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Short communication

Hyperfunction of left lateral prefrontal cortex and automatic thoughts in social anxiety disorder: A near-infrared spectroscopy study

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ABSTRACT

Background: Patients with social anxiety disorder (SAD) experience unusual fear in normal social situations. The verbal fluency task (VFT) was administered while subjects were undergoing near-infrared spectroscopy (NIRS) scanning. The purpose of VFT was to examine the functions of the frontal and temporal lobes.
Methods: Subjects included 145 drug-naïve patients with SAD and 152 healthy controls (HCs). All subjects underwent psychological testing to determine levels of anxiety and depression and to evaluate cognition.
Results: The scores of patients with SAD indicated significantly higher anxiety and depressive states than those in HCs on several measures: Leibowitz Social Anxiety Scale (LSAS), Profile of Mood States (POMS), Spielberger Anxiety Inventory (STAI), Beck Depression Inventory (BDI), and Social Adaptation Self-evaluation Scale (SASS). The patients with SAD also had higher scores on the future denial, threat prediction, self-denial, past denial, and interpersonal threat sections of the Depression and Anxiety Cognition Scale (DACS). NIRS scanning revealed hyperactivity in the left frontal cortex of patients with SAD. Threat prediction scores on DACS were negatively correlated with oxy-Hb responses in the right frontal cortex.
Limitations: Further studies with a larger sample size are required to verify our findings.
Conclusions: The results of this study demonstrate the different mechanisms of the right and left frontal cortex in situations of social anxiety disorder.

1. Introduction

Social anxiety disorder (SAD) has been recognized as a phobic disorder. In the Diagnostic and Statistical Manual of Mental Disorders (DSM 5), SAD is described as a persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others.

Cognitive-behavioral models of social anxiety suggest that negative self-evaluations in social situations are crucial in the occurrence and continuation of social anxiety (Clark and Wells, 1995). Recent studies have emphasized the role of cognitive processes in the maintenance of SAD (Holas et al., 2014). One study showed how eye contact with another person can be an aversive and highly arousing experience for adolescents with SAD. The anxiety stereotypes should be considered as a possible source of the fear of negative assessment among patients with SAD.

The prefrontal cortex has been strongly associated with the primary formation of fear memories, providing new possibilities for studying the neurobiology of underlying unusual fear in anxiety disorders. The prefrontal cortex accelerates fear memory through the incorporation of sensory and emotional signals and through the organization of memory storage in an amygdala-based network (Dejean et al., 2015).

Near-infrared spectroscopy (NIRS) is an advanced, noninvasive neuroimaging procedure with a good chronological resolution that measures concentrations of oxy- and deoxy-hemoglobin (referred to herein as oxy-Hb and deoxy-Hb, respectively) as they alter the cerebral cortex. The anxiety index can be predicted from alterations in the oxy-Hb and deoxy-Hb concentrations using prefrontal cortex NIRS data (Sato et al., 2013a, b). The utility of NIRS in effectively assessing real-time changes in cerebrovascular response as a function of natural social behavior supports the possible utility of this technology in the study of neurophysiology of social anxiety (Tuscan et al., 2013).

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Therefore, we investigated the function of the frontal and temporal lobe in SAD using NIRS while performing verbal fluency task (VFT).

2. Methods

2.1. Participants

This study included 145 patients and 152 healthy controls (HCs) (Table 1). All patients were diagnosed on the basis of clinical interviews and all underwent SAD testing according to DSM-IV criteria. The diagnoses of current Axis I disorders were made by a trained psychiatrist (JA) using the Mini International Neuropsychiatry Interview (MINI) (Sheehan et al., 1998). Patients were excluded if they had comorbid psychiatric disorders, or any physical illness. To ensure that the participants were right-handed, all participants completed the Edinburgh handedness inventory (Oldfield, 1971). All subjects provided written informed consent. This study was approved by the Human Ethics Committees of the Oita University Faculty of Medicine.

2.2. VFT

VFT (letter version) consisted of a 30 s pre-task (baseline), a 60 s activation task, and a 70 s post-task. During the activation task period, the participants were trained to make as many Japanese words beginning with a designated syllable as possible. The three sets of initial syllables were presented in a random order; each presented syllable changed every 20 s during the 60 s activation task. During the pre-task and post-task periods, participants were instructed to repeat a sequence of Japanese vowel syllables aloud.

Table 1
Characteristics of Control and SAD.

	Control (n=152)	SAD (N=145)	Statistics
Age	26.0 ± 6.3	26.5 ± 7.7	$p=0.60$
Sex (F/M)	53/99	61/84	$p=0.20$
BMI	22.3 ± 3.4	22.8 ± 4.1	$p=0.63$
Smoking (no. cig)			
< 10/day	131	123	
> 10/day	21	22	$p=0.75$
Education (years)	16.8 ± 3.1	16.4 ± 2.7	$p=0.83$
Number of words (VFT)	16.6 ± 4.1	15.8 ± 4.9	$p=0.14$
LSAS	16.8 ± 7.4	50.1 ± 14.7	$p<0.01$
POMS			
Tension-Anxiety	38.8 ± 6.8	44.3 ± 9.3	$p<0.01$
Depression-Dejection	42.1 ± 4.9	45.3 ± 6.8	$p<0.01$
Anger-Hostility	39.9 ± 5.1	41.3 ± 6.6	$p<0.01$
Vigor	50.8 ± 10.8	46.7 ± 10.9	$p<0.01$
Fatigue	41.0 ± 6.0	44.0 ± 8.3	$p<0.01$
Confusion	41.8 ± 7.3	46.1 ± 8.7	$p<0.01$
STAI			
Trait Anxiety	45.8 ± 13.2	46.1 ± 9.7	$p=0.34$
State Anxiety	42.3 ± 12.3	45.1 ± 11.9	$p<0.05$
BDI	2.1 ± 3.0	4.3 ± 4.7	$p<0.01$
SASS	42.4 ± 5.5	36.7 ± 7.4	$p<0.01$
DACS			
Future denial	43.8 ± 8.9	49.2 ± 11.5	$p<0.01$
Threat prediction	38.2 ± 13.4	47.7 ± 12.7	$p<0.01$
Self-Denial	41.5 ± 10.5	52.6 ± 11.9	$p<0.01$
Past denial	38.8 ± 10.2	46.7 ± 12.5	$p<0.01$
Interpersonal threat	36.8 ± 15.4	43.5 ± 12.4	$p<0.01$
HRV			
LF	52.5 ± 20.5	54.3 ± 20.3	$p=0.16$
HF	45.7 ± 20.3	45.7 ± 20.3	$p=0.19$
LF/HF	1.9 ± 2.6	1.9 ± 2.4	$p=0.98$

SAD=Social Anxiety Disorder, BMI=Body Mass Index, VFT=Verbal Fluency Task, LSAS=Liebowitz Social Anxiety Scale, POMS=Profile of Mood States, STAI=Speilberger Anxiety Inventory, BDI=Beck Depression Inventory, SASS=Social Adaptation Self-evaluation Scale, DACS=Depression and Anxiety Cognition Scale, HRV=Heart Rate Valiability

2.3. NIRS measurement

For frontal and temporal lobe function tests, we used NIRS, which employed a near-infrared, noninvasive device for measuring brain function from the scalp. We chose [oxy-Hb] as an indicator because it better reflects cortical activity and demonstrates stronger correlations with fMRI blood-oxygenation level-dependent signals compared to [deoxy-Hb] (Sato et al., 2013a, b). We used a 47-channel (CH) NIRS system (ETG-7100; Hitachi Medical Co., Tokyo, Japan).

2.4. Psychological and physiological tests

The Depression and Anxiety Cognition Scale (DACS), which measures automatic thoughts that cause depression and anxiety, consists of five subscales that correspond to future denial (FD), threat prediction (TP), self-denial (SD), past denial (PD), and interpersonal threat (IPT). The DACS has good test–retest reliability and internal consistency, and the scale demonstrated excellent internal consistency (Arimitsu and Hofmann, 2015). Depressive symptoms were assessed using the Beck Depression Inventory (BDI) (Beck et al., 1961). The Profile of Mood States (POMS) was administered to the participants (McNair et al., 1992). Each patients also completed the 40-item State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1970) and Leibowitz Social Anxiety Scale (LSAS) to assess SAD severity (Liebowitz, 1987) and general and social anxiety symptoms. SASS evaluated social motivation and awareness factors (Goto et al., 2005). We also measured heart rate variability (HRV) immediately after VFT. Low frequency (LF; 0.04–0.15 Hz) and high frequency (HF; 0.15–0.4 Hz) fluctuations of HR on R-R intervals were calculated by an APG Heart-Rater SA-3000 P (Tokyo Iken Co, Ltd, Japan). After VFT, we administered DACS, LSAS, POMS, STAI scores, BDI, SASS, and HRV to the participants.

2.5. Statistics

NIRS uses two wavelengths of near-infrared light (695 and 830 nm) and calculates the amount of absorbed near-infrared light based on the modified Beer–Lambert law. This method allows for the calculation of signals reflecting changes in Hb levels, which were calculated in arbitrary units (mM–mm). The sampling rate-wassetat100 ms. To assess the cortical localization of each CH, we used the simulated registration method (Matsubara et al., 2014), which allows the simulated registration of NIRS data onto the Montreal Neurological Institute (MNI) coordinate space (Fig. 1). Group comparisons of each of the 47 CHs were performed. For each subject, the change of oxy-Hb concentration in each CH was analyzed for the task period. The pre-task baseline was defined as the mean over a 30 s period immediately prior to the task period, and the post-task baseline was defined as the mean over the last 70 s of the post-task period. A Linear fit was applied to the data between these two baselines. The records of changes in oxy-Hb concentration in a statistical analysis were obtained by subtracting the baseline data (calculated by using the integral mode) from the original measurement data in oxy-Hb. In all the groups, the clinical variables were compared using various tests; *t*-tests and one-way ANOVA (with Bonferroni corrections) were used for the comparison of the means of variables. We used the χ^2 tests for sample