



Neural correlates of processing harmonic expectancy violations in children and adolescents with OCD



Judith Buse*, Veit Roessner

Department of Child and Adolescent Psychiatry, Faculty of Medicine of the TU, Dresden, Germany

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ABSTRACT

It has been suggested that patients with obsessive–compulsive disorder (OCD) exhibit enhanced awareness of embedded stimulus patterns as well as enhanced allocation of attention towards unexpected stimuli. Our study aimed at investigating these OCD characteristics by running the harmonic expectancy violation paradigm in 21 boys with OCD and 29 healthy controls matched for age, gender and IQ during a functional magnetic resonance imaging (fMRI) scan. Each trial consisted of a chord sequence in which the first four chords induced a strong expectancy for a harmonic chord at the next position. In 70% of the trials the fifth chord fulfilled this expectancy (harmonic condition), while in 30% the expectancy was violated (disharmonic condition). Overall, the harmonic condition elicited blood-oxygen-level dependent (BOLD) activation in the auditory cortex, while during the disharmonic condition the precuneus, the auditory cortex, the medial frontal gyrus, the premotor cortex, the lingual gyrus, the inferior frontal gyrus and the superior frontal gyrus were activated. In a cluster extending from the right superior temporal gyrus to the inferior frontal gyrus, boys with OCD exhibited increased activation compared to healthy controls in the harmonic condition and decreased activation in the disharmonic condition. Our findings might indicate that patients with OCD are excessively engaged in processing the implicit structure embedded in music stimuli, but they speak against the suggestion that OCD is associated with a misallocation of attention towards the processing of unexpected stimuli.

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1. Introduction

Obsessive–compulsive disorder (OCD) is characterized by intrusive thoughts and time-consuming repetitive behaviors often causing significant impairment. Approximately 2% of the population are affected (Ruscio et al., 2010). Many patients with OCD report about sensations of incompleteness or something being “not-just-right” accompanying their symptoms. These sensations – often referred to as Not-just-right experiences (NJRE) – can be evoked by visual, auditory or tactile perceptions and often entail the urge to perform a compensatory compulsion (Leckman et al., 1994; Prado et al., 2007; Summerfeldt, 2004).

NJRE are more frequent in patients with early-onset OCD (Rosario-Campos et al., 2001), which has been suggested to represent a distinct subtype of OCD (Chabane et al., 2005). Besides the higher frequency of NJRE, early onset OCD is also associated with a higher frequency of tic-like compulsions, a greater familial aggregation of OCD and tic disorders

and a male predominance (Chabane et al., 2005; Geller et al., 2007; Nestadt et al., 2003; Roessner et al., 2005; Rosario-Campos et al., 2001).

Although NJRE have gained some attention in recent years, most studies have not gone beyond a description of their phenomenology and prevalence and the underlying mechanisms of NJRE remain elusive.

Rauch and Savage (2000) proposed that cognitive intrusions in OCD might stem from a misallocation of attention towards stimuli that would normally be processed without conscious awareness. The underlying neural mechanism might be a disbalance between the direct cortico–pallido–thalamic pathway, which amplifies attention towards salient stimuli and the indirect pathway, which helps to inhibit distraction from nonsalient cues. This assumption got empiric support from a study utilizing an implicit procedural learning task. While patients with OCD had deficits in implicit procedural learning, they showed enhanced awareness of the stimulus pattern that was embedded in the implicit learning task (Goldman et al., 2008).

It has also been proposed that patients with OCD exhibit a hypersensitivity of the stimulus-driven attentional system (Mathews and Mackintosh, 1998), assessable in the orienting response towards unexpected stimuli. An enhanced cortical orienting response is reflected in enhanced P3 event-related potential amplitudes. Indeed, a heightened P3b and shortened P3b latencies following target sounds have been found in patients with OCD (Gohle et al., 2008; Ischebeck et al.,

* Corresponding author at: Department of Child and Adolescent Psychiatry, Medizinische Fakultät Carl Gustav Carus, Technische Universität Dresden, Fetscherstrasse 74, 01307 Dresden, Germany.

E-mail address: judith.buse@uniklinikum-dresden.de (J. Buse).

2011; Johannes et al., 2001; Mavrogiorgou et al., 2002). The P3b is largely generated in temporal-parietal regions as well as in the hippocampus (Huang et al., 2015; Molnár, 1994).

An ideal probe for studying how patients with OCD a) process implicit structures of stimuli and b) respond to the presentation of unexpected stimuli might be the harmonic expectancy violation paradigm by Koelsch et al. (2000, 2005). The harmonic expectancy violation paradigm is based on tonal music constructed in accordance to specific regularities, sometimes called the musical syntax. Listeners brought up in a western culture are familiar with these regularities and detect violations of the expected harmonic structure (Koelsch, 2005; Koelsch et al., 2000). In a previous study it was shown that the violation of music-syntactic regularities by disharmonic chord sequences provokes feelings in healthy controls that are similar to NJRE reported in the context of obsessive-compulsive (OC) symptomatology (Buse et al., 2015).

The detection of music-syntactically irregular chords is reflected in a negative Event-Related Potential (ERP) that occurs at about 200 ms after onset of the disharmonic chord and is strongest over right-frontal electrode leads (Koelsch, 2005; Koelsch et al., 2000). Functional neuroimaging studies show that the processing of harmonic expectancy violations is located in the inferior frontolateral cortex (often denoted as 'Broca's area', an area that has also been implicated in the processing of linguistic syntax) (Koelsch, 2005; Maess et al., 2001) but also the superior temporal gyrus and the premotor cortex (Koelsch et al., 2002, 2005).

The aim of the current study was to investigate the neural correlates of a) the processing of music-syntactic regularities and b) the detection of violations of those regularities in children and adolescents with OCD.

We hypothesized that boys with OCD exhibit altered BOLD activation as compared to healthy controls during the harmonic expectancy violation paradigm in the inferior fronto-lateral cortex, the superior temporal gyrus and the premotor cortex, but potentially also in temporal-parietal regions and in the hippocampus.

2. Methods

2.1. Sample characteristics

Participants with OCD were recruited among referrals to the Child and Adolescent Psychiatry of the University Medical Centre Dresden. The OCD diagnoses were made by board certified child and adolescents psychiatrists using ICD-10 criteria. Additionally, all potential participants were screened for psychiatric disorders with the Mini International Neuropsychiatric Interview for Children and Adolescents (M.I.N.I.-Kid, Sheehan et al. (1998)).

The recruitment was restricted to boys aged between 11–17 years. We chose to examine only children and adolescent, because the phenomena of interest are particularly present in the early-onset OCD subtype.

Initially, 21 boys with OCD and 29 healthy controls were recruited. The healthy controls were matched with the patients with regard to age, sex and IQ. We excluded patients with any comorbid diagnosis to OCD, except related disorders such as phobia ($n = 3$), panic disorder ($n = 1$) and depressive episode in the past ($n = 1$) since they were no current source of impairment. Four boys with OCD had to be excluded because of movement artifacts, resulting in a total of 17 boys with OCD. One of the controls had to be excluded because of claustrophobia, one because of a previously undetected large intracranial cyst and one because he exhibited motor tics during the examination. Three controls were excluded because of movement artifacts, resulting in a total of 23 boys in the control group.

Two boys with OCD were currently taking medication (both fluoxetine).

Written informed consent was obtained from both the participants and their parents after the procedure had been fully explained. The study was approved by the ethics committee of the TU Dresden and

Table 1
Demographics and clinical characteristics of the sample.

		Boys with OCD N = 17	Healthy control boys N = 23		
		Mean (SD)	Mean (SD)	t(38)	p
Age (in years)		14.88 (1.73)	14.26 (1.89)	1.07	.293
IQ		114 (27.66)	110 (13.08)	0.60	.553
Age at OCD onset		10.47 (3.32)			
Duration of OCD		4.41 (2.94)			
CY-BOCS	Obsessions	7.59 (5.29)	–	–	–
	Compulsions	8.29 (5.02)	–	–	–
	Total score	15.88 (8.58)	–	–	–
OCI-R	Global score	21.35 (19.82)	4.35 (6.01)	3.90	<0.001
OCTCDQR	Harm avoidance	6.77 (4.48)	1.78 (2.81)	4.32	<0.001
	Incompleteness	11.41 (8.46)	3.13 (4.61)	4.00	<0.001
ZWIK-E	Total score	82.65 (18.57)	24.13 (25.23)	8.07	<0.001
ZWIK-K	Total score	65.59 (32.52)	21.44 (25.48)	4.82	<0.001

IQ = assessed with the short version of the Hamburg-Wechsler-Test for Intelligence for children (HAWIK-IV, German version of the WISC-IV) (Petermann and Petermann, 2010), CY-BOCS = Children's Yale-Brown Obsessive-Compulsive Scale (Scahill et al., 1997), OCI-R = Obsessive-Compulsive Inventory (Foa et al., 2002), OCTCDQR = Obsessive-Compulsive Trait Core Dimensions Questionnaire – Revision (Summerfeldt et al., 2001), ZWIK = Zwangsinventar für Kinder und Jugendliche (Goletz and Döpfner, 2011) (ZWIK-E = parent-report version, ZWIK-K = self-report version).

was carried out in accordance with the latest version of the Declaration of Helsinki. The demographics and clinical characteristics of the sample are presented in Table 1.

2.2. Assessment of OC symptoms and motivational core dimensions

The Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) (Scahill et al., 1997) was obtained from all boys with OCD. The CY-BOCS is a half-structured interview to determine the severity of symptoms in pediatric OCD.

Both boys with OCD and healthy controls completed the Obsessive-Compulsive Inventory (OCI-R) ((Foa et al., 2002), German version by Gönner et al. (2007)), a self-report instrument measuring dimensional OC symptoms on six subscales (washing, obsessing, hoarding, ordering, checking and neutralizing) and one global symptom scale.

The Obsessive-Compulsive Trait Core Dimensions Questionnaire – Revision (OCTCDQ-R) developed by Summerfeldt et al. (2001) assesses the two motivational core dimensions underlying OCD-like symptoms: harm avoidance and incompleteness. We used the German short version of the questionnaire (Ecker et al., 2011). The OCTCDQ-R was obtained from all participants.

In addition, the Zwangsinventar für Kinder und Jugendliche (ZWIK) (Goletz and Döpfner, 2011), a German questionnaire to dimensionally assess pediatric OC symptoms was completed by all participants (ZWIK-K: self-report form) and their parents (ZWIK-E: parent-report form). It provides scores on four subscales (contamination fears and washing compulsions, controlling and repeating, obsessions about the harm or injury of oneself or others, counting and questioning) as well as one total symptom score.

2.3. Task

The harmonic expectancy violation paradigm (e.g. Koelsch et al., 2000) is based on tonal music constructed in accordance to specific implicit regularities. It enables the assessment of reactions to violations of those regularities.

The stimuli were chord sequences, identical to those used by (Koelsch et al., 2005), consisting of five chords each. The first four chords corresponded to the rules of classical harmony with the fourth

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