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Region of Interest Analysis Results of Children with Dyslexia and Dysgraphia During Word Reading Task

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ABSTRACT

Developmental dyslexia is a neurodevelopmental disorder characterized by adequate intelligence, delays, and impairments in reading and writing processes despite educational opportunity. Developmental dysgraphia, which is associated with dyslexia, is manifested by weakness and impairments in the writing process. In this study, the similarities and differences between the two learning disabilities on the functionality of the brain were examined. The task-based functional magnetic resonance imaging (fMRI) data used in the study were taken from OpenfMRI. At the time of the fMRI, the subjects were instructed to read aloud normal words and pseudo-homophone words to German-speaking children with dyslexia (20) and dysgraphia (16) and to normal children that form the control (22) group. Region of interest (ROI) analysis was performed by selecting the regions of the fusiform gyrus, the inferior frontal gyrus (IFG), the precuneus, and the precentral gyrus, which include regions related to reading in the literature. As a result of the study, among the selected ROIs, differences were found between the groups in the left fusiform gyrus, the right IFG, and the precuneus regions. The number of studies examining dyslexia and dysgraphia together is insufficient in the literature. Our study contributes to the literature , by revealing the functional differences of dyslexia, dysgraphia, and normal brain in reading task.

***Index Terms*—**Developmental dysgraphia, developmental dyslexia, Functional magnetic resonance imaging, Region of interest analysis

I. INTRODUCTION

Developmental dyslexia is a specific learning disorder that is heterogeneous in cognitive and behavioral conditions with a genetic and neurobiological basis [1]. Despite this heterogeneity, the generally accepted main deficiency is the deterioration in speech sounds, that is, in phonological skills [2]. Developmental dyslexia is the most common learning disability, affecting 7–17% of children worldwide, and is characterized by normal intelligence, poor reading performance despite adequate education, and poor spelling [3]. People with dyslexia have cognitive deficits in visual processing, selective and sustained attention, and executive functions [4]. They have difficulty in phonological processing, distinguishing sounds in words, and recognizing rhyming words [5]. It is assumed that the source of the deficiency in dyslexia is a functional disorder of the left hindbrain system [6]. Studies have reported that readers with dyslexia show hypoactivation in the left hindbrain system [7, 8].

Developmental dysgraphia, a subtype of dyslexia, is characterized by impairment and weakness in skills that are important in the writing process, such as writing speed, legibility of letters, and fine motor coordination [9]. The two learning difficulties can occur together or can be seen separately [10]. The incidence of both learning disabilities is higher in boys than in girls [11, 12].

Functional magnetic resonance imaging (fMRI), which is one of the imaging methods used in dyslexia and dysgraphia research, is divided into task-based fMRI and resting state fMRI. The resting state is realized by the measurement of the Blood-Oxygen-Level-Dependent (BOLD) signal, which occurs due to the change in the blood oxygen level in the brain in the absence of a conscious thought, that is, in the resting state [13]. The working process of task-based fMRI is that the time-series data of the acquired functional images are compared with a predetermined model of neural function based on the cognitive task performed. Then, the statistical inference method is performed and a hypothesis is established, which can be accepted or rejected for each voxel, and a map of the brain regions that respond to the task is created [14]. However, one of the analyses used to analyze fMRI data, region of interest (ROI) analysis, is to control type 1 error by limiting

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the number of statistical tests to a few ROIs. In addition, it is often helpful to see the signal formed in the ROI plotted for each condition or against other relevant variables [15].

When the literature on dyslexia was examined, a study evaluated the connections of brain regions related to visual attention. Normally reading and dyslexic children performed the reading task. In executive functions of the ventral attention and dorsal attention networks, it was found that children with normal reading increased their functional connectivity compared to children with dyslexia [16]. In a study in which dyslexia and control groups were evaluated by ROI analysis, the selected ROIs were the bilateral superior temporal gyrus, left fusiform, and right superior frontal gyrus. In the results obtained, lower activation was found in the left fusiform ROI in the dyslexia group compared to the control group. No group differences were found in the other two ROIs [17]. Centanni et al. investigated the left and right fusiform gyrus regions with ROI analysis in a longitudinal study they conducted. The tasks performed by children at risk for dyslexia and dysgraphia and control group participants are to look at normal letters, wrong fonts, and emotional and neutral faces and make decisions. As a result of ROI analysis, the dyslexia group in the left fusiform gyrus differed from the other two groups, but no significant difference was found between the groups in the right fusiform gyrus [18]. In a study of adolescents with developmental dysgraphia and adolescents with good spelling skills, a decrease in functional activation was found in adolescents with dysgraphia compared to those who spell well in the left lower frontal gyrus, left middle frontal gyrus, and right cerebellum posterior lobe—structures important for language processes [19]. In a study of children with dyslexia and dysgraphia, Diffusion Tensor Imaging (DTI) and fMRI images were obtained at the time of writing. As a result of Richards et al.'s study, children with dysgraphia showed increased activation in the left precuneus region compared to children with dyslexia. In the dyslexia group, they observed increased activation in the left supramarginal gyrus and left occipital-temporal regions. As a result of the DTI analysis, it was observed that the control group had more structural white matter integrity than the other groups. In functional connectivity, the dyslexia and dysgraphia groups showed more connectivity than the control group, which they explained as a neural disability [20]. Nielsen et al. examined the emotional and behavioral connections of dyslexia, dysgraphia, and learning disabilities of children with normal reading. In task-based fMRI, participants decided whether the word displayed on the screen was a correctly spelled real word or a pseudoword. In the study, the connection between the precuneus, inferior frontal gyrus (IFG), left occipital temporal region, left supramarginal gyrus, and amygdala, which are selected five ROIs regions, were evaluated. In the findings, children with dyslexia and dysgraphia showed a connection between the amygdala and different regions in the limbic system, while the control group did not show any connection with any region [21]. Dębska et al., in their study with fMRI, found hypoactivation of the posterior superior temporal cortex in children with dyslexia and dysgraphia during visual word processing. As a result of the study, it is reported that the region associated with reading deficit is mostly the left ventral occipitotemporal region [22].

In this study, in the dataset with dyslexia, dysgraphia, and control groups, children performed two different reading-aloud tasks during fMRI. One of these tasks is the normal (real) word reading task and the other is the pseudouhomophone word reading task. In this study, the regions of the fusiform gyrus, IFG, precuneus, and precentral gyrus were selected, which are ROIs that show overactivation and match the literature as a result of the first-level analysis performed with general linear model (GLM) analysis. With the ROI analysis, while the participants were performing the reading tasks, the activation in the selected ROI and the intergroup differences between the tasks were examined.

II. MATERIAL AND METHOD

The data used in this study were obtained from the publicly accessible OpenfMRI [23]. The dataset consists of 58 participants. Their ages are between 9 and 11. The dyslexia group consists of 20 children (8 girls and 12 boys), the typographical group (dysgraphia) consists of 16 children (6 girls and 10 boys), and the control group consists of 22 children (10 girls and 12 boys). Literacy and cognitive measures did not differ by gender in the three groups. The first language of the participants is German. All participants scored 85 and above on the nonverbal IQ test. Hearing and visual impairments are absent, and there is no clinical diagnosis of attention-deficit and hyperactivity disorder [23].

A. Experimental Stimuli and Procedure

The stimuli consist of 60 pseudohomophones consisting of 60 words and at least three and at most eight letters. The task design is event related, and each stimulus is presented in white on a black background for 3 s. After the stimulus, a fixation cross, a marker, was displayed for 4 s. Words and pseudohomophones are randomly displayed. Children were instructed to read aloud the stimuli that appeared on the screen. The tasks were carried out in three consecutive sessions to prevent the children from getting tired. There are short breaks of 3-5 min between each session [23]. In each session, 20 words and 20 pseudouhomophones were presented as stimuli. In this study, only the first session was selected, and a single session was analyzed.

B. Functional Magnetic Resonance Imaging *Data Collection*

Imaging was performed on a 3.0 T Skyra scanner using a 20-channel head coil (Siemens Healthineers, Erlangen, Germany). Anatomical images, 3D-T1 MPRAGE high-resolution scans ([repeat time (TR) = 1600 ms, echo time (TE) = 1.81 ms], Field of view (FOV) = 224 mm, flip angle = 8 degrees, 176 slices, voxel resolution 1 × 1 × 1 mm^3), and BOLD sensitive T2*-weighted functional images were acquired using a single-shot gradient-echo Echo Planar Imaging (EPI) pulse sequence (TR = 2340 ms, TE = 33 ms; FOV = 192 mm, flip angle = 90 degrees, 0.3 34 slices with 0.3 mm gaps, voxel resolution 3 × 3 × 3 mm^3, decreasing order of acquisition). A tight padding is used around the head to prevent head movement. While the participants were performing the tasks, their verbal responses were recorded with an MR-compatible microphone (FOMRI-III, Optoacoustics Ltd, Moshav Mazor, Israel).

C. Preprocessing Steps

Within the scope of this study, a series of preprocessing steps were first applied to the raw fMRI data in the dataset. Preprocessing and analysis of fMRI data was performed using FSL 6.0 FEAT [24]. The data preprocessing steps are as follows: motion correction using FSL's MCFLIRT tool by aligning each functional run and functional volume to the center volume, to shift the time series in fMRI data by an appropriate fraction of a TR relative to the middle of the TR period (Hanning window) using sinc interpolation, slice timing correction, removal of extra-brain structures using FSL's BET tool, spatial smoothing using an FWHM 5.0 mm Gaussian kernel to reduce

noise without reducing current activation, performed separately on each volume of fMRI data, general average intensity normalization of the entire four-dimensional (4D) dataset with a single multiplicative factor, and high-pass filtering (100 s) to remove low-frequency artifacts from the data. Functional data were recorded on high-resolution anatomical images and performed with 12 Degree of Freedom (DOF) in the FLIRT, linear recording tool located in FSL. Registration of structural images on the 2-mm Montreal Neurological Institute (MNI) standard space template was done using the nonlinear registration tool FNIRT.

D. Region of Interest Analysis

After applying the preprocessing steps to the functional images, first-level, GLM analysis was performed for each participant within the scope of this study. First, separate contrasts were created for the normal word reading task and the psedouhomophonic word reading task. Then, ROIs were determined by forming spheres with a radius of 10 mm. With the Featquery tool in FSL, the contrast images resulting from the analysis and each of the ROIs and numerical data with contrast estimation for each participant were obtained. The averages of contrast estimates obtained for both tasks were analyzed in the statistical analysis program IBM SPSS Statistics (26) (IBM Corp., Armonk, NY, USA) [25]. The normality test was first applied to the input data with the Kolmogorov–Smirnov test, and all of the data showed a normal distribution. Then, two-way (task group) 2 × 3 analysis of variance (ANOVA) analysis was performed. Post hoc analysis was performed using the Tukey Honestly Significant Difference (HSD) method in order to see between which groups this difference occurred in the ROIs where a significant difference was found between the groups as a result of the ANOVA analysis.

III. RESULTS

In this study, ROI analysis was performed with the fusiform gyrus, IFG, precuneus, and precentral gyrus regions, which showed overactivation as a result of the first-level analysis performed with GLM analysis and were selected in the literature. ROIs are shown in Fig. 1 [26].

As a result of the two-way ANOVA analysis, the *P*-value was examined in order to see that there was a significant difference between the tasks and between the groups. Although the *P*-value is a statistical value, it is calculated by Student's *t*-test and is used by two different groups to calculate whether the numerical data differ significantly from each other. When the *P*-value is below 0.05 as a result of the Student's *t* test, it is concluded that there is a significant difference between the two groups.

TABLE I. LEFT FUSIFORM GYRUS ROI ANOVA ANALYSIS RESULT

	Left Fusiform Gyrus		
	F	*P*	ηp2
Task	1.181	0.280	0.011
Group	3.193	0.045*	0.055

*Significant.
ANOVA, analysis of variance; ROI, region of interest.

In this study, it was observed that there was no significant difference between the tasks in the left fusiform gyrus ROI, with $F=1.181$, $P=0.28$, and $\eta p2=0.011$. As seen in Table I, $F=3.193$, $P=0.045$, and $\eta p2=0.055$ among groups, and a significant difference was found. As a result of the Tukey HSD method and post hoc analysis, it was observed that there was a significant difference between dyslexia and dysgraphia groups ($P=0.047$).

The marginal mean estimation is calculated from the graph shown in Fig. 2. The marginal mean for each category of a factor can be defined as the average response adjusted for other variables in the model. As seen in the graph for the dyslexia group, the average of the left fusiform gyrus ROI was higher in both tasks compared to the other groups. More interaction was obtained in the left fusiform gyrus ROI in all three groups during the pseudo-homonymous word reading task compared to the normal word reading task. However, the bars on the graph represent the standard error.

As a result of ANOVA analysis in the ROI of the right IFG, no significant difference was found between the tasks, with $F=3.312$, $P=0.072$, and $\eta p2=0.029$. As seen in Table II, $F=5.513$, $P=0.005$, and $\eta p2=0.091$ among groups, and a significant difference was found. As a result of post hoc analysis, it was observed that there was a significant difference between the dyslexia and dysgraphia groups, $P=0.036$, and between the dysgraphia and control groups, $P=0.005$.

As a result of the ROI analysis of the right IFG region, it is seen in the graph shown in Fig. 3 that there was a negative interaction in all three groups. The mean signal strength of this ROI was lower in both tasks, especially in the dysgraphia group compared to the other groups.

As a result of the ANOVA analysis of the precuneus ROI, no significant difference was obtained between the tasks, with $F=0.296$, $P=0.588$, and $\eta p2=0.003$. As seen in Table III, $F=4.340$, $P=0.015$, and $\eta p2=0.073$ among the groups, and a significant difference was

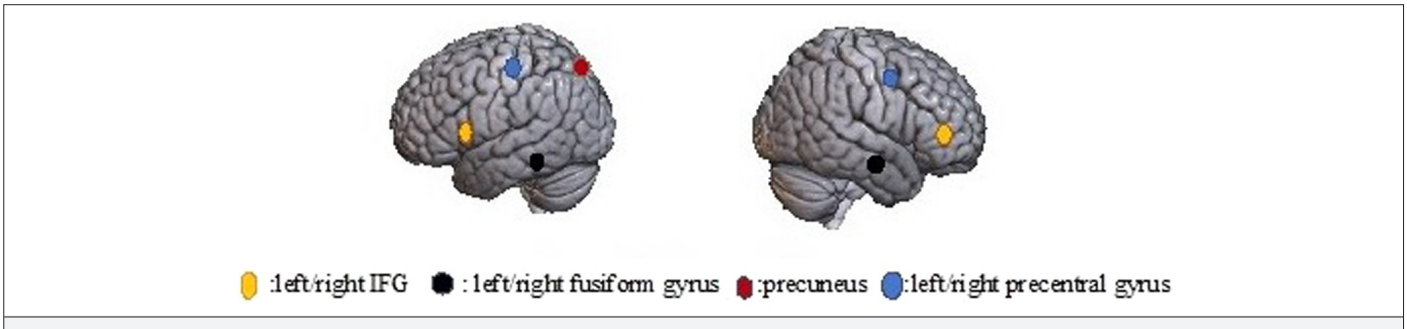

Fig. 1. ROI regions

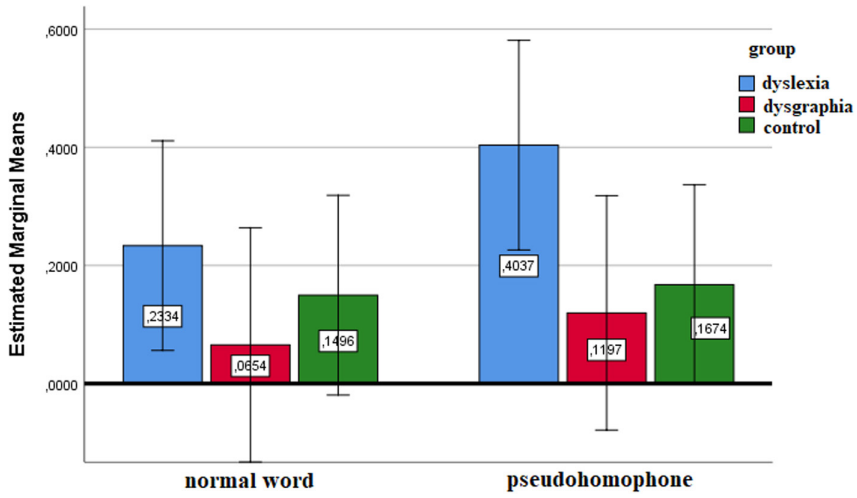

Fig. 2. Marginal mean estimation plot of the left fusiform gyrus ROI region

TABLE II. RIGHT INFERIOR FRONTAL GYRUS ROI ANOVA ANALYSIS RESULT

	Right Inferior Frontal Gyrus		
	F	*P*	ηp2
Task	3.312	0.072	0.029
Group	5.513	0.005*	0.091

*Significant.
ANOVA, analysis of variance; ROI, region of interest.

TABLE III. PRECUNEUS ROI ANOVA ANALYSIS RESULT

	Precuneus		
	F	*P*	ηp2
Task	0.296	0.588	0.003
Group	4.340	0.015*	0.073

*Significant.
ANOVA, analysis of variance; ROI, region of interest.

found. As a result of the post hoc analysis, it was observed that there was a significant difference between the dyslexia and dysgraphia groups, $P=0.02$, and between the dysgraphia and control groups, $P=0.04$.

As seen in the graph shown in Fig. 4, a negative interaction was found in three groups as a result of the ROI analysis of the precuneus region. In the dyslexia group, the interaction, which decreased negatively, was more in the normal word reading task than in the so-called homophonic word reading. In the dysgraphia and control groups, there was not much difference between the two tasks, and a decreasing interaction was found for the precuneus region in the so-called homophonic word reading task.

Region of interest analysis was performed in seven ROIs in total. As a result of the statistical evaluation, no significant difference was found between the tasks and groups in the right fusiform gyrus, left IFG, and the left and right precentral gyrus regions. In this study,

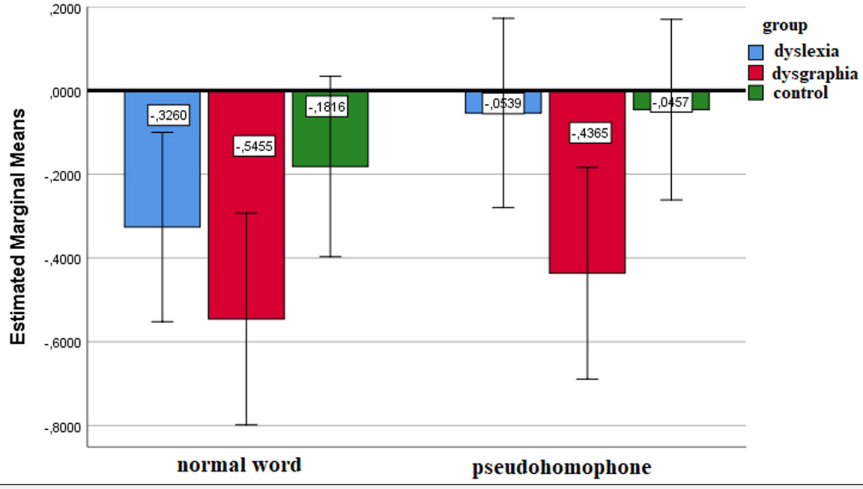

Fig. 3. Marginal mean estimation plot of the ROI region of the right inferior frontal gyrus

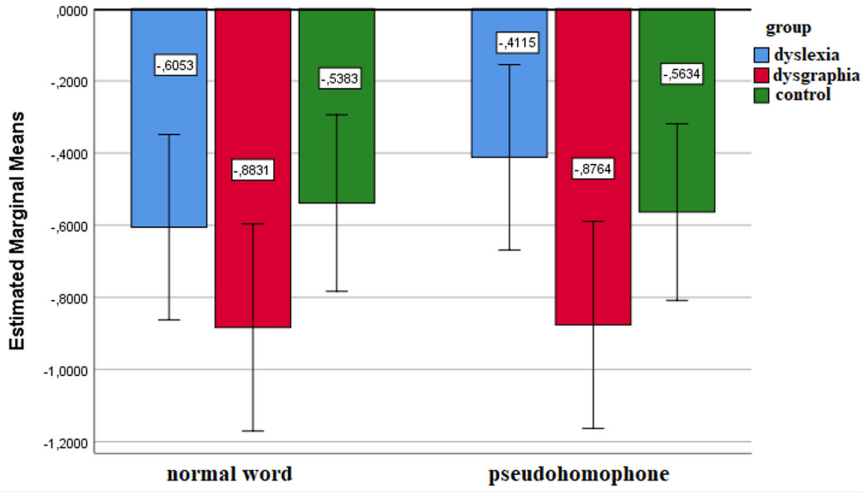

Fig. 4. Marginal mean estimate plot of the Precuneus ROI region

TABLE IV. CONTRAST IMAGE OF ROIS WITH FEATQUERY TOOL-GENERATED STATISTICAL RESULTS

		Left Fusiform Gyrus			Right Inferior Frontal Gyrus			Precuneus		
	Group									
Fea.	Task	Dyslexia	Dysgraphia	Control	Dyslexia	Dysgraphia	Control	Dyslexia	Dysgraphia	Control
Min	Nor.	–0.4635	–0.5019	–0.5085	–0.7106	–0.9182	–0.4193	–1.233	–1.657	–1.166
	Ph	–0.2887	–0.5404	–0.5012	–0.4867	–0.75	–0.2415	–0.7913	–1.433	–1.194
10%	Nor.	–0.1892	–0.2257	–0.1899	–0.551	–0.6662	–0.2489	–0.7667	–1.177	–0.6917
	Ph	–0.04	–0.2016	–0.1646	–0.3432	–0.3812	–0.1613	–0.5499	–1,108	–0.7353
Aver.	Nor.	0.2142	0.0599	0.1775	–0.2358	–0.4683	–0.1115	–0.5015	–0.8112	–0.4789
	Ph	0.3584	0.1287	0.1913	–0.0529	–0.3812	–0.0158	–0.357	–0.7935	–0.5462
Med	Nor.	0.2381	0.0636	0.1939	–0.2587	–0.4648	–0.1487	–0.4876	–0.7849	–0.4561
	Ph	0.3874	0.1372	0.2064	–0.0961	–0.3569	–0.0732	–0.3454	–0.7751	–0.5363
90%	Nor.	0.6002	0.3591	0.508	0.1093	–0.3029	0.0906	–0.2499	–0.4818	–0.2997
	Ph	0.7554	0.4684	0.5088	0.3644	–0.2117	0.228	–0.1678	–0.496	–0.3398
Max	Nor.	0.8197	0.5881	0.7149	0.9755	0.3472	0.6991	–0.0858	–0.2835	–0.2217
	Ph	0.9546	0.7104	0.6715	0.9739	–0.0186	0.5907	–0.0623	–0.2992	–0.1828
Stds	Nor.	0.2937	0.2316	0.2605	0.2618	0.1559	0.1605	0.2061	0.2661	0.1607
	Ph	0.2939	0.2595	0.2552	0.2605	0.153	0.1685	0.1523	0.2367	0.1662

ANOVA test results of ROIs with significant differences are given. In addition, in Table IV, the results of seven features obtained on the contrast images of the groups of ROIs selected in the Featquery tool are given collectively (minimum, 10% signal change, average, median, 90% signal change, maximum, and standard deviation).

IV. DISCUSSION AND CONCLUSION

Region of interest analysis measures the baseline signal generated by a particular ROI in the whole brain. ROIs, are usually selected from the clusters showing maximum activation as a result of other analyses [15]. The ROIs selected in this study were the bilateral IFG, fusiform gyrus, precuneus, and precentral gyrus regions. As a result of the ROI analysis, a significant difference was obtained between the groups in the right IFG, fusiform gyrus, and precuneus regions.

Analysis of variance of left and right IFG ROIs revealed a significant difference between dyslexia–dysgraphia and dysgraphia–control groups in the right IFG region. This difference was negative in the right IFG region and showed a lower activation during normal word reading. No significant difference was found between the groups in the left IFG region. It is noted that the left and right IFG regions

may participate in executive function to coordinate phonological and orthographic processing. In children, decreased activation of the right IFG region after trainer treatments has been associated with improvements in phonological decoding [27]. In a study in which left and right IFG were selected as ROIs, significant differences were found between groups in both ROIs [28]. In our study, no significant difference was found between the groups in the left IFG, but a negative significant difference was found in the right IFG ROI. Gebauer et al. [29] investigated children with dyslexia and dysgraphia by selecting five ROIs in a task-based fMRI study. Regions of interest are right supramarginal gyrus, right superior parietal lobe, right IFG, middle frontal gyrus, and left occipitotemporal regions. Unlike our findings in the right IFG region, they did not find a significant difference between the groups. They found a significant difference between the groups in the other ROIs they selected [29]. Olulade et al. in a study comparing children with dyslexia with a control group, the ROIs selected for ROI analysis were six ROIs from the left and right occipitotemporal cortex and five ROIs from the left and right IFG regions. In the findings obtained the study, ROIs in the left occipitotemporal cortex were also found higher activation in the control group compared to the dyslexia group, but no significant difference was found in the homologous ROIs regions in the right hemisphere [30]. In our study, significant differences were found between the groups in the right IFG region.

As a result of the ANOVA analysis of the fusiform gyrus ROI, a positive interaction was observed in all groups in the left fusiform gyrus region, and a significant difference was obtained between the dyslexia and dysgraphia groups. The fusiform gyrus region is the region that covers the visual word form area. This region shows rapid development in the first years of learning to read [31]. In addition, it is stated that the activation of the fusiform gyrus region increases during spelling and access to words [32]. In a study examining the fusiform region, Centanni et al. determined the left and right fusiform gyrus region as the ROI. In the study, which included children at risk for dyslexia, with dyslexia and a control group, as a result of the left fusiform gyrus ROI analysis, dyslexia and control group showed more interaction than children at risk group. They found no difference between the groups in the control and at-risk groups, but they found a significant difference in the dyslexia group compared to the other two groups, consistent with our study. In the right fusiform ROI, they did not find a significant difference between the groups, which is consistent with our study [18]. In another study in which the left fusiform gyrus region was selected as the ROI, children with dyslexia and a control group were examined in a task-based fMRI study with visual and auditory stimuli. The ROIs selected in the study are bilateral superior temporal gyrus, left fusiform, and right superior frontal gyrus. As a result of the ROI analysis, unlike our study, they found lower activation in the left fusiform ROI in the dyslexia group compared to the control group. This difference in results may be because the tasks were not the same. No group differences were found in the other two ROIs [17].

The precuneus region is involved in complex functions such as visual, attention, information integration, and visuo-spatial imagery [33]. The decreased activation in the precuneus seen in children with dyslexia may reflect less efficient or less complete processing of visuo-spatial and orthographic information during reading and handwriting. Studies have consistently demonstrated reduced brain activation [34, 35] and structural changes [36] in this region in dyslexia. In addition, it is stated that the activation of the precuneus region during fluent and accurate reading decreases over time with age [37]. In our findings, a significant difference was obtained between dyslexia, dysgraphia, and the control groups as a result of the ANOVA analysis of the precuneus ROI. A negative decreasing interaction was found in all groups. Richards et al. compared children with dysgraphia and a control group in a study they conducted. ROI analysis was performed in the study, and as a result of the ROI analysis of the precuneus region, a significant difference was found between the groups, consistent with our study; negative interaction was obtained in both groups. Also, they found a lower interaction in the dysgraphia group compared to the control group [37]. Consistent with our findings, in a task-based fMRI study comparing the ROI analysis of dyslexia and control groups, decreased activation was found in the right precuneus ROI in the orthographic decision task in children with dyslexia compared to the control group [38].

In this study, ROI analysis was performed between dyslexia and dysgraphia groups and the control group, and the activation differences in the relevant ROIs were compared. The statistical magnitude of the activation in the groups of the selected ROIs raises the hope that the related ROIs may be indicative of the functional distinctiveness of diseases with each other and with the control group. This should be supported by more data and further analysis in future studies.

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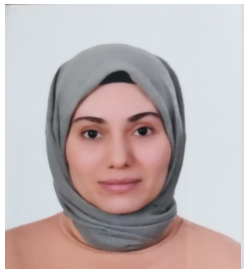

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