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Depression affects working memory performance: A Functional Near Infrared Spectroscopy (fNIRS) Study

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ABSTRACT

Depression is a complex disorder that can be caused by psychosocial and biological conditions, and it not only affects to emotional life, but also cognitive functions, specifically the executive functions, attention, psychomotor speed, and memory. Some results of the studies in the literature show that depressed individuals perform worse on cognitive tasks than healthy individuals, while others indicate that there is no difference. Moreover, there is also no consensus about the depressed people brain functionalities. We aimed to compare the people who has high and low depression score measured with Beck Depression Inventory in terms of their working memory performance by using n-back paradigm and their brain activity by using optical imaging with this study. The age of lower BDI group ($n = 11$) is 23,9 ± 3,04 and higher BDI group ($n = 23$) is 22,2 + 2,28. The fNIRS were recorded from each subject while neutral words-faces and emotional words-faces are given to the subjects in the visuospatial 2-back WM task. There are no significant differences between the two groups behaviorally during the working memory performance, however, the high BDI group's PFC activation in right hemisphere is founded to be higher than the lower group. Our findings support the literature who is claiming the difference brain activity in depressed brain but not cognitive performance. Though, the small group size and the task difficulty (easy) could be the explanation of the behavioral results.

1. Introduction

Depression affects some cognitive functions such as attention, memory, learning, and decision making, although this disorder is included within the category of mood disorders in the DSM-5 (American Psychiatric Association 2013; Helvacı Çelik et al., 2016; Zaninotto et al., 2015; Lee et al., 2012). Cognitive disorders observed in depression are mostly the difficulties in decision makings due to slowing down of the thought system and tendency to negative thoughts. Memory impairment increases with the severity of depression, delusions that may lead to suicide due to mood disorders and attention disorders (Helvacı Çelik et al., 2016).

The anatomical and functional changes are also observed in the depressive people's brain (Savitz and Drevets, 2009). Although attention, memory and executive functions have been shown to be negatively affected (Zaninotto et al., 2015, Lee et al., 2012, Evans et al., 2014) in some studies, anothers have not found any abnormal results regarding these cognitive processes, but it has been shown neuroimaging findings to indicate some differences in neural activity (Yüksel et al., 2018). These abnormalities were seen in the prefrontal cortex (PFC) and in subcortical structures such as some regions of the striatum, amygdala, and thalamus (Drevets, 2000).

A neuropsychological test battery was applied to people diagnosed with major depressive disorder in a study (Mohn and Rund, 2016) to examine the relationship between the severity of major depression symptoms and the subjective memory complaints. The results show that the test scores of patients with depressive disorder were significantly lower than the healthy controls. It has been reported that people with high depression scores which are specific to the right hemisphere (Levin et al., 2007) are lower than health people.

According to the results of the NIRS study conducted by Liu et al., which deals with the differentiation in brain activity in depression, the

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oxyhemoglobin (oxyHb) changes were observed in bilateral PFC and anteromedial PFC in the Major Depressive Disorder (MDD) (Liu et al., 2014). In a review study, it is said that people with depression perform poorly in cognitive tests related to areas such as recognizing emotional faces, line direction, 3-D structure perception, spatial learning, pattern recognition, and it is shown that the severity of depression negatively affects these cognitive functions (Levin et al., 2007).

There are many neuroimaging studies examining working memory (WM) and brain connectivity. According to the neuroimaging studies, places that show increased activity in tasks related to WM include the posterior cingulate cortex and medial frontal areas, which are also parts of the resting state network (Hampson et al., 2006). Studies provide evidence that the frontal cortex is associated with WM (Hampson et al., 2006, Baker et al., 2018, Nystrom et al., 2000, Kring et al., 2007, Smith and Kosslyn, 2013).

Researches using fNIRS has generally focused on verbal fluency, and publications on visuospatial WM are limited. In the verbal fluency experiment of Kawano et al. with functional near infrared spectroscopy (fNIRS), a negative correlation was observed between depression score and frontal lobe activity (Kawano et al., 2016). In the study of Kinou et al., people with MDD showed reduced frontopolar PFC and DLPFC activity compared to the healthy controls (Kinou et al., 2013). In an fNIRS study using the n-back task, it is stated that MDD patients show a decreased activation in the inferior prefrontal region compared to the healthy controls (Zhu et al., 2018). In the visual-spatial WM experiments of Schecklmann et al. using NIRS, groups with depressive features showed reduced PFC activity, ventrolateral and dorsolateral, compared to the healthy controls (Schecklmann et al., 2011). In another study, although there was no behavioral difference between the MDD and the healthy control groups during the verbal fluency task, it was reported that there was hypoactivation in the left DLPFC as a result of brain imaging performed with NIRS in the MDD group (Akiyama et al., 2018). In another NIRS study, hypoactivation in the bilateral frontal cortex was observed in depressed individuals in the n-back task performed before the ECT application, and an increase in the bilateral frontal cortex activation was observed after the ECT application (Hirano et al., 2017).

In addition to emotional problems, depressed individuals also experience cognitive impairments in the form of visuospatial WM impairment. Therefore, understanding the brain structures and processes that mediate these cognitive functions will facilitate the planning of cognitive rehabilitation based on neuromodulation.

The aim of the study is to examine the effects of high depression symptoms on visuospatial WM performance and to compare WM task related brain activities of the groups who has high and low depression scores on BDI with fNIRS.

2. Method

2.1. Participants

The study was carried out in Istanbul Medipol University Functional Imaging and Cognitive-Affective Laboratory (fINCAN). In the first step, Beck Depression Inventory (BDI) were administered online to 501 volunteered subjects, who were university students/graduates, aged between 18-35 and sex is balanced. Participants who had a neuropsychiatric diagnosis, or head trauma or having psychoactive drugs for any reason for last 6 months were not included the studies. Also, those whose pre-experiment anxiety level measured with STAI was two standard deviations above the mean were not included in the experiment. Among these 501 subjects, 60 individuals who has highest and lowest BDI scores invited to the laboratory for the experiments. Only 23 subjects from the high score BDI group (BDI $\geq$ 23; education = 15.76 $\pm$ 1.96 years; age = 22.24 $\pm$ 2.28 years) and 20 subjects from the low score BDI group (BDI $\leq$ 11; education = 16.84 $\pm$ 2.29; age = 23.95 $\pm$ 3.04) participated the working memory tasks (2-back visuo-spatial WM paradigm).

During the experiments the hemodynamic responses were recorded with fNIRS from these 43 subjects. We used all the subject's behavioral data but not all the fNIRS data. Some of them were excluded because of the poor quality of the recordings. Moreover, when the number of people in one group decreased to eleven, we removed fNIRS data randomly from the other group and equated the two groups to eleven.

2.2. Behavioral and fNIRS measurement

In this study, three measurements were used to see the effect of depression level on the working memory and the brain activity. The Beck Depression Inventory (BDI) was used to create two groups with high and low depression scores. It is a 21-item self-report inventory to measure the symptoms of the depression and higher scores indicate higher depressive symptoms. The scale was developed by Beck (Beck et al., 1961) and adopted to Turkish in 1989 (Hisli, 1989).

Experiment-induced anxiety is measured with State-Trait Anxiety Inventory. A total of 40 self-reported and developed by Spielberg used to measure state or trait anxiety (Spielberger et al., 1983) ant it was adapted into Turkish in 1983 (Öner and LeCompte, 1983). The "State Anxiety Inventory" section score of the scale is used an exclusion criterion.

The purpose-tailored n-back paradigm (Kirchner, 1958) was used to measure visuo-spatial WM performance in this study and the task was adapted from Vermeij et al. (Vermeij et al., 2014). The stimuli, the words and faces were presented with e-Prime (Psychology Software Tools 2022) for 500ms and ISI were jittered between 3-5 s. In the study, the subject was presented with a series of sequential stimuli which appeared in one of ten possible places in a circle which the diameter was 12 cm. The participant was expected to decide whether the last stimulus was "in the same place" as the two trials preceding stimulus (visuo-spatial 2-back) (Soveri et al., 2017).

The emotional and neutral faces were selected from KDEF (Lundqvist et al., 1998) and the words (see Table 1) were selected depending on their arousal and valence scores from a previous study (Kapucu et al., 2018). There are four blocks and during the 'emotional face' condition the faces with emotion expression were given, and during the 'neutral faces' condition, neutral faces were given. Like the face conditions, emotionally loaded words were used in the 'emotional words' condition, and neutral words were used in the 'neutral words' condition.

During the WM task, the hemodynamic responses were recorded with the NIRS device (NIRScout 8-16, NIRx Medizintechnik GmbH, Germany). 15 optodes (8 sources and 7 detectors) were placed in the right and left dorsal-dorsolateral PFC areas, 18 symmetrically and 2 in the midline, to form 20 channels (look at the Fig. 1 for the channel positions). Optodes are placed on the international EEG 10/20 system elastic caps, and the distance between the source and the detector is

Table 1
Verbal stimuli used for WM task and their arousal and valence scores.

Words	Emotion	Valence	Arousal
Friend	Positive	8,21	6,65
Delight	Positive	8,18	6,13
Smile	Positive	8,19	6,75
Peace	Positive	8,03	6,38
Vacation	Positive	7,78	6,38
Bomb	Negative	3,73	7,94
Sadness	Negative	3,95	5,89
Cruelty	Negative	4,89	7,42
Mourning	Negative	4,37	5,66
Slaughter	Negative	4,35	6,32
Door	Neutral	5,21	2,79
Letter	Neutral	5,42	2,94
Clasp	Neutral	5,38	3,14
Corner	Neutral	5,14	3,22
Sample	Neutral	5,25	3,28

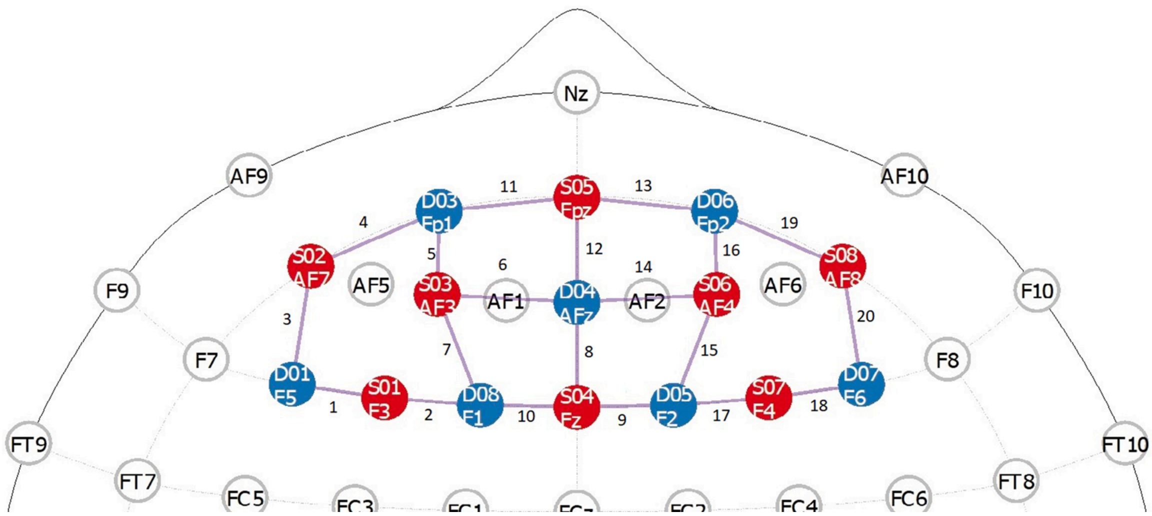

Fig. 1. Layout of source, detector and channels (red: sources, blue: dedectors and purple: channels).

fixed at 3 cm. NirSite 2021.4 program was used while creating this montage.

The data were collected by the block design method. There is a single block for each condition (neutral faces, neutral words, emotional faces, and emotional words). The recordings are in continuous wave form and the oxyHb and deoxyHb concentration changes were monitored on the screen simultaneously with the experiment. This variation is calculated according to the modified Beer Lambert Law (Obrig and Villringer, 2003). The "detrend" process is applied to the baseline fluctuations in the continuous wave that continues throughout the recording with the recorder's own software. Hemodynamic brain activation during the task was recorded with the NirStar 15.3 and analyzed with the nirsLAB software. Noises created by heartbeat, pulse, and unwanted movements in the fNIRS data were eliminated by applying a band pass filter (0.01-0.2 Hz).

2.3. Statistical analysis

The age, education, BDI, STAI and WM performances averages and standard deviations were analyzed descriptively and as the normality conditions were not met WM performances were compared with the Mann Whitney-U Test, using statistical software Jamovi (Jamovi 2021). After the determined parameters were applied to the hemodynamic data, the HRF graph was selected using the GLM at the SPM 1 level only for the oxyHb in nirsLAB, for analysis at the individual level. ANOVA was used for analyzes at SPM 1 level. Independent groups Student's t-Test was used in the analyzes at SPM 2 level. The significance level was determined as $p < 0.05$ for both behavioral and fNIRS data.

3. Results

3.1. Behavioral results

At the first step, the subjects were divided into two group depending on their BDI scores. The high group BDI scores average was 30.65 ± 4.80 ($n = 20$) and the low group BDI is 5.83 ± 3.03 ($n = 23$) which is shown at Table 2. When we compared the two groups by Student's t Test, high group's BDI score is significantly higher than low BDI group's ($t(41) = 20.49$; $p < 0.001$). Two groups age and education were founded to be similar ($p > 0.05$).

During the visuo-spatial WM task, correct answers are counted for the all conditions separately (neutral words-faces, emotional words-faces; all neutral and emotional stimuli and all words and faces) shown in Table 3. High and low BDI group's WM task results were compared with Mann Whitney-U test. There was no behavioral difference between the low BDI scores and high BDI scores ($p > 0.05$).

When the group factor was ignored, the difference seems to be significant in favor of the emotional words comparing to the neutral words (with Paired sample t Test: $t(42) = 8.07$; $p < 0.001$). However, this difference was not seen for the faces.

3.2. fNIRS results

Initially, we looked for a topographical difference in the hemodynamic responses to stimuli in each condition during working memory performance. This difference was examined separately in the low and high BDI groups. In these analyzes, only in the low BDI group and only in the neutral face condition, one channel in the right DLFC was more active than the others ($p < 0.05$), while there was no significant difference in the other conditions (emotional faces, neutral and emotional words) ($p > 0.05$).

Table 2
Age, education, BDI and STAI scores of low and high BDI groups and group differences.

								Shapiro-Wilk			
	Group	N	Mean	Median	SD	Min	Max	W	p	t (df=41)	df
Age	Low BDI	23	23.3	23	1.96	20	27	0.933	0.127	1.33	0.19
	High BDI	20	22.4	22	2.48	19	26	0.882	0.019		
Education	Low BDI	23	16.52	17	1.78	13	20	0.953	0.344	1.3	0.202
	High BDI	20	15.75	15.5	2.12	12	19	0.949	0.352		
BDI	Low BDI	23	5.83	7	3.05	0	11	0.877	0.009	20.49	< .001
	High BDI	20	30.65	31	4.8	23	43	0.955	0.443		
STAI	Low BDI	23	31.78	34	9.73	0	47	0.882	0.011	4.81	< .001
	High BDI	20	44.55	43.5	7.29	33	60	0.953	0.421		

Table 3
The WM (behavioral) scores of low and high BDI groups.

	Group	N	Mean	Median	SD	Min	Max	MWU*	p
Neutral Face	Low BDI	23	29.4	30	5	19	35	217	0.75
	High BDI	20	29.9	32	4.6	21	35		
Neutral Words	Low BDI	23	26.6	27	3.9	18	31	188	0.31
	High BDI	20	27.9	28	3.2	17	33		
Emotional Words	Low BDI	23	30.6	31	3	24	35	193	0.37
	High BDI	20	29.9	31	2.6	23	33		
Emotional Face	Low BDI	23	30	33	5.9	16	35	227	0.94
	High BDI	20	31.2	32	4.2	22	35		
Neutral	Low BDI	23	56	58	8.2	39	66	208	0.60
	High BDI	20	57.8	59	6.9	38	67		
Emotional	Low BDI	23	60.6	64	8.5	42	70	205	0.55
	High BDI	20	61.1	62.5	5.7	45	68		
Words	Low BDI	23	57.2	58	6.6	42	65	226	0.93
	High BDI	20	57.8	58.5	5.2	40	64		
Faces	Low BDI	23	59.3	65	9.9	37	70	223	0.87
	High BDI	20	61.1	64	7.5	43	69		

* Mann-Whitney U Test

In the next step, the channels of the high and low BDI groups are compared individually in each condition:

When the stimuli are faces; In the neutral faces condition, no differentiation was observed in any channel between the groups ($p > 0.05$), but in the emotional faces condition (see Fig. 2), there was a significant difference in favor of the high BDI group in three regions in the right lateral and anterior PFC (t(2.15 to 2.46); $p < 0.05$).

When the stimuli are words; In the neutral words condition (see Fig. 3), a significant difference was observed in five regions in favor of the high BDI group, in the right lateral and near the midline anterior PFC (t(2.12 to 2.65); $p < 0.05$). In the emotional words condition (see Fig. 4), again in favor of the high BDI group, a significant difference was observed in the two regions in the right lateral and anterior PFC (t(2.10 and 2.30); $p < 0.05$).

When the stimulus type (word-face) is ignored, in the neutral and emotional stimuli condition, in favor of high BDI, when the stimuli are neutral (see Fig. 5), between two channels in the right anterior and lateral PFC (t(2.17 and 2.23); $p < 0.05$); when the stimuli were emotional (see Fig. 6), there was a significant difference between the two channels in the right anterior and lateral PFC (t(2.17 and 2.20); $p < 0.05$).

4. Discussion

The primary aim of this study is to investigate whether there will be a difference between behavioral and brain hemodynamic responses during the visual-spatial WM task in groups with low and high depression scores, although the participants have no clinical diagnosis. Even if there is no behavioral difference between the groups due to sample size and task difficulty, it has been predicted that there will be a difference in brain activities.

In this section, the findings of the study are discussed in the light of previous studies in the literature. When similar studies in the literature, it is seen that individuals between the ages of 35-45 generally constitute the sample of the studies, the ages of the groups are not equal, or the participants have used psychoactive drugs in the past or present (Yüksel et al., 2018, Kawano et al., 2016, Kinou et al., 2013, Schecklmann et al., 2011, Akiyama et al., 2018, Hirano et al., 2017, Harvey et al., 2005, Hugdahl et al., 2004, Okada et al., 2003, Norbury et al., 2014, Wagner et al., 2006). In this study, the education, and ages of the low and high BDI groups were equalized, and the mean age was smaller than other studies in the literature in order to see the relationship between depression symptom level and WM in the young population.

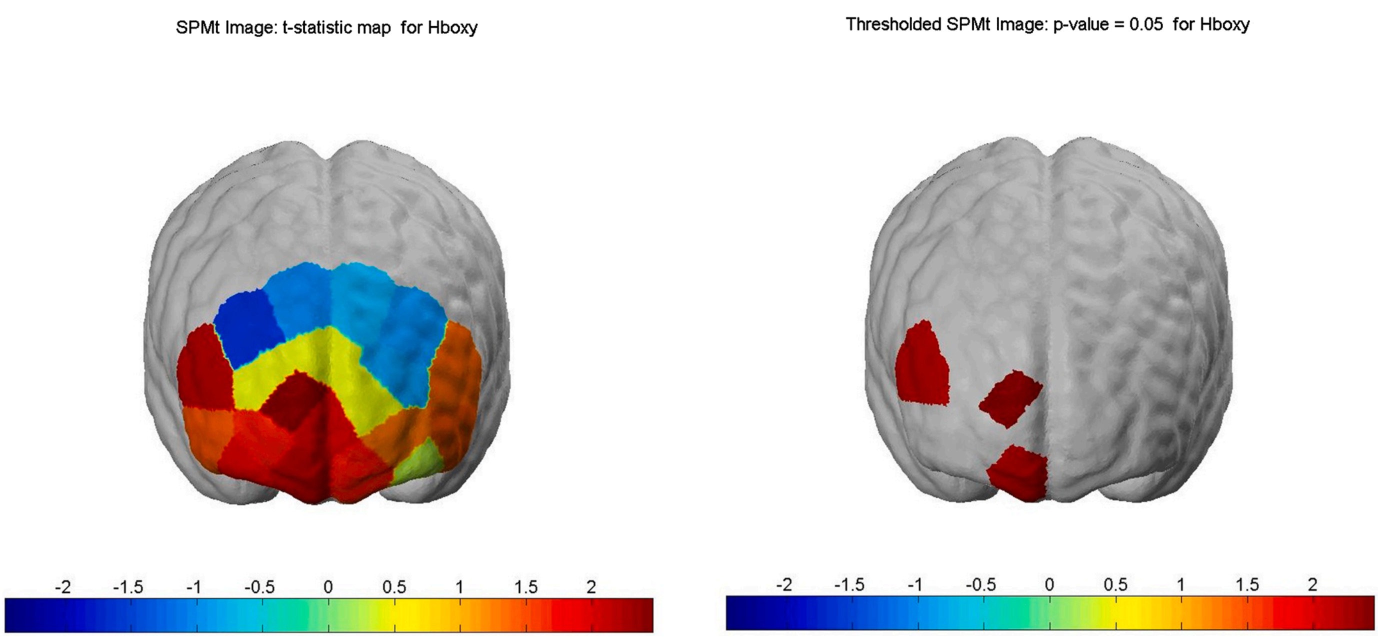

Fig. 2. Hemodynamic brain activities in the emotional face condition (left: activation of all channels, right: channels where difference is significant).

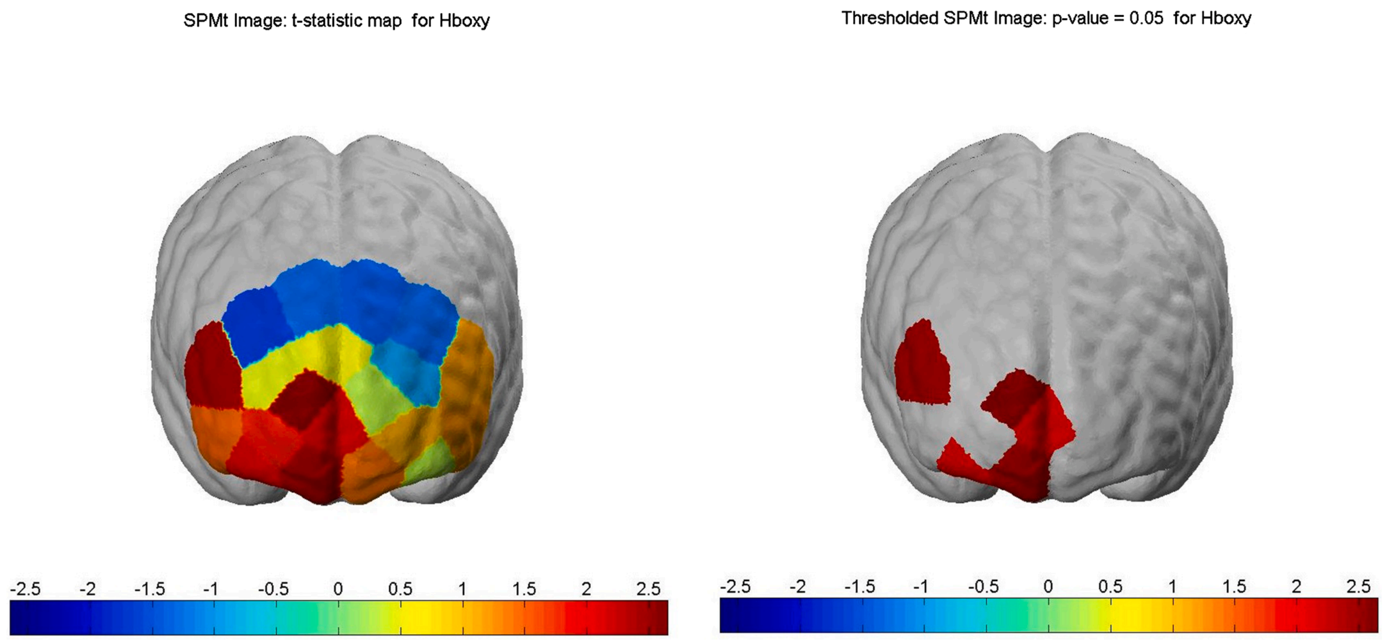

Fig. 3. Hemodynamic brain activities in the neutral word condition (left: activation of all channels, right: channels where difference is significant).

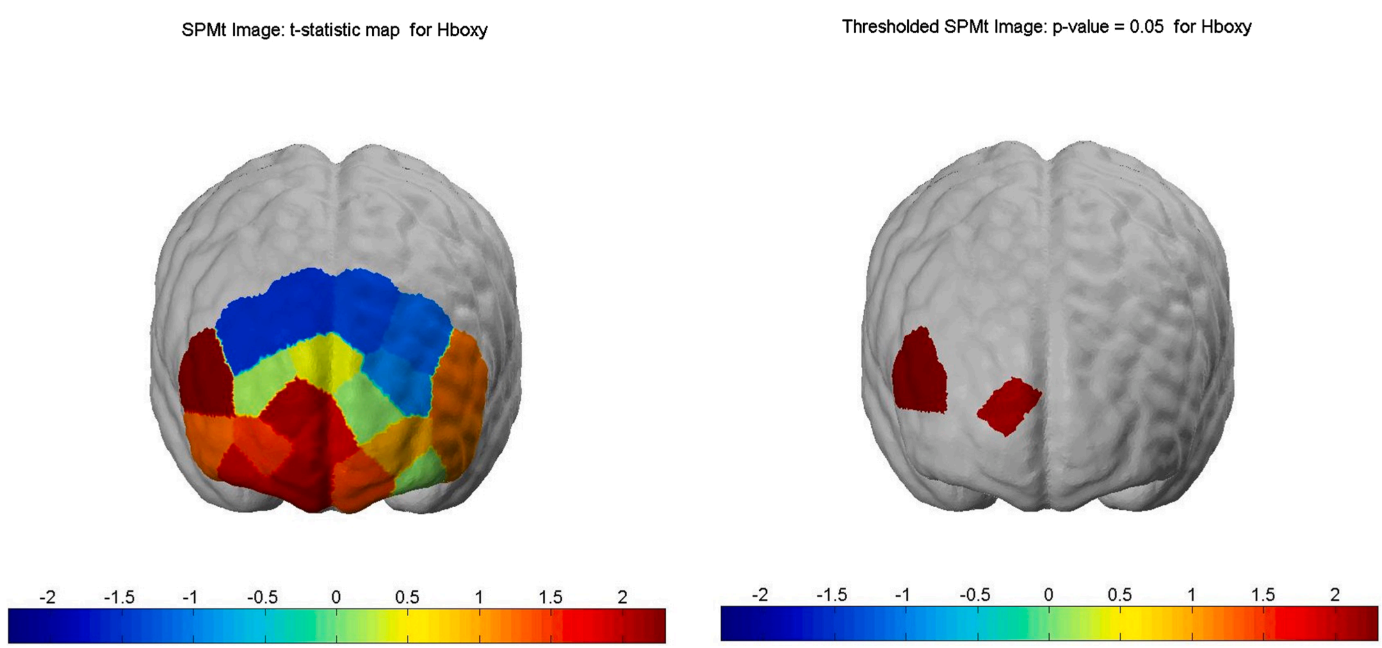

Fig. 4. Map of hemodynamic brain activity in the emotional words condition (left: activation of all channels, right: channels where the difference is significant).

Some previous studies have been done with only the patient group, without a control group, while others have included both the patient and control group. When we take those with low BDI scores as the control group in our study, it differs from some studies in the literature in terms of including a control group, but the patients with high BDI scores in this study did not have a clinical diagnosis.

Generally, n-back (Yüksel et al., 2018, Zhu et al., 2018, Hirano et al., 2017, Harvey et al., 2005, Norbury et al., 2014, Matsuo et al., 2007) and verbal fluency tests (Kawano et al., 2016, Kinou et al., 2013, Akiyama et al., 2018, Okada et al., 2003) are used to measure WM, but there are also different experiments (Schecklmann et al., 2011, Hugdahl et al., 2004, Wagner et al., 2006). In this study, an n-back task was designed to measure visuospatial WM performance. Participants were expected to keep in mind the location of the stimuli they saw on the screen and to decide whether the last stimulus they saw was in the same place as the two previous ones (2-back WM). Keeping the positions of the stimuli in mind during the experiment is the function of the visuospatial sketch-book component in Baddeley and Hitch's WM model.

Both neutral and emotional stimuli were used in the experiment to see whether the stimuli were emotional or not, especially in the high BDI group, on WM performance and brain activity. On the other hand, it was also diversified into words and faces, as it was wondered whether evolutionarily advantageous faces would amplify this possible effect. The visual-spatial n-back WM task is a unique paradigm in that it consists of both verbal and visual stimuli and allows emotional and neutral stimuli to be measured together.

Some previous studies have reported behavioral differences during the WM task between mildly depressed and healthy groups, while others

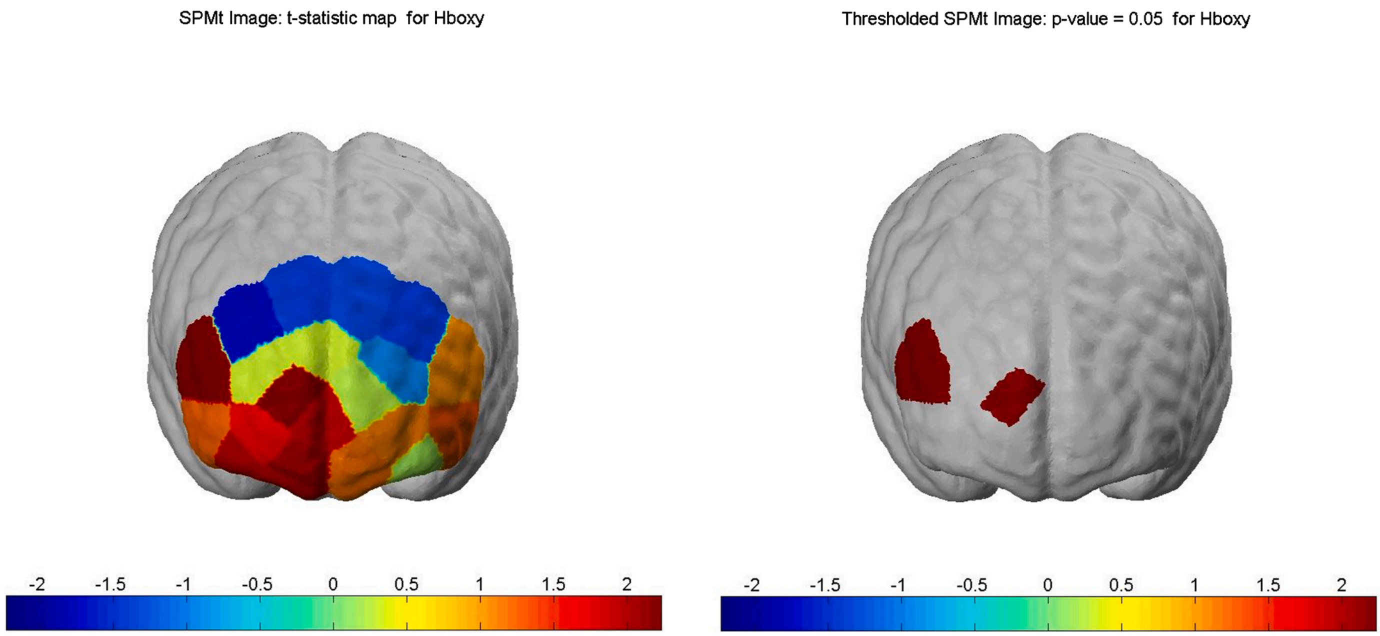

Fig. 5. Map of hemodynamic brain activities in the neutral stimulus condition (left: activation of all channels, right: channels where difference is significant).

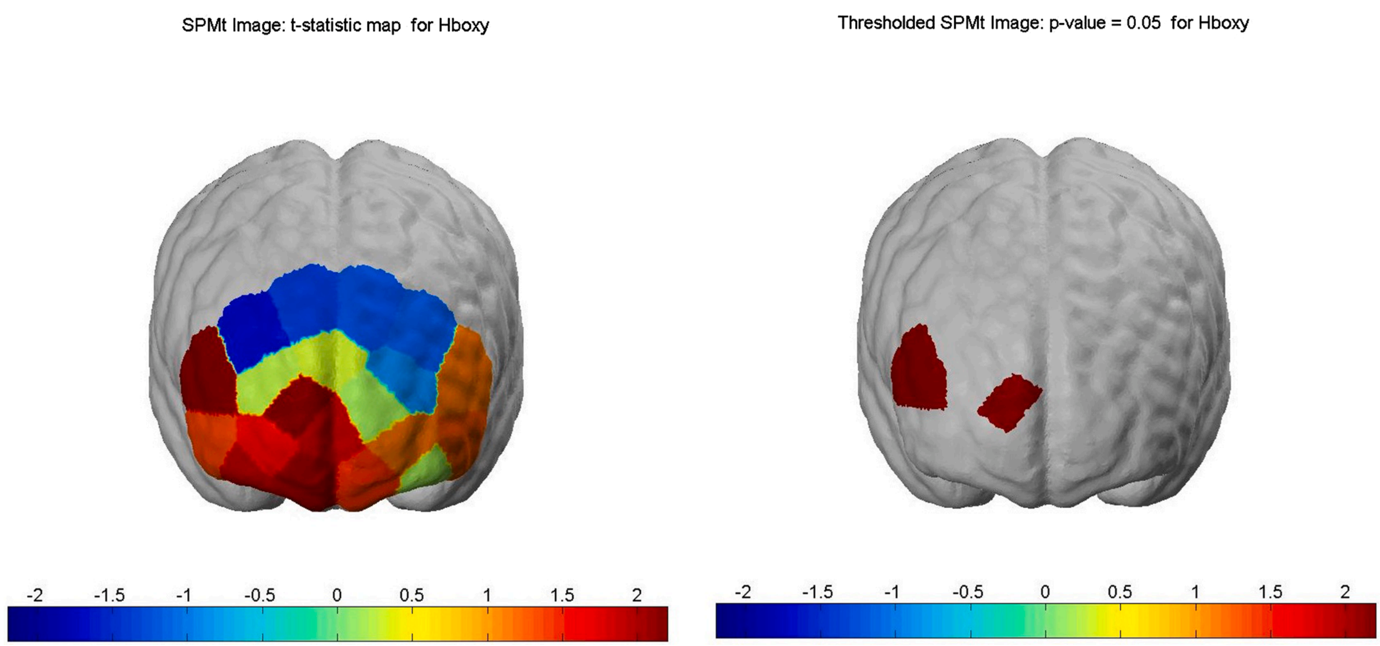

Fig. 6. Map of hemodynamic brain activities in the condition of emotional stimuli (left: activation of all channels, right: channels where difference is significant).

have shown no difference. Inconsistent results show that there is no consensus in the literature. In this study, no significant behavioral difference was observed between the high and low BDI groups. The young population of the sample may be a reason for this result. Participants with high BDI scores performed similarly to participants with low BDI scores (healthy).

On the other hand, when the group factor is ignored, it is seen that the performance of the participants is significantly higher when emotional words are used in the n-back task than in the neutral condition. However, this difference is not seen when faces are used in the task. The fact that presenting emotional faces, which we consider to be more evolutionarily important, as a stimulus does not change the performance may be due to the experiment itself or to the "attention-grabbing" effect of the faces. Another simple explanation is that stimuli given for 500 milliseconds may not have the desired effect.

In this study, brain activity measurement was carried out using fNIRS, which has been used frequently in recent years, is easy, inexpensive, has high ecological validity and can be applied quickly. Although it is similar to magnetic resonance imaging (MRI) in terms of measuring the hemodynamic response, it cannot measure the activation of deep brain regions. While reviewing the literature for this study, fMRI and fNIRS studies were focused on, since the working principles were similar.

Although the high BDI group showed similar behavioral performance to the low group in our study, increased oxyHb exchange was observed in the right PFC, especially in the DLPFC, in the high BDI group. It had been reported in some previous studies (Yüksel et al., 2018). In line with this finding, we can say that the group with depressive features exhibited more PFC activation to achieve the same success.

Contrary to our findings, some studies show that there is a decrease in prefrontal cortex activity in depression. When the aforementioned studies were examined, it was seen that clinical groups and healthy groups were compared (Ho et al., 2020, Husain et al., 2020, Husain et al., 2020, Li et al., 2022, Schecklmann et al., 2011). The absence of a clinical group in our study may explain the conflicting results with these studies. The findings in the literature indicate that there is a hemispheric asymmetry in depression and this asymmetry is observed as hypoactivation in the left PFC or hyperactivation in the right PFC. Although contradictory with some other studies, our findings support the theory of hyperactivation in the right PFC (Thibodeau et al., 2006).

It is seen that the findings of our study are compatible with some previous research findings and contradictory with some results. The reason for this discrepancy may be that the average age of the participants in our study was lower than the others, there were people with a clinical diagnosis in other studies or the groups with major depression were using drugs, the difference in WM tasks, the difference in the difficulty level of the WM tasks or the number of participants.

5. Conclusion

No behavioral differences were observed between the groups with low and high depression scores during the visuospatial WM task. This may be because the task was not difficult enough. According to the fNIRS results, the group with higher depression scores showed increased activation in the right DLPFC during the WM task. As a result, the group with higher depression scores made a compensatory effort to achieve the same performance and their PFCs became more active.

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Ethics approval

This study was approved by the ethics committee of Istanbul Medipol University Non-Invasive Clinical Research.

Contributions

EY and ÖVK designed the study. ÖVK collected the data. EY and ÖVK processed the data and wrote the manuscript. EY helped with statistical analysis and revised the manuscript. All authors reviewed the paper and approved the final version to be published.

Informed consent

All participants were given written informed consents.

Consent to publish

All authors consent to publication of the work.

Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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