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Lower prefrontal activity in adults with obsessive–compulsive disorder as measured by near-infrared spectroscopy

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ABSTRACT

Recent developments in near-infrared spectroscopy (NIRS) have enabled the non-invasive elucidation of the neurobiological underpinnings of psychiatric disorders. Functional neuroimaging studies in human patients have suggested that the frontal cortex and subcortical structures may play a role in the pathophysiology of obsessive–compulsive disorder (OCD). Here we used NIRS to investigate neurobiological function in 12 patients with OCD and 12 age- and sex-matched, healthy control subjects. The relative concentrations of oxyhemoglobin (oxy-Hb) were measured with prefrontal probes every 0.1 s, during performance of a Stroop color-word task, using 24-channel NIRS. Oxy-Hb changes in the prefrontal cortex of the OCD group were significantly smaller than those in the control group, especially in the left lateral prefrontal cortex. These results suggest that patients with OCD have reduced prefrontal hemodynamic responses as measured by NIRS.

1. Introduction

Obsessive–compulsive disorder (OCD) is one of the most common mental disorders in the general population, with a prevalence rate of 2% to 3% (Weissman et al., 1994). The main clinical manifestations in OCD patients are recurrent, intrusive, and distressing thoughts and/or repetitive behaviors, resulting in significantly impaired occupational and social functioning (Koran et al., 1996). However, while the clinical manifestations are well-characterized, the neurobiological mechanisms responsible for the disorder remain unknown.

It has been hypothesized that the cortico-striato-thalamic circuits play a key role in the pathophysiology of OCD (Menzies et al., 2008). Studies of OCD patients using positron emission tomography (PET) have identified abnormally high, functional activity in localized regions of the brain, including the orbitofrontal cortex, anterior cingulate cortex, and caudate nucleus (Baxter et al., 1987; Swedo et al., 1989a, 1989b). In addition, studies of OCD patients using single photon emission computed tomography (SPECT) indicate dysfunction of the orbitofrontal cortex and caudate nucleus (Busatto et al., 2000; Machlin et al., 1991). Whiteside et al. (2004) performed a meta-analysis of PET and SPECT findings and reported consistent abnormalities in the orbital gyrus and the head of the caudate nucleus in OCD patients. In another meta-analysis of functional magnetic resonance imaging (fMRI) findings in OCD patients, Menzies et al. (2008) found consistent abnormalities in the orbitofrontal cortex and striatum as well as other areas. Many studies have reported the dysfunction of the prefrontal cortex, it is possible that OCD patients have abnormal prefrontal hemodynamic responses.

Functional brain imaging methodologies such as PET, SPECT, and fMRI have the disadvantage of requiring large apparatuses, which prevents their use in a bedside setting for diagnostic and treatment purposes. Furthermore, these functional brain imaging methodologies do not offer high time resolutions. In contrast, multi-channel near-infrared spectroscopy (NIRS) systems have recently been developed to allow non-invasive and bedside functional mapping of the cerebral cortex, with high time resolution (Koizumi et al., 1999; Maki et al., 1995; Yamashita et al., 1996).

NIRS is a method that enables functional imaging of brain activity (Villringer and Chance, 1997). It measures changes in the concentration of oxy-hemoglobin (oxy-Hb) and deoxy-hemoglobin (deoxy-Hb), and changes in the redox state of cytochrome c oxidase by their different specific spectra in the near-infrared range between 700 and 1000 nm.

Abbreviations: OCD, obsessive–compulsive disorder; NIRS, near-infrared spectroscopy; Hb, hemoglobin; PET, positron emission tomography; SPECT, single photon emission computed tomography; fMRI, functional magnetic resonance imaging; ADHD, attention deficit hyperactivity disorder; DSM-IV-TR, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; SCID, Structured Clinical Interview for DSM-IV Axis I Disorders Patient Edition; SCID-NP, Structured Clinical Interview for DSM-IV Axis I Disorders Non-Patient Edition; FIQ, full-scale intelligence quotient; Y–BOCS, Yale–Brown Obsessive–Compulsive Scale; MOCI, Maudsley Obsessive–Compulsive Inventory; SCWC-1, Stroop color-word task number of correct answers for the first presentation; SCWC-2, Stroop color-word task number of correct answers for the second presentation; SCWC-3, Stroop color-word task number of correct answers for the third presentation.

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Because of neurovascular coupling (Gratton et al., 2001; Villringer and Dirnagl, 1995), brain activation leads to an increase in cerebral blood flow without a proportionate increase in oxygen consumption, and, consequently, to an increase in the concentration of oxy-Hb and a decrease in the concentration of deoxy-Hb (Villringer and Chance, 1997).

NIRS is a neuroimaging modality that is especially suitable for psychiatric patients for the following reasons (Matsuo et al., 2003). First, because NIRS is relatively insensitive to motion artifact, it can be used in experiments that might cause some motion in the subjects, such as those requiring the subject to produce a vocalization. Second, the subject can be examined in a natural sitting position, without any surrounding distractions. Third, the cost of this technique is much lower than other neuroimaging modalities, and implementing this procedure is relatively easy. Fourth, the high temporal resolution of NIRS is useful in characterizing the time course of prefrontal activity in psychiatric disorders (Kameyama et al., 2006; Suto et al., 2004). Accordingly, NIRS has been used to assess brain functions in many psychiatric disorders, including schizophrenia, bipolar disorder, depression, dementia, post-traumatic stress disorder, pervasive developmental disorders, and attention deficit hyperactivity disorder (ADHD) (Fallgatter et al., 1997; Kameyama et al., 2006; Kubota et al., 2005; Kuwabara et al., 2006; Matsuo et al., 2003; Negoro et al., 2010; Suto et al., 2004). In the context of OCD, Ota et al. (in press) examined reduced prefrontal hemodynamic responses in pediatric OCD children as measured by NIRS. Moreover, they determined cerebral hemodynamic changes in response to the Stroop color-word task in 12 OCD children and 12 healthy age- and sex-matched controls. They found that oxy-Hb changes in the control group were significantly larger than those in the OCD group in the prefrontal cortex, especially in the frontopolar cortex, during the Stroop color-word task.

To our knowledge, however, there are no reports of prefrontal hemodynamic responses in adult OCD patients as measured by NIRS. Previous studies have discussed whether the neural bases of adult OCD are similar to those of pediatric OCD (Kalra and Swedo, 2009; Maia et al., 2008). Previously published studies on OCD patients using SPECT have suggested that early-onset OCD cases show decreased regional cerebral blood flow in the right thalamus, left anterior cingulate cortex, and bilateral inferior prefrontal cortex, compared to late-onset subjects (Busatto et al., 2001). Few studies have provided evidence for pathophysiological distinct subtypes of OCD that vary in symptoms present in childhood versus those that emerged de novo, in adulthood (Busatto et al., 2001; Eichstedt and Arnold, 2001; Geller et al., 1998). Another resting state SPECT study suggested that the regions of dysfunction in pediatric OCD were largely consistent with those in adult OCD (Diler et al., 2004). Based on another study using NIRS in pediatric OCD patients, and previous studies using other neuroimaging techniques that showed dysfunction of the prefrontal cortex, we hypothesized that adult OCD patients have reduced prefrontal hemodynamic response as measured by NIRS, as well as pediatric OCD patients. Thus, in the present study, we used similar design that was used in pediatric OCD patients, i.e., we used multi-channel NIRS to examine the characteristics of prefrontal cerebral blood volume changes during the Stroop color-word task in adult OCD patients, and in age- and sex-matched control subjects.

2. Methods

2.1. Subjects

Twelve subjects (7 males and 5 females) aged 19–50 years and diagnosed with OCD, according to the DSM-IV-TR [American Psychiatric Association, 2000], were compared with 12 age-, sex-, and intelligence quotient (IQ)-matched healthy control subjects (7 males and 5 females) (Table 1).

The subjects with OCD were recruited from the outpatient units of the Department of Psychiatry at Nara Medical University. They underwent a standard clinical assessment comprising a psychiatric evaluation, a structured diagnostic interview (Structured Clinical Interview for DSM-IV Axis I Disorders Patient Edition; SCID), and a medical history evaluation under the supervision of an experienced psychiatrist. Two experienced psychiatrists confirmed the diagnosis of OCD in each patient. Of the subjects with OCD, none had comorbid major depressive disorder, schizophrenia, or bipolar disorder. One subject had comorbid social anxiety disorder. Patients who presented with a neurological disorder, a head injury, a serious medical condition, or a history of substance abuse/dependence were excluded. Intelligence was assessed using the Wechsler Adult Intelligence Scale — Third Edition by a trained psychologist, and patients whose full-scale IQ (FIQ) scores were below 70 were excluded. Two of the 12 OCD patients selected for the study were not medicated for the disorder (hereafter, drug naive), whereas the remaining 10 subjects were receiving medication for OCD symptoms (six, fluvoxamine; two, paroxetine; two, clomipramine). We then used factor analysis, developed by Leckman et al. (1997), to categorize the patients by symptom subtypes. The individual symptom subtypes included contamination and cleaning (33.3%, n = 4), obsessions and checking (41.7%, n = 5), symmetry and ordering (16.7%, n = 2), and hoarding (8.3%, n = 1).

Healthy control subjects were recruited through local print advertising, and 15 participants were recruited in this study. They also underwent a standard clinical assessment comprising of psychiatric evaluation, a structured diagnostic interview (Structured Clinical Interview for DSM-IV Axis I Disorders Non-Patient Edition; SCID-NP), and an evaluation of medical history by an experienced psychiatrist. Intelligence was assessed using the Wechsler Adult Intelligence Scale — Third Edition by a trained psychologist. Three participants were excluded as they did not meet the assessment criteria. Therefore, a total of 12 healthy subjects who did not have OCD and had no history or symptoms of psychiatric or neurological disorders were enrolled in the present study.

All subjects were right-handed and Japanese. Ethical approval for the present study was obtained through the Nara Medical University, and written informed consent was obtained from all subjects before the study.

2.2. Assessment of OCD symptoms

The Yale–Brown Obsessive–Compulsive Scale (Y–BOCS) (Nakajima et al., 1995) and the Maudsley Obsessive–Compulsive Inventory (MOCI) (Sánchez-Meca et al., 2011) were used to evaluate symptoms in the subjects with OCD.

The Y–BOCS is a well-accepted 10-item semi-structured clinician-rated instrument designed to assess the presence and severity of current OCD symptoms. The MOCI is a self-administered questionnaire with a true-false question format that was developed for evaluating the types

Table 1
Characteristics of the subjects.

	OCD mean(SD)	Control mean(SD)	p-value
Number[sex ratio: M:F]	12[7:5]	12[7:5]	1.00
Age (years)	32.1(10.0)	33.0(9.2)	0.81
Age of onset (years)	21.9(6.3)	NA	NA
Duration of illness (years)	11.8(8.1)	NA	NA
FIQ(WAIS-III)	92.0(19.5)	90.5(12.1)	0.83
Y–BOCS	24.5(3.5)	NA	NA
MOCI	16.7(4.4)	4.6(3.1)	<0.001
SCWC-1	44.0(11.2)	46.4(10.2)	0.58
SCWC-2	45.3(9.9)	48.0(12.3)	0.55
SCWC-3	49.0(11.8)	52.9(12.3)	0.43

Group differences tested with *t*-tests.
F, female; FIQ (WAIS-III), Full scale IQ score of the Wechsler Adult Intelligence Scale -Third Edition; M, male; MOCI, Maudsley Obsessional–Compulsive Inventory; NA, not applicable; OCD, Obsessive–compulsive disorder; SCWC-1, Stroop color-word task number of correct answers first time; SCWC-2, Stroop color-word task number of correct answers second time; SCWC-3, Stroop color-word task number of correct answers third time; Y–BOCS, Yale–Brown Obsessive–Compulsive Scale.