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RESEARCH ARTICLE

VISUAL EVOKED RESPONSES IN ADOLESCENT IDIOPATHIC SCOLIOSIS

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ABSTRACT

Purpose: In electrophysiological studies conducted with adolescent idiopathic scoliosis (AIS) patients, no prior studies examining the visual evoked potentials of AIS patients were found in conjunction with objective vertical perception. The aim of this study was to examine the visual evoked potentials of individuals with AIS and healthy individuals in terms of their brain responses.
Material and Methods: Twelve AIS patients (12.75±0.86 years) and 10 healthy subjects (13.80±1.68 years) participated. A 64-channel electroencephalography (EEG) recording system, Embedded Microcontroller Unit (EMISU), visual stimulation unit, EEG cap, and video recording system were used to examine brain responses after applying visual stimulus.
Results: In AIS and control groups (CG), three positive and two negative peaks were observed after applying the stimulus. In the AIS, the first and second negative, and second positive peaks, and in the CG, the second positive and negative peaks appeared significantly earlier in the frontal region. The amplitude of the third positive peak in all regions was found to be higher in the AIS. In AIS and CG, the second positive peak was found to be significantly higher in the parieto-occipital region.
Conclusion: It can be judged that AIS patients use more sources for processing the vertical visual stimuli than procedures compared to healthy individuals. In light of the findings obtained, the effect of treatments applied to AIS patients with the method used in this study can be evaluated in terms of brain responsiveness. In addition to the subjective visual perception of individuals with AIS, this method can also evaluate objective vertical perception.

Keywords: Adolescent Idiopathic Scoliosis, vertical perceptions, electroencephalography

INTRODUCTION

Scoliosis is a three-dimensional spine deformity with multiple epidemiological causes (eg congenital, neuromuscular, etc). Adolescent idiopathic scoliosis (AIS) is the most common (80-90%) type of scoliosis (1, 2). Etiopathogenetic factors of AIS are genetic, neurological, bone growth abnormalities, metabolic, hormonal dysfunction etc. (3, 4). Studies investigating neurological changes in AIS have mainly focused on explaining the etiopathogenesis, brain structures, and functions (5, 6). EEG is a non-invasive and easily applicable method, has an important place in clinical observations as well as being of great importance in brain research. The brain responses to stimuli (i.e. visual) given from outside during the spontaneous activity of the brain are called the (visual) evoked potentials (7).

The number of studies investigating brain responses in AIS is very limited. These EEG studies differ in terms of the number of electrodes used and the analysis approach, whereas the methodology of comparing AIS with the control group (CG) was utilized in a similar fashion like other neurological studies. In this context, Robb et al. indicated that there was no difference in EEG results similar between AIS and CG (8). In contrast, It was suggested that pathological changes may have occurred in subcortical structures due to increased low-frequency brain activities and observation of paroxysmal activity in AIS and that cerebellar dysfunction may be related to its etiology (9, 10). Besides differences in brain responses, hemispheric changes associated with the type of curvature has drawn attention. Pathological EEG results were found in contralateral hemisphere in AIS with lumbar curvature, in ipsilateral hemisphere in those with thoraco-lumbar curvature, and in the bilateral hemisphere in those with thoracic curvature (10). In contrast, Petersen et al. (11) did not find a systematic relationship as Dretakis et al. stated (10). Pinchuk et al. reported increased bioelectrical activity in the left hemisphere, especially left thalamus (12). Although there are differences of opinion among these studies, the cause of functional impairment in the puberty process may be related to the overloading of the adaptation-compensation mechanism of the central nervous system. In addition, EEG could not provide a method to predict the prognosis of scoliosis and to determine the relationship between the convex side and the hemisphere with changes (12).

The aim of this study was to examine the VEPs of individuals with AIS and CG. In former literature, there are no EEG records while the participants were in balance standing. Besides, no studies examining VEPs of scoliosis patients were found in the literature. In this respect, the current study targets a specific focus of research in the cognitive related brain responses of this neurospinal disorder..

MATERIAL AND METHODS

The study was approved by Dokuz Eylul University, Non-Interventional Research Ethics Committee, (Date: 21.11.2013, Number 2013/42-07) while the children and their parents were informed about the study, and written consent were obtained. Twelve patients with AIS (11 female, 1 male) and 10 healthy subjects (8 female, 2 male) participated in the study. The average age of the AIS group was 12.75 ± 0.86 years, and 13.80 ± 1.68 years for controls. The inclusion criteria were as follows; having a diagnosis of AIS, being between 10-16 years old, having a Cobb angle of 20° to 50°, a Risser sign determined to be 0-

Table 1. Demographic characteristics of individuals according to AIS and control groups.

	AIS Group (n:12) X±SD	**Control Group (n:10) X±SD**	**z**	***P***
Age (years)	12.75 ± 0.86	13.80 ± 1.68	-1.591	*0.112*
Height (cm)	160.58 ± 6.00	173.00 ± 7.94	-1.587	*0.113*
Weight (kg)	50.50 ± 9.03	54.00 ± 10.24	-0.265	*0.791*
BMI (kg/m^2)	19.50 ± 2.80	19.82 ± 2.89	-0.363	*0.717*

X: Average, SD: Standard deviation, BMI: Body mass index, z: Mann-Whitney U value

3. The exclusion criteria were selected as; former spinal operation, accompanying mental problems, other neurologic, muscular, or rheumatic diseases.

The Lenke classification was used to classify AIS patients' curvature types and the Cobb method to determine the curvature size.

EEG was recorded in an isolated and dark room that blocks electromagnetic waves, electrical and acoustical noise. The isolated room was monitored with a video camera with the knowledge of the individuals, and communication was provided by a sound system.

A 64-channel EEG recording system (Jasper 10-20 system), Embedded Microcontroller Unit (EMISU) (13), visual stimulation unit, EEG cap, and video recording system were used.

An electro gel (ECI Electro-Gel, ElectroCap International, Inc. ABD) was used to ensure the conductivity between the electrodes on the EEG caps and the scalp. The electrical potential of the earlobes was assumed to be zero and was referenced accordingly. The impedances of the electrodes were kept at 5 kOhm during recording. Electrooculography (EOG) records were taken with electrodes placed around the right and left eye area of the participants.

Line-alignment Visual Setup

The stimuli prepared in the MATLAB software environment for visual stimuli were applied to the participants through the EMISU device. To process vertical line perception, a set of pseudorandomized preset vertical lines have been prepared. In order to estimate the individual behavioral responses, the midline deviation values were obtained. The individual reference values were then taken as reference for each session. All the visual stimuli were created with red lines with angle values determined by the system, randomly within ± 15 degrees of this vertical reference value. These visual stimuli were applied to the participants through a 19-inch LCD screen in the form of red lines on a black background (Figure 1). In the records, 120 stimuli were sent and the inter stimulus interval (ISI) was around 3 to 3.5 seconds.

EEG analysis has been conducted offline via Scan 4.5 software (Neuroscan, USA). The epochs of 1000

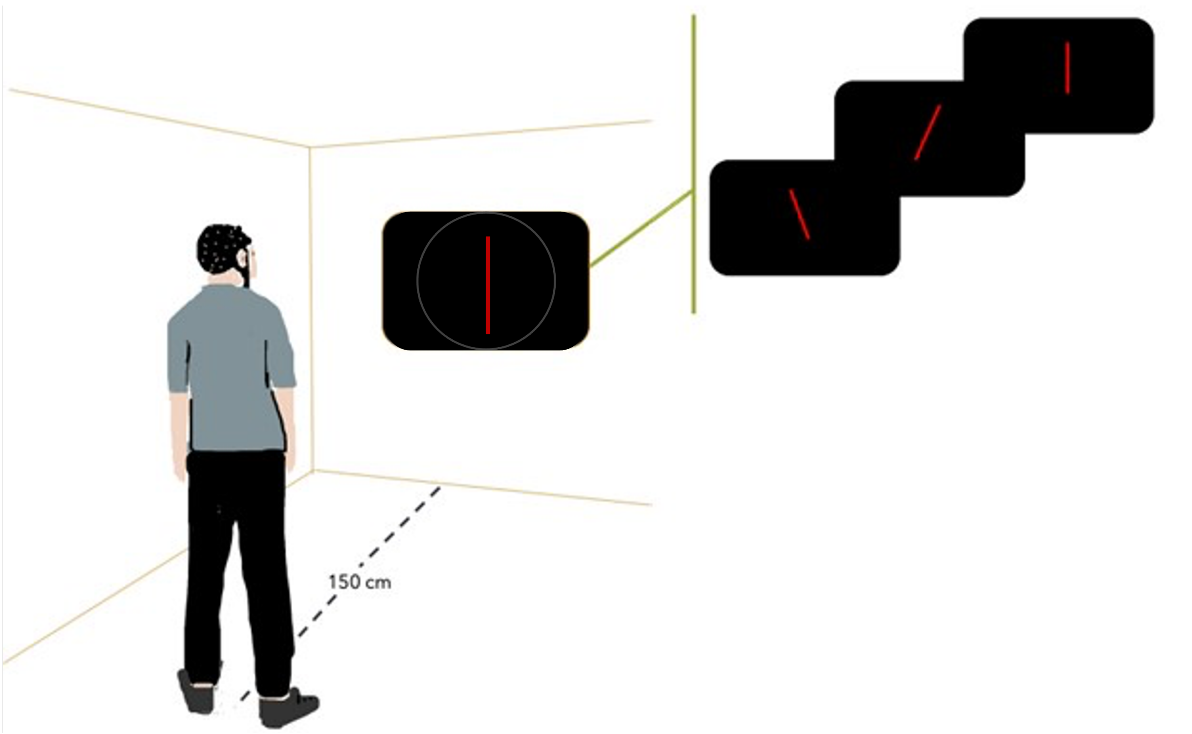

Figure 1. Subjective visual vertical perception tests environment: There should be a distance of 150 cm between the screen on which the experimental pattern is projected and the participant. A black camouflage with a circle-shaped gap in the middle of the screen is used in order not to refer to the verticality of the screen's edges. The participant can only see alerts through the circle-shaped space. In addition, the whole experiment was carried out in a dark environment in order to prevent reference to the quality of the wall lines, ceiling or various objects in the room.

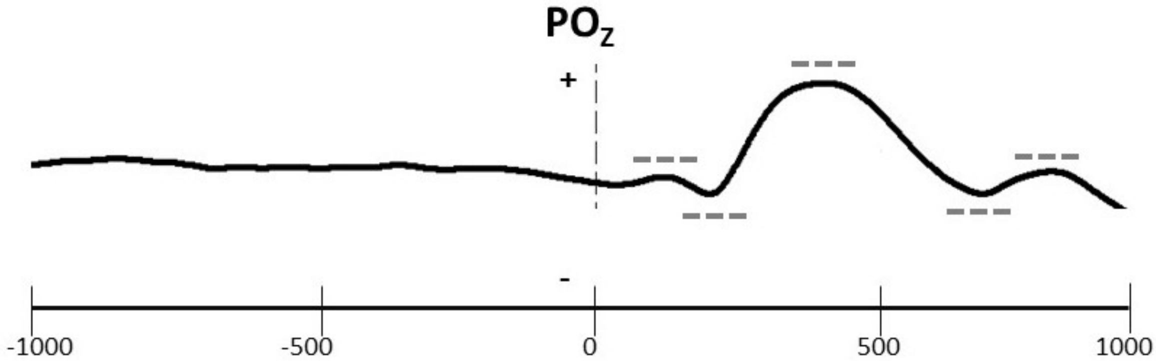

Figure 2. The average (N=12) brain response that occurs after the visual stimulus. The sample brain responses at the POZ electrode of the central parieto-occipital region are shown. The gray dashed lines show the brain response components examined. The moment of stimulation is indicated by the dashed line at "0.0". The horizontal axis is the time axis, 1000 msec before the stimulus and 1000 msec after the stimulus. The bottom side shows the negative direction, and the top side shows the positive direction to show the vertical axis amplitude (μV) values.

ms before and 1000 ms after the stimulus were created and were examined. In these epochs, those with an amplitude greater than ± 50 μV in the EOG electrode channels and those containing noise were eliminated.

The files obtained for each participant were baseline corrected based on the time axis and filtered with a digital bandpass filter with 0.5 - 3.5 Hz limit values (12 dB / oct and zero phase shift, Neuroscan 4.5). After the filtering process, the mean file was created for each individual. In measuring the amplitude of electrophysiological responses, the responses with the greatest amplitude between 0-1000 ms were measured and evaluated in μV. EEG recordings were taken from 64 channels. However, primarily the F3, FZ and F4 electrodes in the frontal region, which is the primary area for cognitive processing and PO3, POZ and PO4 electrodes in the parieto-occipital region, which is the primary area for visual stimuli, were examined. For the comparison between regions, F3-PO3, FZ-POZ and F4-PO4 electrodes were used. Excitation potentials comprise a series of electrical changes in the peripheral and central nervous system and are usually associated with sensory pathways and cognitive processing.

The processing of any external stimulus in our brain is completed within an average of 1000 ms after the stimulus is applied during wakefulness. After the stimulus is applied, different positive and negative peaks appear in the signals recorded by electroencephalography. Accordingly, a negative amplitude represents a decrease, and as a contrary a positive amplitude represents an increase in signal direction after stimulus application in conjunction with electrode recording site (Figure 2). The timing and the polarity of the signals are thus recorded and labeled, which enables further identification of these peaks and relates them to certain sensory and cognitive functions.

Statistical analysis of the data was made with the SPSS 22.0. Since the data did not show normal distribution, nonparametric tests were used. Differences between the two groups were analyzed using the Mann Whitney U test and in-group evaluations with the Wilcoxon test. In all statistical analysis, p values of less than 0.05 (≤ 0.05) were considered significant.

RESULTS

The distribution of demographic characteristics of the participants by groups is shown in Table 1. There was no difference between the groups in terms of age, height, weight, body mass index (BMI) ($p > 0.05$). The Cobb angle of patients with AIS was 32.33° ± 6.70. According to curvature types, the distribution of AIS patients was Lenke 1 in 41.7%, Lenke 3 in 33.3%, and Lenke 5 in 25%. In both AIS and CG, three positive and two negative peaks were observed after applying the stimulus. The peak that appeared in the positive direction 30 to 209 ms after the stimulus was

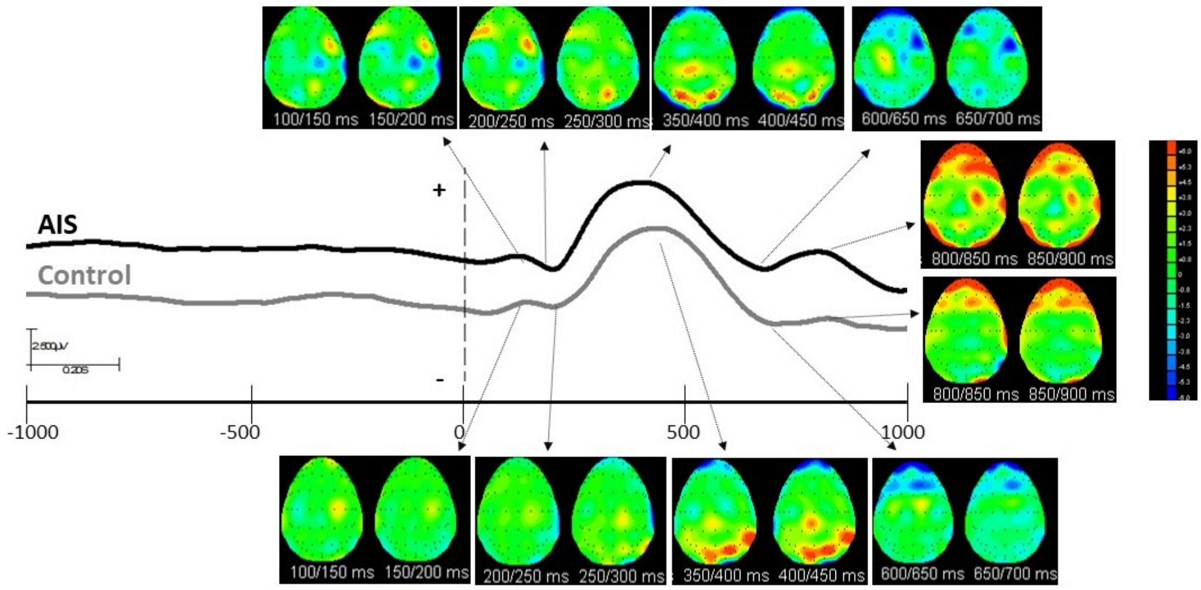

Figure 3. The brain response that occurs after the visual stimulus and topological distributions. Brain responses at the POZ electrode of the parieto-occipital region are shown. Black line indicates patient group (N=12), gray line indicates healthy control group (N=10). The horizontal axis is the time axis, 1000 msec before the stimulus and 1000 msec after the stimulus. The moment of stimulation is indicated by the dashed line at "0.0". The bottom side shows the negative direction, and the top side shows the positive direction to show the vertical axis amplitude (μV) values. The topological distributions are provided in respective time windows as a colormap (red to blue color codes are provided on the right side).

evaluated as the first positive peak, the negative peak at 60 to 313 ms as the first negative, the positive peak at 183 to 500 ms as the second positive, the negative peak at 299 to 799 ms as the second negative, the positive peak at 687 to 948 ms after the stimulus was evaluated as the third positive peak respectively.

In the AIS group, the first positive peak occurs 30 msec to 160 msec after the stimulus, the following peaks were as first negative at 101 to 239 msec, the second positive at 187 to 500 msec, the second negative at 440 to 694 msec, and third positive at 748 to 914 msec (Figure 3).

In the CG, the first positive peak 41 to 209 msec after the stimulus, followed by first negative at 119 to 291 msec, second positive at 190 to 489 msec, second negative at 299 to 799 msec, third positive at 734 to 948 msec (Figure 3).

When the latencies of the brain responses were examined in the frontal region, the first positive peak in the F4 electrode AIS appeared significantly earlier in the CG (p=0.016). The second negative and third positive peaks in POZ and PO4 electrodes in the parieto-occipital region were significantly earlier in the AIS than CG (p=0.011, p=0.025, respectively).

When the amplitude of the brain responses was examined, the amplitude of the third positive peak in all measurement regions was found to be higher in the AIS than in CG (p=0.021 at F3 electrode, p=0.036 at FZ electrode, p=0.030 at F4 electrode, p=0.001 at PO3 electrode, p=0.014 at POZ electrode, p=0.017 at PO4 electrode) (Figure 4).

Topological distribution

In three comparisons (F3-PO3, FZ-POZ, F4-PO4) in the AIS, the first negative peak, second positive and second negative peaks appeared significantly earlier in frontal region than parieto-occipital region (p=0.002 in first negative peak, p=0.002 in second positive peak, p=0.002 in second negative peak in the F3-PO3

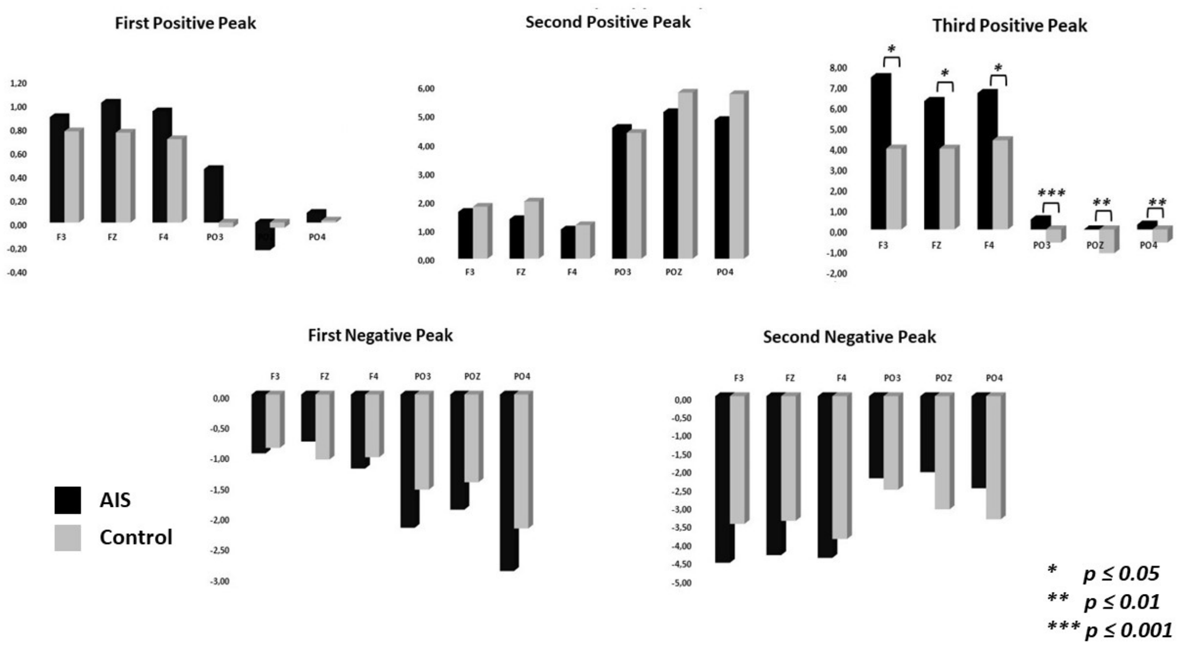

Figure 4. Average values of response peaks after stimulation. y-axis shows the amplitude of the peaks in μV. Gray bars represent control group, black bars represent AIS group The panels are categorized in regard to peaks in consecutive order.

comparison; p=0.002 in first negative peak, p=0.002 in second positive peak, p=0.005 in second negative peak in the FZ-POZ comparison; p=0.041 in first negative peak, p=0.003 in second positive peak, p=0.002 in the second negative peak in F4-PO4 comparison).

In the comparison between the F3-PO3 and FZ-POZ electrodes in the CG, the first positive peak, the second positive peak, and the second negative peak appeared significantly earlier in the frontal region than the parieto-occipital region, whereas in the F4-PO4 comparison, only the second positive peak and the second negative peak appeared significantly earlier than the parieto-occipital region in the frontal region (p=0.008 in the first positive peak, p=0.028 in the second positive peak, p=0.005 in the negative peak in the F3-PO3 comparison; p=0.012 in the first positive peak, p=0.017 in the first negative peak, p=0.009 in the second positive peak, p=0.005 in the second negative peak in the FZ-POZ comparison; p= 0.009 in the second positive peak, p=0.005 in the second negative peak in the F4-PO4 comparison).

In the AIS group, the amplitude of the second positive peak was found to be significantly higher in the parieto-occipital region than the frontal region in the comparison between the F3-PO3, FZ-POZ, and F4-PO4 electrode regions (p=0.002), the amplitudes of the second negative and third positive peaks were found to be significantly higher the frontal region than parieto-occipital regions (p=0.010, p=0.050, p=0.023 in the second negative peaks, p=0.002 in the third positive peaks respectively) (Figure 4).

In the comparison between the F3-PO3, FZ-POZ, and F4-PO4 electrode regions in the healthy CG, the amplitude of the second positive peak in the parieto-occipital regions was significantly higher than the frontal region as in the AIS group (p=0.022, p=0.007, p=0.005, respectively). The amplitude of third positive peaks were significantly higher in the frontal region than parieto-occipital regions (p=0.005) (Figure 4).

DISCUSSION

This study aims to examine the VEPS in AIS in terms of brain responses. For the first time, the experimental design has been utilized in this study to evaluate the alignment related visual evoked potentials of patients with AIS. As the study results showed, the component of late positive brain responses appeared earlier and its amplitudes were higher in the AIS than in the CG, in all measurement regions.

In the literature, EEG studies on patients with AIS are very limited, except for one they were conducted between 1970-1980s. Besides, EEG records were obtained with a limited number of electrodes (such as 12, 16 electrodes). On the contrary, 64 channels were used in the current study. When the results of the studies were examined, a consensus could not be reached in terms of changes in brain responsiveness in patients with AIS.

Robby et al. and Petersen et al. stated no difference in brain responses between AIS and CG (8, 11). Also, Enslein et al., evaluated the change in beta and theta waves during sleep in their research in AIS. The study stated that they encountered abnormal EEG findings in 2 of 28 subjects and possible abnormalities in 7. However, there was a significant difference in brain responses between patients with AIS and CG in this study like other studies (15). Lukeschitsch et al., Deratakis et al., and Sahlstrand et al. reported that the idiopathic scoliosis group differed significantly from EEG results in a healthy population (9, 10, 16). Also, in previous studies, EEG signals were taken in a sitting or lying position. In current study, EEG signals were received while standing as a first in this respect. The standing posture is more appropriate, especially for the evaluation of visual vertical perception. Accordingly, vertical alignment related real-world experience and body position for perception (e.g. not in supine position) were achieved.

When the studies in the literature were reviewed, no studies evaluated the VEPs in AIS. Hence, they are examined for the first time in this study.

In the literature, there are studies investigating differences between the curvature type and hemispheres as well as examining the EEG signals in scoliosis patients. Pathological EEG results were found in the contralateral hemisphere in AIS with lumbar curvature, in the ipsilateral hemisphere in patients with thoraco-lumbar curvature, and in the bilateral hemisphere in patients with thoracic curvature (10). Pinchuk et al. reported increased bioelectrical activity in the left hemisphere, especially left thalamus (12). In this study the difference between the hemispheres was not examined because the curvature types of the subjects were various, only the anterior and posterior regions of the head were compared.

Surely, there are many general theories in the literature about the way the brain works. In one of these, Basar suggested oscillating neural populations (17, 18, 19, 20). This theory states that the brain exhibits oscillatory activity in different frequency bands, which are respectively called delta, theta, alpha, beta, and gamma. In present study, the delta was investigated by filtering the signals in 0.5-3.5 Hz frequency band.

It is stated in the literature that the delta response after the stimulus is related to a conscious and cognitive function, to be obtained during the decision-making phase, and is the result of target stimulus recognition process (21, 22, 23, 24). In addition, if the task given involves decision making the potential responses related to visual and auditory events are more pronounced. In this study, the second positive component, occurring 187-500 msec after the stimulus in AIS, and 190 to 489 msec after the stimulus in CG, is the higher peak after the stimulus. The reason that there was no difference in latencies and amplitudes between CG and AIS may be because the visual lines were applied at different angles, and the processes of recognizing and comparing stimuli were similar in both groups. The reason that the second positive peak appears earlier in the frontal region and its amplitude is higher can be explained that the frontal region is responsible for higher-level cognitive processes.

In AIS, third positive peak occurs 748-914 msec after the stimulus, while in CG at 734-948 msec. The late-positive brain responses component appeared earlier in AIS group in the parieto-occipital region compared to CG, and its amplitudes were higher in all measurement regions (F3, FZ, F4, PO3, POZ, and PO4 electrodes) than in CG.

In studies conducted with electroencephalography in sleep and wakefulness processes, it is known that there are late components in the brain (25, 26). It has been shown that these late components, which occur after the stimulus is applied, are related to complex cognitive processes such as conflict monitoring in wakefulness (26, 27). In this study, the amplitudes of the third positive peak, which is the late response component, were found to be different in AIS and CG.

In the study, the stimuli were randomized to the participants in the range of ± 15°in the experimental design. Since the vertical perceptions of the group with AIS are different compared to the healthy CG, the group with AIS may have attributed more resources in the posterior frontal axis when processing stimuli in their brains. Hence there has been a different degree of frontal and occipital potentials as can be found in the color maps and the statistical data above. These showed that Parieto-Occipital areas as well as Frontal lobes were more involved in AIS to enable a similar task, therefore the patient groups' performance have been apparently less effective than of normal subjects. Furthering from our initial results, this sensory-cognitive domain needs further studies to paint a full picture of complex cortical dynamics in AIS.

This study also had a number of limitations. Firstly, the study was not designed according to curve types of patients with AIS. Secondly, the values of the subject visual vertical perception of patients with AIS were not determined and the experimental design was not based on the perceptions of the participants. On the positive side, our study constitutes a first as the experimental design, the position where the EEG is applied, and the method used during EEG analysis. These are the first use of 64 EEG channels encompassing the standing posture as a dynamic process, and the use of visual evoked potentials during EEG analysis for the first time in patients with AIS.

One of the major problems in scoliosis is false body perception, which may differ due to the type of curve. Due to the comparatively small number of our sample group, the distribution between groups as a result of classification was not possible for further statistical analysis. However, this remains an important issue that should be investigated in our future studies.

CONCLUSION

In the light of these results, the AIS denotes a series of complex phenomena where the brain dynamics remark a rather disturbed cognitive sensory resource management. The experimental design used in this study can be suggested as an objective measurement method in evaluating the vertical visual perception of patients with AIS. In addition to the subjective visual perceptions of patients with AIS, objective vertical perceptions can also be evaluated with these methods. In addition, with the method used in this study, the effect of treatments applied to patients with AIS in terms of brain responsiveness can be evaluated. With the measurement methods used in this study, a new perspective has been gained for the clinical evaluation of patients with AIS.

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Conflict of interests: None.

Ethical approval: Ethics committee approval for the research was obtained from the Non-Interventional Research Ethics Committee of Dokuz Eylul University with the decision number 2013/42-07, dated 21.11.2013 and protocol number 1217-GOA. For the changes made in the method and consent forms, it was taken again with the decision number 2015/16-29, dated 18.06.2015 and protocol number 1217-GOA.

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