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Original Article

A Noteworthy Pathology in Children with Learning Disabilities: Late Latency Response Failure in Central Auditory Processing

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OBJECTIVES: This study investigates the cortical auditory pathways in children with and without learning disability (LD).

MATERIALS and METHODS: A prospective, controlled clinical study was conducted on patients diagnosed with LD and was followed-up for a minimum period of 6 months in the Department of Child and Adolescent Psychiatry were included as study group. The control group comprised of age- and gender-matched healthy individuals. After otolaryngological and psychiatric examination, all participants were tested using pure-tone audiometry, tympanometry, acoustic reflex, and cortical auditory evoked potentials. Test results were evaluated and compared for each group.

RESULTS: The study included a total of 60 children (30 children with LD as study group and 30 healthy children as control group) who met the inclusion criteria. When event-related potentials were taken into consideration, P2 and P300 mean amplitudes for right ears and N1 and P300 mean amplitudes for left ears were significantly lower in study group than those in the control group. Likewise, P2 and P300 mean latency in right ears and P1, N1, and P300 mean latency in left ears were prolonged in study group ($p<0.05$).

CONCLUSION: Patients with LD may have disorders of the cortical auditory processing even if they have normal hearing screening tests. Pathologies in late-latency evoked potentials may have a role in the etiology of these patients.

KEYWORDS: Learning disability, cortical auditory processing, P300, potentials, central

INTRODUCTION

Learning disability (LD) is a developmental and neurobiological disorder that is defined as deficient acquisition of reading, writing, and mathematical skills despite adequate intellectual ability [1]. According to The Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV), LD is frequently seen in childhood and comprises of a spectrum of disorders such as dyslexia, dyscalculia, and dysgraphia [2]. Careful intervention of children with aforementioned disorders using psychological testing pointed out that these individuals usually have a discrepancy between intellectual ability and academic achievement. The main factor accused for the etiology is insufficiency in information processing. In this manner, previous studies emphasize the importance of visual and audiological perception of stimuli in central pathways [3].

Cortical auditory evoked potentials (CAEPs) can be used to evaluate cortical auditory processing by recording event-related potentials (ERPs) in response to auditory stimuli. Early-, mid-, and late-occurring positive and negative waveforms indicate the functions of different parts of the central auditory system [4].

In this study, we aimed to compare the robustness of cortical auditory processing in children with and without LD, hypothesizing that pathologies involving high auditory cortical pathways may be associated with LD.

This study was presented at the 38th Turkish National Otorhinolaryngology and Head and Neck Surgery Congress, 26-30 October 2016, Antalya, Turkey.

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MATERIALS AND METHODS

This prospective, controlled, and double-blinded study was conducted in a tertiary referral hospital, and all clinical examinations and audiological evaluations were carried out in the departments of audiology and otolaryngology. Each patient's parent signed an informed consent form before the study began, and the Declaration of Helsinki's ethical principles on human experimentation were followed. The study was approved by the ethics committee of Kecioren Research and Training Hospital (No: 987).

Patients diagnosed with LD (according to DSM-IV) and followed-up for a minimum period of 6 months in the Department of Child and Adolescent Psychiatry were included in the study group. Control group comprised of age- and gender-matched healthy individuals. Patients with sensorineural, mixed-type or conductive hearing loss, tympanogram other than type A, absent acoustic reflexes (<105 dB), having any type of vestibular diseases, diagnosed with neurological disorders other than LD, history of previous otological operations, and abnormal otoscopy findings were excluded.

All participants underwent a detailed otolaryngological examination prior to initiating the study. Besides study subjects, all children in the control group were also evaluated by the Department of Child and Adolescent Psychiatry in order to exclude any possible pathologies. After otolaryngological and psychiatric examinations, all participants were tested with pure-tone audiometry, tympanometry, acoustic reflex, and CAEP. Test results were evaluated for each group and were statistically compared.

Audiological Evaluation

All audiological tests were performed according to the guidelines of the American Joint Committee on Hearing and Equilibrium [5]. For audiological evaluation, pure-tone audiometry was performed using Orbiter 922® clinical audiometer (Madsen Electronics, Copenhagen, Denmark) at frequencies of 250, 500, 1000, 2000, 4000, and 8000 Hertz (Hz). A 226-Hz tympanometry was performed using AT235® impedance audiometer (Interacoustics, Copenhagen, Denmark) device. All patients were assessed by the same audiometrist. Acoustic reflexes were also measured using the same tympanometry device with a 226 Hz probe tone at 1000 Hz.

CAEPs were recorded using Bio-Logic Navigator Pro (Natus Med, USA, 2014) system. Auditory ERPs were elicited using an auditory "oddball" paradigm. Tone stimuli (30-ms duration, 10-ms rise and fall time) at 70 dB, above the patients' hearing threshold, were presented binaurally through headphones at an inter-stimulus interval of 1 per 1.8 s. Eighty percent of the tones were of 1000 Hz (background tones) and the remaining 20% were of 1500 Hz (target tones). The sequence of tones was randomly intermixed with the constraint that no two target tones were presented in succession. A total of 500 stimuli at a frequency of 0.3–1 Hz were presented with a 15% oddball stimulus. The standard tone was delivered at 1000 Hz, and the 'oddball' tone at frequency of 2000 Hz. P300 scoring was performed at the baseline to peak by an automated system based on the detection of a change in the sign of the gradient of the P300 component within a 280–550 ms latency window. P1, N1, P2, N2, and P300 latency and amplitudes were measured. P1-N1 and N1-P2 amplitudes were also measured and compared between the groups. The tests were repeated by masking the contralateral ear with 70-dB tone burst white noise (WN, Bio-logic) to verify the suppression effect. The right and left ears were separately assessed in all participants.

Statistical Analysis

Descriptive statistics were obtained from each group; mean values, standard deviations, and medians were calculated. Fisher's exact test and chi-square test were used to compare the results between the groups. Statistical Packages for Social Sciences (SPSS) version 22.0 for Windows (IBM Corp., Armonk, NY, USA) was used for all statistical analyses, and a p-value less than 0.05 was considered as significant.

RESULTS

The study included a total of 60 children who met the inclusion criteria. There were 30 children in the study group with ages between 7 and 14 (10.53±2.81) years and 30 children in the control group with ages between 8 and 13 (9.03±2.01) years. There were no significant differences among gender and ages between the groups. Demographical data is summarized in Table 1. Among the study group, 19 children were diagnosed with dyslexia, seven with dyscalculia, and four with dysgraphia. Three children with dyslexia had accompanying attention deficit and hyperactivity disorder. The average duration of the disease in study group was 2.3 years. Owing to the study criteria, two patients who had serous otitis media were excluded from the study. All participants had normal PTA and tympanometry results, and acoustic reflexes were present in all children.

When ERPs were taken into consideration, P2 and P300 mean amplitudes for right ears and N1 and P300 mean amplitudes for left ears were significantly lower in study group than those in the control group. Likewise, P2 and P300 mean latency in right ears and P1, N1, and P300 mean latency in left ears were prolonged in the study group ($p<0.05$). Mean amplitude and latency measurements for late latency responses in right ears are indicated in figure 1 and 2 respectively.

CAEP measurements are summarized in Table 2. Other important parameters to mention in late latency response are P1-N1 and N1-P2 amplitudes. According to our data, P1-N1 and N1-P2 amplitudes were significantly lower for both the ears in the study group than those for both the ears in the control group (Table 3).

When the subgroups of the study group were taken into consideration mean P1, N1, P2, and P300 amplitudes and latencies for both the ears were similar among the children with dyslexia, dyscalculia, and dysgraphia. However, the number of participants was not enough to obtain any statistical data.

Table 1. Demographical data

	Study group (n=30)	Control group (n=30)	p
Age (years)	10.53±2.81	9.03±2.01	0.062*
Gender (n)			
Male	20 (66.7%)	19 (63.3%)	0.787**
Female	10 (33.3%)	11 (36.7%)	

*Mann–Whitney U Test; **Chi-square test

Table 2. CAEP measurements of all participants

		Study group (n=30)		Control group (n=30)			
Waveform	**Side**	**Amplitude (μv)**	**Latency (msn)**	**Amplitude (μv)**	**Latency (msn)**	**pamplitude***	**platency***
P1	Right	2.52±2.19	60.13±9.63	5.08±3.05	57.91±4.92	<0.001	0.267**
	Left	2.90±1.58	64.09±7.64	3.41±1.80	60.48±5.54	0.267	0.011
N1	Right	−1.99±1.21	123.39±11.30	−3.39±2.34	122.38±9.17	0.021	0.705**
	Left	−2.39±1.64	123.26±11.60	−2.57±1.63	124.79±8.13	0.600	0.386
P2	Right	1.98±1.45	182.14±9.52	2.62±2.12	172.87±11.61	0.487	0.001**
	Left	2.38±1.70	176.38±12.81	2.53±1.49	174.92±10.80	0.745	0.261
N2	Right	−3.04±1.80	227.04±15.66	−4.88±4.23	220.48±13.13	0.196	0.084**
	Left	−3.86±1.91	227.74±16.90	−3.68±2.12	221.00±8.49	0.731**	0.057**
P300	Right	2.75±1.52	352.67±7.58	4.23±1.89	315.56±14.37	0.001**	<0.001**
	Left	2.98±2.28	354.11±12.90	4.02±1.73	316.52±13.85	0.007	<0.001**

*Mann–Whitney U Test; **Student t-test; Bold numbers: statistically significant

Table 3. CAEP measurements of all participants

Waveform	**Side**	**Study group (n=30)**	**Control group (n=30)**	**p***
P1-N1 Amplitude (μv)	Right	4.73±1.98	8.50±5.69	<0.001
	Left	4.98±2.21	6.92±2.86	0.005
N1-P2 Amplitude (μv)	Right	5.06±2.11	8.38±6.01	0.026
	Left	4.64±1.93	6.56±2.57	0.004

*Mann–Whitney U Test; Bold numbers: statistically significant

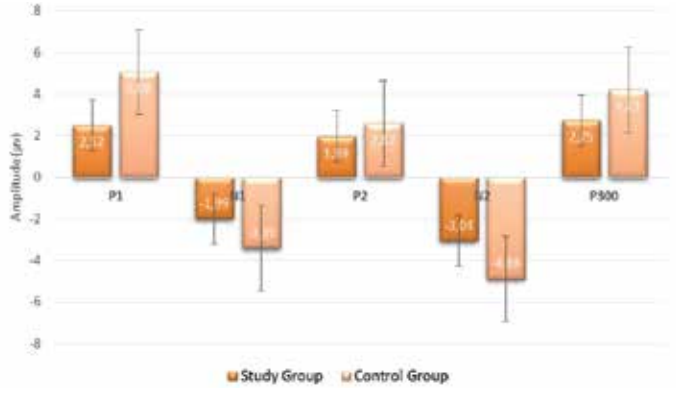

Figure 1. Mean amplitude measurements for late latency response in right ears

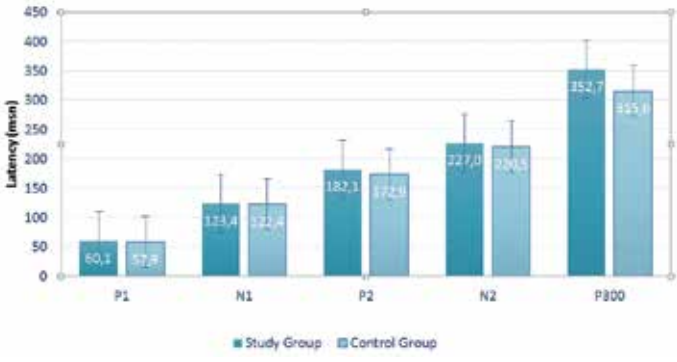

Figure 2. Latency measurements for late latency response in right ears

DISCUSSION

LD is a frequently occurring disorder with an estimated prevalence of 5% among children [1]. Although a vast majority of affected children are diagnosed after school age, the symptoms usually start earlier. The insignificant characteristics of most symptoms make the diagnosis even difficult. There have been theories trying to explain the underlying pathology of the disease based on physiological, anatomical, or behavioral disorders [6, 7].

In recent years, researchers are focusing on pathologies involving cortical auditory processing. There are some studies corroborating temporal processing theory in which majority discussed only patients with dyslexia [8, 9]. An increasing number of researches are supporting and are against disorders in high cortical auditory pathway in patients with dyslexia. From this point of view, we evaluated children with LD, not limited to dyslexia, by CAEPs.

Late-latency auditory evoked potentials (LLEPs), a subgroup of CAEPs, are defined as P1 (50–80 ms), N1 (100–150 ms), P2 (150–200 ms), N2 (180–250 ms), and P300 depending on the timeframe after the auditory stimulus. P300 is an LLEP that reflects mainly the thalamic and cortical activity. It is first described in 1965 by Sutton et al [10] while evaluating cognitive functions. It is a positive wave of 5–20 mV within the timeframe of 250–600 ms measured during a cognitive activity and is used for assessing higher cortical functions such as memory and attention. Many studies were performed about the clinical importance of P300, and latency period was correlated mostly with high cognitive functions, whereas amplitudes were informative about memory and attention [11, 12].

Previously, LLEPs were studied in neurological and physiological sciences for diseases such as schizophrenia, dementia, attention deficit and hyperactivity disorder, depression, and autism [13, 14]. These potentials were associated with visual-orthographic and auditory-phonological systems. Studies demonstrated that disrupted LLEPs may be correlated with early orthographic and late phonological integration deficits [15, 16]. In a study by Frank et al. [17] children with attention and reading disabilities showed abnormalities in ERPs. Another study by

Cohen-Mimran et al. [18] demonstrated that temporal processing deficits may play an important role in the pathophysiology of children with reading disabilities.

According to our data, children with LD had lower amplitudes for positive and negative ERPs as well as P300. These patients also had prolonged latency periods in ERPs, including P300 (Table 2). Our results were consistent with the literature as Papagiannopoulou et al demonstrated abnormalities in P300 latency in children with dyslexia. The greatest abnormality was recorded in the frontal brain region [19]. Likewise Kraus et al. [20] stated that P300 amplitudes were initially smaller among readers with dyslexia and tended to decrease further in the late phases. Another study reported poorer listening scores and lower amplitudes in P3 waves in the LD group [21].

Although a majority of LD spectrum present with dyslexia, there is a considerable amount of patients with dyscalculia and dysgraphia [22]. Unlike previous studies we did not focus only on children with dyslexia. Thus, we think that the findings of this study might be helpful in understanding the pathophysiology of the LD spectrum. The poor performance of the study group regarding LLEPs demonstrate that one of the underlying pathologies in LD spectrum may be relevant to temporal processing disorders. The results of our study corroborate with those of another research by Ingelghem et al. [8] investigating the cortical auditory pathway in patients with dyslexia compared with a control group of subjects with normal development. As understanding the pathophysiology of the disease is the key to adequate therapy, studies investigating LD spectrum may change the way clinicians treat their patients. Several studies were performed to assess the effects of music on the auditory cortex and findings suggest that musical therapy positively affects LLEPs [23-25].

The limitation of this study was the effects of the medication that were ignored in study group. However, all patients were followed-up in the same department with the same protocol. Further studies involving more patients with different medication protocols will increase the knowledge about drug effects to CAEPs.

In the light of our results and comparison with the literature, we can conclude that patients with LD may have disorders in cortical auditory processing even if they have normal hearing screening tests. Pathologies in LLEPs may have a role in the etiology of these patients. Thus, we recommend performing CAEP and evaluating LLEPs in this group of patients. With the support of further studies on the subject, disrupted waveforms in LLEPs may change the philosophy of the therapy in the future, like musical therapy as mentioned above.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Kecioren Research and Training Hospital (Approval No: 987).

Informed Consent: Written informed consent was obtained from patients' parents who participated in this study.

Peer-review: Externally peer-reviewed.

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