients in comparison to healthy controls, depressed bipolar patients with reduced BR echogenity interestingly showed significantly higher depressed scale scores (Krogias et al., 2011b).

In the present study, a complete sonographic evaluation was performed for the first time in OCD. Aim of our study was to evaluate BR echogenicity of patients with obsessive–compulsive disorder as compared to healthy controls. In regard to the serotonin deficit hypothesis of OCD, it was hypothesized that hypoechogenic BR should be detected more frequently in OCD patients.

A second hypothesis was that OCD patients more frequently show alterations of the basal ganglia, especially the striatum, as based on the neuroanatomical model of OCD.

## 2. Materials and methods

### 2.1. Subjects

Thirty-one patients with unequivocal diagnosis of obsessive–compulsive disorder were recruited from the outpatient clinic for OCD at the Department of Psychiatry, Ruhr University Bochum. Diagnosis was based on the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV, APA, 2000).

Exclusion criteria were organic psychiatric disorders or recent concomitant neurological or other medical disorders and the presence of severe alcohol or substance abuse. No patient met the criteria for Tourette syndrome and any psychotic disorder. Comorbid major depression and anxiety disorders were not considered as a exclusion criteria. Table 1 shows the demographic and clinical data of the thirty-one patients being included in the study. Most patients were receiving a variety of constant medications including antidepressant and/or an adjunct antipsychotic agent (Table 2). Cognitive behavioral therapy was not administered to anyone at any time of this study.

Initially, a control group of 13 healthy volunteers was created. These 13 persons underwent the Structural Clinical Interview for DSM-IV (Sheehan et al., 1998), the psychometric tests for obsessive–compulsive symptoms as well depressive and anxiety symptoms.

To improve statistical analysis, the control group was expanded with 18 further age-matched healthy persons from a pre-existing group of healthy persons forming the reference group of our sonography laboratory.

Thirty-one healthy volunteers without any neurological or psychiatric disorders in personal or family history served as an age-matched control group. They were recruited from persons within and externally of the hospital staff and medical students. Their demographic data are also shown in Table 1.

All subjects gave written consent, after the study was fully explained to them. In accordance to the Helsinki Declaration of 1975, the study was approved by the local university ethics committee of the Ruhr University Bochum, Germany.

**Table 1**
Demographic and clinical characteristics of OCD patients and healthy controls.

| | OCD ($n = 31$) | Healthy controls ($n = 31$) | Statistics *t*-test |
|---|---|---|---|
| Gender (m/f) | 20/11 | 19/12 | |
| Age, mean (SD), years | 37.2 (10.3) | 34.9 (12.0) | $p = 0.431$ |
| Illness duration mean (SD), years | 16.8 (9.7) | – | |
| HAM-D score, mean (SD) | 17.3 (7.2) | 8.0 (0.9) | $p < 0.001$ |
| BDI, mean (SD) | 19.5 (11.5) | 8.0 (1.5) | $p < 0.001$ |
| Y-BOCS obsessions, mean, (SD) | 12 (4.5) | – | |
| Y-BOCS compulsions, mean (SD) | 12 (3.3) | – | |
| Y-BOCS total score mean (SD) | 23.9 (7.6) | – | |
| MOCI mean (SD) | 17.6 (5.6) | – | |
| STAI I mean (SD) | 43.5 (6.4) | – | |
| STAI II mean (SD) | 47.9 (8.9) | – | |
| CGI mean (SD) | 4.7 (1.0) | – | |
| PSP mean (SD) | 50.5 (15.5) | – | |

HAM-D = Hamilton-Depression Scale; BDI = Beck-Depressions-Inventory: Y-BOCS = Yale-Brown Obsessive-Compulsive Scale; MOCI = Maudsley Obsessional–Compulsive Inventory; CGI = Clinical Global Impressions; STAI = State-Trait Anxiety Inventory; PSP = Personal and Social Performance Scale.

### 2.2. Clinical assessment

Severity of obsessive–compulsive symptoms was assessed by the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS, Goodman et al., 1989a,b) and Maudsley Obsessive–Compulsive Inventory (MOCI, Hodgson &, Rachman, 1977). To validate the presence of OCD (sub)symptoms we use the Yale-Brown Obsessive–Compulsive symptom checklist.

Severity of depressive symptoms was assessed using the Hamilton Depression Rating Scale (HAM-D, Hamilton, 1967), and self-ratings with Beck's Depression Inventory (BDI, Beck et al., 1961).

**Table 2**
Psychopharmacological medication and daily dose.

| | $N = 31$ (%) | Daily dose (mg) median (range) |
|---|---|---|
| Citalopram | 2 (6.5) | 70 (60–80) |
| Clomipramine | 2 (6.5) | 125 (50–200) |
| Escitalopram | 9 (29.0) | 21 (10–40) |
| Fluoxetine | 7 (22.6) | 53 (20–80) |
| Paroxetine | 5 (16.1) | 56 (40–80) |
| Sertraline | 4 (12.9) | 213 (150–300) |
| St. Johns wort | 1 (3.2) | 900 |
| None | 1 (3.2) | – |

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