Hearing profile in Egyptian children with attention-deficit hyperactivity disorders
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Received 8 November 2016
Accepted 15 January 2017
The Egyptian Journal of Otolaryngology 2018, 34:76–83

Background
Attention-deficit hyperactivity disorder (ADHD) is a common neuropsychiatric syndrome with onset in childhood, most commonly becoming more apparent during the first few years of grade school. The aim of this study is to assess peripheral hearing and central auditory processing as well as cognitive function in 30 children diagnosed with ADHD. Their age ranged from 6 to 16 years (16 males and 14 females) and their IQ of at least 70. All of them were subjected to a basic audiological evaluation, and assessment of auditory brainstem responses, slow vertex response, and P300 waves using the oddball paradigm.

Results
No significant differences were found between pure tone thresholds and speech audiometry between the study and the control groups. There was a statistically significant increase in auditory brainstem response (ABR) absolute latencies (III and V) and interpeak latencies (I–III and I–V) at both low repetition rate and high repetition rate. Also, an increase in latencies of N1, P2, N2, and P300 latencies was observed with decreased P300 amplitude of the study group compared with the control groups. A significant mild positive correlation was found between P300 and both wave V latency and I–V interpeak latency.

Conclusion
The results of this study provide more evidence of central auditory processing involvement in children with ADHD and show the role of ABR and P300 in the management of these children.

Keywords:
ABR, attention-deficit hyperactivity disorder, children, P300

Introduction
Attention-deficit hyperactivity disorder (ADHD) is a common neuropsychiatric syndrome with onset in childhood, most commonly becoming apparent during the first few years of grade school [1]. Reports on the incidence of ADHD in the USA have varied from 2 to 20% of grade school children. Boys have a higher incidence than girls, with the ratio ranging from 3 to 1 to as high as 5–1 [2].

According to Diagnostic and Statistical Manual of Mental Disorders, 4th ed., (DSM-IV) [3], the essential feature of ADHD is ‘... a persistent pattern of inattention and/or hyperactivity-impulsivity which is more frequent and severe than is typically observed in individuals at a comparable level of development’. Symptoms of ADHD must be present before the age of 7 years, and must interfere with developmentally appropriate social, academic, or occupational functioning in a least two settings (e.g. at home and at school, or at home and at work). Although the disorder is usually not diagnosed before school entry, problems are often noted before age 4.

Anderson et al. [4] noted that ~80% of elementary school students (ages 4–10 years) suffer from temporary hearing loss at some time during the school year. These hearing losses were largely undetected by parents or teachers, and the typical hearing loss was determined to be 25–30 dB. When children with minimal or mild hearing loss present with behaviors that mimic ADHD/attention-deficit disorder (ADD) behaviors, the child might be managed with educational intervention, medications, and/or accommodations that are perfectly appropriate for ADHD/ADD, but clearly inappropriate for treating hearing loss.

There is another medical condition that has many of the symptoms of ADHD. Riccio argued that Central Auditory Processing Disorder (CAPD) and ADHD may be overlapping but independent disorders [5],

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whereas other investigators Cook et al. [6] argued that there are similarities between both disorders. There is a similarity between CAPD and ADHD in symptomatology as well as in psychoeducational and behavioral sequelae. Research findings concluded that a diagnosis of ADHD places the child at risk (50–80%) for CAPD [5].

Chermak and Musiek [7] suggested that understanding the relationship between the attention deficits of ADHD and CAPD hinges on the interaction between perception and higher level cognitive processing. Although several studies were carried out to evaluate CAPD in ADHD, debate still exists on the relation of both disorders.

Aim
This study aimed to evaluate peripheral hearing and central auditory functions as well as cognitive function in children diagnosed with ADHD.

Materials and methods

Study group
The study group included 30 children ranging in age from 6 to 16 years (16 males and 14 females), their IQ of at least 70, and they had not received treatment for ADHD. They were referred from the outpatient clinic of the psychiatry and pediatric psychiatry clinic at Assiut University Hospital after they were diagnosed with ADHD by a competent psychiatrist.

All caretakers of the children provided written consent for their children to be participants in the study after a full explanation of the study procedures was provided. All patients fulfilled the DSM-IV-TR [8] diagnostic criteria for ADHD.

Exclusion criteria
Children with IQ less than 70, a history of head trauma and major neurological deficit, and also children whose caretakers refused to write informed consent were excluded.

Thirty control volunteered children age and sex matched with the patient group participated in the study. They were selected from the general population at the outpatient clinic and fulfilled the same inclusion and exclusion criteria as the study group.

Methods
Children in both the study and the control group were subjected to the following:

1. Detailed assessment of history from parents.
2. Diagnosis of ADHD:
   According to the DSM-IV-TR [8] using the ADHD criteria of Swanson, Nolan and Pelham Questionnaire fourth ed.
3. Assessment of IQ (Stanford Binet fourth ed.).
4. Otoscopic examination.
5. Basic audiologic evaluations including (pure tone audiometry, speech audiometry, speech audiometry (speech reception threshold using Arabic spondee words for children [9] and speech recognition score) using Arabic Kindergarten Phonetically Balanced words [10] were performed using a calibrated pure-tone audiometer (Dual Channel clinical audiometer Madsen OB 922; GN Otometrics, Copenhagen, Denmark) with TDH-39 earphones in a sound-treated booth (Industrial Acoustic Company IAC model 1602-A; Industrial Acoustic Company, USA) and immitancemetry measurement including tympanometry and acoustic reflex thresholds of frequencies 500–4000 Hz (Interacoustics AZ 26, Assens, Denmark).

Slow vertex response (N1, P2, N2) and P300 test
Slow vertex response and P300 waves were elicited using the oddball paradigm. Two tones were presented in a random series at a rate of 1.1/s. A frequent tone (1000 Hz) was presented for 80% of the testing time and a target tone (2000 Hz) was presented randomly for 20% of the testing time. The two stimuli had a rise/fall time of 50 ms and a plateau duration of 200 ms. Each ear was examined separately. The stimuli were presented at an intensity of 80 dBHL [11].

The responses were obtained with the active electrode at Cz (after the hair was parted referenced to the right mastoid). The ground electrode was placed at Fz. The negative electrodes were placed on the ipsilateral and contralateral mastoids. The children were resting comfortably in bed throughout the testing session.

Children were trained and instructed to count the total number of target tones (the 2000 Hz tone). The accepted percent of correct identification of the number of the target stimuli was judged to be 90% or more. If a lower percentage was obtained, retest was performed after training.

The recording filter was set to band pass 0.5–20 Hz. The time window (sweep time) was 1 s with an amplifier sensitivity of 5 UV/division.
Analysis of the slow vertex response (N1, P2, N2) and P300 involved waveform identification, amplitude, and latency measurement.

P300 was identified as a positive peak or a series of peaks in the vicinity of P300 millisecond that was presented in the waveform evoked by the infrequent (target) tone [11,12]. Three measures were taken; the first and second measures were trough to maximum peak of the ascending and descending limbs of the P3 waveform. The third measure was the average of the first and second ones, which was taken as the response amplitude [11,13].

**ABR**

For recording the auditory brainstem response (ABR), electrodes were placed as follows: active electrode at the vertex (Cz), reference and ground electrodes at the left and right ears (A1 and A2), and recording between vertex and ear (Cz–A1 for the left side and Cz–A2 for the right side). One thousand and five hundred click stimuli at the rate of (21.1 and 61.1 Hz) with a duration of 0.1 ms were delivered at (90 dBnHL) through supra aural headphones TDH-39.

Signals were filtered with a 100 Hz to 3 kHz band pass and averaged over 1500 stimuli.

Peak latencies of all the waves (I, III, V) and IPLs (I–III, III–V, and I–V) were determined for each ear separately.

**Statistical analysis**

Data were collected and an analysis was carried out using the computer program ‘IBM SPSS, version 20’ (USA). Data were expressed as mean, SD using the t-test to determine significance for quantitative variables. A χ² was used to determine significance for qualitative variables. Furthermore, correlations between different parameters were assessed using Pearson’s correlation test.

**Results**

The study group included 30 children of both sexes diagnosed previously with ADHD/C at the Psychiatric Department (16 males and 14 females); their age ranged from 6 to 16 years, with mean±SD (8.4±2.2). The control group included 30 children age and sex matched with the study group.

**Basic audiologic evaluation**

**Pure tone audiometry**

The average of the pure tone threshold of the right and left ears for both study and control groups is shown in Table 1.

As the initial analysis of the results did not show statistically significant differences between the pure tone threshold of the right and the left ears, the results of the right and left ears are grouped together in the following analysis.

Averages of pure tone audiometric thresholds and speech audiometry for both the study and the control groups are shown in Table 2.

No statistically significant differences were found between the average pure tone thresholds at all frequencies in the study and control groups. The same result was found for the results of speech audiometry (average speech reception threshold and word recognition scores of participants in both the study and the control groups are shown in Table 2.

### Table 1  Comparison of the mean±SD of pure tone thresholds of right and left ears (dBHL) for both the study and control groups using the Student t-test

<table>
<thead>
<tr>
<th>Frequencies (kHz)</th>
<th>Ear</th>
<th>Study group</th>
<th>P-value</th>
<th>Control group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25</td>
<td>RT</td>
<td>16.5±5.0</td>
<td>0.342</td>
<td>15.5±5.3</td>
<td>0.543</td>
</tr>
<tr>
<td></td>
<td>LT</td>
<td>16.0±5.3</td>
<td></td>
<td>15.2±5.0</td>
<td></td>
</tr>
<tr>
<td>0.5</td>
<td>RT</td>
<td>15.3±5.2</td>
<td>0.674</td>
<td>14.5±4.4</td>
<td>0.783</td>
</tr>
<tr>
<td></td>
<td>LT</td>
<td>15.3±4.5</td>
<td></td>
<td>13.3±4.4</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>RT</td>
<td>14.0±4.2</td>
<td>0.732</td>
<td>13.7±3.9</td>
<td>0.329</td>
</tr>
<tr>
<td></td>
<td>LT</td>
<td>13.8±3.9</td>
<td></td>
<td>13.2±4.8</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>RT</td>
<td>12.7±5.0</td>
<td>0.431</td>
<td>12.2±4.5</td>
<td>0.651</td>
</tr>
<tr>
<td></td>
<td>LT</td>
<td>11.0±4.6</td>
<td></td>
<td>12.3±5.0</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>RT</td>
<td>11.0±5.0</td>
<td>0.839</td>
<td>11.2±4.7</td>
<td>0.881</td>
</tr>
<tr>
<td></td>
<td>LT</td>
<td>11.2±4.5</td>
<td></td>
<td>9.8±4.8</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>RT</td>
<td>11.2±7.2</td>
<td>0.247</td>
<td>9.7±7.1</td>
<td>0.439</td>
</tr>
<tr>
<td></td>
<td>LT</td>
<td>12.2±6.1</td>
<td></td>
<td>10.3±7.1</td>
<td></td>
</tr>
</tbody>
</table>

LT, left; RT, right.
Immitance measurements

All participants in the study and control groups had a (type A) tympanogram. The acoustic reflexes were present at the expected sensation levels when elicited contralaterally at 500, 1000, 2000, and 4000 Hz for both groups.

Results of ABR

The average absolute latencies of waves (I, III, V) and interpeak latencies (I–III, I–V, III–V) at a low repetition rate (LRR: 21.1 Hz/s) and a high repetition rate (HRR: 61.1 Hz/s) for both the study and the control groups are shown in Table 3.

As the initial analysis of the results did not show statistically significant differences in the evoked potentials between the right and the left ear, the results of the right and left ears are grouped together in the following analysis.

This table showed that there were statistically significant increases in most ABR waves’ absolute latencies (III and V) and interpeak latencies (I–III and I–V) for both LRR and HRR between the study and the control groups, suggesting an abnormal brainstem transmission and a deficit in the activation of the central auditory process (Fig. 1).

Results of slow vertex response and event-related potential (P300)

As the initial analysis of the results did not show statistically significant differences between the latency of N1, P2, and N2 of the right and left ears, the right and left ears were grouped together in the following analysis.

Table 4 shows that there were statistically significant differences between the mean N1, P2, and N2 latencies for both the study and the control groups, suggesting that there was an abnormal processing of sound detection in children with ADHD.

There was an increase in P300 latency (Fig. 2), with statistically significant differences between the mean P300 latency for both the study and the control groups (Table 5).

The Pearson correlation coefficient was determined to uncover any correlation between brainstem and cortical measures in ADHD and it was found that there were significant mild positive correlations between P300 and

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Table 2 Comparison of the mean±SD of pure tone thresholds (dBHL) and speech audiometry [speech reception threshold (dBHL) and word recognition scores (%)] for both the study and control groups using the Student t-test

<table>
<thead>
<tr>
<th>Frequencies (kHz)</th>
<th>Group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Study group</td>
<td>Control group</td>
</tr>
<tr>
<td>0.25</td>
<td>16.3±5.1</td>
<td>15.3±5.1</td>
</tr>
<tr>
<td>0.5</td>
<td>15.3±4.9</td>
<td>13.9±4.4</td>
</tr>
<tr>
<td>1</td>
<td>13.9±4.0</td>
<td>13.4±4.4</td>
</tr>
<tr>
<td>2</td>
<td>11.8±4.9</td>
<td>12.3±4.7</td>
</tr>
<tr>
<td>4</td>
<td>11.1±4.7</td>
<td>10.5±4.8</td>
</tr>
<tr>
<td>8</td>
<td>11.6±6.6</td>
<td>10.0±7.0</td>
</tr>
</tbody>
</table>

Speech audiometry

<table>
<thead>
<tr>
<th>SRT</th>
<th>Study group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.9±3.7</td>
<td>14.3±4.3</td>
<td>0.171</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>WD%</th>
<th>Study group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>99.5±2.0</td>
<td>99.7±1.0</td>
<td>0.898</td>
</tr>
</tbody>
</table>

SRT, speech reception threshold; WD, word discriminationscore.

Results of ABR at LRR (21.1 Hz/s)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Study group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>I latency</td>
<td>1.5±0.2</td>
<td>1.5±0.2</td>
</tr>
<tr>
<td>III latency</td>
<td>3.8±0.3</td>
<td>3.6±0.3</td>
</tr>
<tr>
<td>V latency</td>
<td>5.6±0.3</td>
<td>5.4±0.3</td>
</tr>
<tr>
<td>I–III</td>
<td>2.2±0.2</td>
<td>2.0±0.2</td>
</tr>
<tr>
<td>III–V</td>
<td>1.9±0.3</td>
<td>1.9±0.3</td>
</tr>
<tr>
<td>I–V</td>
<td>4.1±0.2</td>
<td>3.9±0.3</td>
</tr>
</tbody>
</table>

Results of ABR at HRR (61.1 Hz/s)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Study group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>I latency</td>
<td>1.6±0.2</td>
<td>1.7±0.3</td>
</tr>
<tr>
<td>III latency</td>
<td>3.9±0.3</td>
<td>3.8±0.3</td>
</tr>
<tr>
<td>V latency</td>
<td>5.8±0.3</td>
<td>5.7±0.3</td>
</tr>
<tr>
<td>I–III</td>
<td>2.3±0.3</td>
<td>2.1±0.3</td>
</tr>
<tr>
<td>III–V</td>
<td>1.9±0.2</td>
<td>2.0±0.2</td>
</tr>
<tr>
<td>I–V</td>
<td>4.2±0.3</td>
<td>4.0±0.3</td>
</tr>
</tbody>
</table>

HRR, high repetition rate; LRR, low repetition rate. *P value E 05. Significant. ***P value highly significant.

Figure 1

Showed ABR waves on low and high repetition rate from a child with ADHD.
wave V latency of ABR (LRR and HRR) \( r = 0.3 \leq 0.024 \) and between P300 and I–V interpeak latency (LRR and HRR) \( r = 0.3 \leq 0.04 \).

There were no statistically significant correlations between age and the different measures of ABR and P300, \( r = 0.04 \), \( P \)-value of more than 0.05.

**Discussion**

ADHD is among the most common chronic behavioral problems encountered during childhood and adolescence [14]. El-Tellawy et al. [15] reported that ADHD affects 5% of Assiut school-age children.

Some researchers argued that CAPD and ADHD may be overlapping, but independent disorders. Thus, no single tool is sufficient for the diagnosis of ADHD and evaluation should consist of a broad-based approach including screening for hearing and vision to exclude sensory deficits [5].

Statistically significant differences were not found in the results of the basic audiological evaluation (pure tone audiometry, speech audiometry, and immittancecmetry) between both the study and the control group as they were all within normal ranges, and this is in agreement with Reiff et al. [14] Barbaresi [16] and Kaplan et al. [2].

Although the participants of this study did not have any peripheral hearing disorders at the time of this research, some investigators such as Anderson et al. [4] reported that ~80% of elementary school students (ages 4–10 years) suffer from temporary hearing loss at some time during school year and undetected mild sensorineural hearing loss that mimics ADHD. Thus, a child with a peripheral hearing disorder may be misdiagnosed as having ADHD; Therefore, he recommended hearing assessments for any child diagnosed with ADHD.

Sininger and Starr [17] suggested that an accurate manifestation of stimulus timing in the auditory brainstem is a hallmark of normal perception; thus, deviations within fractions of milliseconds are clinically significant in the assessment of brainstem function and increases in latency are objective evidence of clinical or subclinical disease [18].

In this study, there was a statistically significant increase in absolute latencies of wave III and wave V and interpeak latencies of I–III and I–V at both a LRR and a HRR (21.1 and 61.1 Hz/s, respectively); this is in agreement with Puente et al. [19], who found prolonged latencies of waves III and V in children with ADD and significant differences between the mean interwave intervals I–III and I–V in ADD patients compared with controls.
These findings suggested abnormal brainstem transmission and a deficit in the activation of the central auditory process. It is possible that a response de-synchronization in the auditory pathway might exist in these disorders and the degree of myelination, axonal growth, and synaptic function could be the reason for this underlying deficit [20].

A temporal perception deficit in the range of milliseconds in ADHD may impact other functions such as perceptual language skills and motor timing. Furthermore, Yang et al. [21], supported the existence of a generic time perception deficit in this population. These results suggested that asymmetrical conduction of the auditory stimulus in the brainstem plays a role in the pathophysiological process of ADD/ADHD [22]. However, Schochat et al. [23] found that all ADHD patients had normal ABR.

The study group showed statistically significant increase in N1, P2, N2, and P300 latencies compared with the control group. Kemner et al. [24], reported that increased P3 latency in a set of event related potentials (ERP) responses reflects a defect in the cerebral processing of attention and a reduction in the speed of processing in children with ADHD. They concluded that there is an abnormal processing of cognitive information in children with a predominantly inattentive type of ADHD and thus a dysfunction in attentional mechanisms [24].

In this study, there was a decrease in the P300 amplitude in comparison with the control group; however, this did not show statistical difference. This small P3 amplitude can be explained by a reflection of behavioral disinhibition, a failure of behavioral control, and central nervous system hyperexcitability [25]. This is in agreement with Barry et al. [26] who suggested that a reduction in P3 amplitude elicited from an auditory oddball task is specific for children with ADHD in contrast to healthy children and children with autism or dyslexia [27].

The results of this study are in agreement with those of Puente et al. [19] and Idiazábal-Alecha et al. [28], who found a significant increase in the P300 latency and a significant decrease in the P300 amplitude in ADHD patients compared with controls. Lazzaro et al. [29] found a significant delay in N200 latency across midline sites along with a delay in P300 latency in the ADHD group.

P3 in ERPs has been used as a predictor of the response to treatment with central nervous system stimulants such as methylphenidate and atomoxetine. Administration of methylphenidate normalizes ERP indices, P3 amplitude, and latencies in children with ADHD [30].

In the present study, abnormal auditory brainstem timing and reduced cortical functions were detected (mild positive correlations between ABR and P300; Fig. 3); these results suggest an association between auditory processing at the brainstem and the cortex. This relation could be explained by two mechanisms.

**Bottom-up influence**

Subtle timing deficit at the brainstem typically impedes the cortical ability to process sound under acoustic stress (noise, small differences between stimuli). This was supported by listening training that resulted in enhanced robustness of the cortical response in individuals with abnormal brainstem timing [31].

**Top-down influences**

Brainstem timing may be impaired as a result of abnormal feedback from the cortex. Because the auditory brainstem receives efferent inputs from the cortex, it could be argued that abnormal cortical function results in impaired cortical feedback on the brainstem, which ultimately generates an abnormal brainstem response [32]. Also, the descending pathway could exert its influence by affecting selective attention, which in turn aids in gating of sensory information to the cortex.

Interestingly, the above-mentioned dual relation was supported recently by the fMRI study that highlighted the relation between brainstem and cortical activation [33]. They showed that the degree to which a given patient activated the brainstem subcomponent was
highly predictive of the degree to which that same patient activated the right frontal subcomponent [34].

Conclusion

(1) Children with ADHD showed statistically increased latencies of wave (III, V) and interpeak latencies of (I–III and I–V) of ABR at a LRR and a HRR.

(2) There were statistically increased latencies of N1, P2, N2, and P300 waves in children with ADHD compared with the control group with a decrease in P300 amplitude, but failing to reach the level of significance.

(3) The above findings/results indicate that ADHD pathophysiology impairs brain Functions that are important for allocating attention and using cognitive representation to guide cognition and behavior. Attention-related neural dysfunction is thus an important factor to consider in neurobiological theories of ADHD.

(4) The results of this study add more evidence to central auditory processing involvement in patients with ADHD and showed the role of ABR and P300 in the management of these children.

Recommendations

(1) Efforts should be made to attract attention of neuropsychiatrists as well as the public to the importance of hearing evaluation in children with ADHD for a proper diagnosis.

(2) Electrophysiological tests should be used to assess central auditory processing and cognitive functions, which can also monitored to measure the efficacy of treatment.

(3) Speech ABR should be included in the assessment as it utilizes a more complex signal than click ABR, which could provide more information on the mechanism of processing.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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