Obstructive Sleep Apnea–Hypopnea Syndrome and Hearing in Children

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Abstract
Objective To explore the relationship between hypoxemia and hearing in children with obstructive sleep apnea–hypopnea syndrome.

Methods Auditory brainstem responses (ABRs) were recorded in 68 ears and distortion product otoacoustic emissions (DPOAEs) in 60 ears in children with OSAHS and type “A” tympanograms, and in 30 ears in normal children. Results ABR latencies of waves I, III and V, and I-III, III-V and I-V intervals were not statistically different between OSAHS and normal children. Wave I latency was delayed in children with OSAHS compared to normal children (P < 0.05). DPOAE amplitudes in children with mild OSAHS were lower than normal children at 8 kHz (P < 0.05). DPOAEs were lower at 6 kHz and 8 kHz in children with moderate/severe OSAHS than normal children (P < 0.05). Conclusion Cochlear function was affected when AHI was at or greater than 10/hour. ABR and DPOAE can be used to detect early changes in auditory function in children with OSAHS.

Key words obstructive sleep apnea–hypopnea syndrome, children, auditory brainstem response, otoacoustic emissions

Introduction Obstructive sleep apnea–hypopnea syndrome (OSAHS) refers to sleep respiration disorders characterized by long time partial and/or intermittent complete obstruction of upper airway. It disturbs normal sleep ventilation and sleep formation. The morbidity rate in childhood is about 1–3%, especially in 2–8 years old children. Long-term sleep apnea–hypopnea may influence child growth and development and can sometimes result in serious complications. The primary pathophysiological mechanism is recurrent attacks of hypoxemia and hypercapnia. Auditory brainstem responses (ABRs) and otoacoustic emissions (OAEs) have been used as neurophysiological indexes of influences of hypoxemia in adult OSAHS patients. In light of the research on adults, ABRs were recorded from 68 ears and distortion product otoacoustic emissions (DPOAEs) from 60 ears in children with OSAHS between July 2005 and July 2006 at the 2nd Affiliated Hospital of Sun Yat-sen University.

Materials and methods

Clinical data

ABRs were recorded in 34 children with OSAHS (23 males and 11 females), aging 3–13 years (mean=7 years). The disease course was from 1 months to 10 years (mean=2 years). OSAHS was mild in 19, moderate in 9 and severe in 6 of these children. DPOAEs were recorded in 30 children with OSAHS (21 males and 9 females), aging 3–12 years (mean=6.8 years). The disease course was between 1 month and 10 years (mean=2.3 years). OSAHS was mild in 17, moderate in 7 and severe in 6 of these children. The control group included 15 children (10 males and 5 females), aging between 3 and 13 years (mean=7 years).

1 Diagnosis of OSAHS: According to the diagnostic criteria for children by Peking Capital Medical University and overseas studies, hypopnea is identified as a decrease in the mouth–nose airflow during sleep by more than 50% compared with the baseline level that lasts longer than 6 seconds and is accompanied by a ≥4% decrease in blood oxygen saturation or light awakeness. Sleep apnea occurs when cease of airflow lasts longer...
than 6 seconds. OSAHS was diagnosed when sleep apnea index (AHI) was $\geq 1 / h$ or sleep apnea–hypopnea index (AHI) $\geq 5 / h$, accompanied by LSaO2 $< 92\%$. Using the same diagnostic criteria, we further categorized OSAHS as mild (AHI $\geq 5 / h$), moderate (AHI $\geq 10 / h$) and severe (AHI $\geq 20 / h$).

2. Pathological adenoid hypertrophy was diagnosed when A/N was $\geq 0.76$ on lateral nasopharyngeal X-ray. The tonsil was considered hypertrophic when $2^\text{nd}$ or $3^\text{rd}$ degree enlargement was seen.

3. All children involved had type “A” tympanograms.

4. Patients with ear or maxillofacial abnormalities, or history of noise exposure, neurologic diseases, use of ototoxic medicines or upper respiratory tract infection one week prior to the monitoring were excluded. History of snoring and chronic respiratory tract diseases were ruled out in Children enrolled in the control group.

**Lab tests**

1. Polysomnography (PSG): A polysomnography recorder (model MS–SW2000C, Peking Mingsi Co., Beijing, China) was used. Patients were monitored for longer than 7 hours in natural sleep. Indices monitored included ECG, mouth–nose airflow, chest and abdominal wall movement, blood oxygen saturation and snoring. Results were analyzed on a PC computer.

2. ABRs: ABRs were recorded using an auditory evoked potential system (HIS, USA) in a sound-proof and electrically-shielded chamber while at sleep. Oral 10% chloral hydrate (0.4ml/kg) was used to induce sleep in children having difficulties falling asleep. The recording electrode was placed at Fz and the reference electrode at the ipsilateral mastoid process. Sweeps were 10 ms long and filtered between 100–3000 Hz. Clicks were presented at a rate of 19.3/s at 80 dB nHL, and 1024 sweeps were averaged for each recording. The left and right ears were tested separately. Latencies of waves I, III and V and intervals between waves I–III, III–V and I–V were analyzed. Testing was repeated at least twice for each recording.

3. Otoacoustic emissions: An otoacoustic emission system (IHS, USA) was used to record DPOAEs in a sound-proof and electrically-shielded chamber while the patient was awake. The f1 and f2 tones were set at 65 and 55 dB SPL respectively, with a frequency ratio (f2/f1) of 1.22. After levels of the primary tones had stabilized, amplitudes of the geometric mean of f2, f1 (2f1–f2) were measured at 0.5 to 8 kHz, using nonlinear sampling. Testing was repeated for each frequency.

**Statistical analysis**

Statistical analysis was performed using the SPSS for Windows (v. 11.5) software. All results were described as $\bar{x} \pm s$. The Student “t” test was used for comparison. Differences were considered statistically significant for $P < 0.05$.

**Results**

**ABRs**

We combined the moderate and severe OSAHS patients for analysis. ABR wave latencies and intervals showed no difference between children with mild OSAHS and those in the control group. Children with moderate/severe OSAHS, when combined together, showed delayed wave I latency ($P < 0.05$) but no difference in intervals between waves I–III, III–V and I–V when compared with normal children (Table 1).

**DPOAEs**

DPOAE amplitudes at 8 kHz were found to be lower in children with mild OSAHS than children in the control group ($P < 0.05$). DPOAE amplitudes at 6 and 8 kHz were lower in children with moderate/severe OSAHS than normal children ($P < 0.05$) (Table 2, Figure 1).

**Table 1** Comparison between mild, moderate/severe OSAHS group and the control group in the latency of wave I, III, V, and interval of wave I~III, III~V, I~V

<table>
<thead>
<tr>
<th>Groups</th>
<th>Latency (ms)</th>
<th>Interval (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>III</td>
</tr>
<tr>
<td>Mild OSAHS</td>
<td>1.75±0.18*</td>
<td>3.88±0.19</td>
</tr>
<tr>
<td>Moderate–severe OSAHS</td>
<td>1.72±0.13</td>
<td>3.84±0.21</td>
</tr>
<tr>
<td>Control</td>
<td>1.67±0.11</td>
<td>3.82±0.14</td>
</tr>
</tbody>
</table>

*compared with control group, * $P < 0.05$. 

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Journal of Otology 2008 Vol. 3 No. 2
Table 2  Comparison between mild, moderate/severe OSAHS group and the control group in DPOAE amplitude values

<table>
<thead>
<tr>
<th></th>
<th>1 kHz</th>
<th>1.4 kHz</th>
<th>2 kHz</th>
<th>3 kHz</th>
<th>4 kHz</th>
<th>6 kHz</th>
<th>8 kHz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate/severe OSAHS</td>
<td>9.00±6.60</td>
<td>11.38±5.42</td>
<td>8.54±4.99</td>
<td>1.42±6.15</td>
<td>-2.58±5.92</td>
<td>-2.12±5.95*</td>
<td>3.77±6.76*</td>
</tr>
<tr>
<td>Mild OSAHS</td>
<td>9.91±5.79</td>
<td>11.50±7.10</td>
<td>9.79±6.64</td>
<td>2.76±7.89</td>
<td>-2.21±6.18</td>
<td>1.97±5.80</td>
<td>-1.74±5.85*</td>
</tr>
<tr>
<td>Control</td>
<td>11.87±4.16</td>
<td>13.93±4.45</td>
<td>8.53±6.53</td>
<td>1.13±5.76</td>
<td>-3.93±3.22</td>
<td>3.00±7.60</td>
<td>2.83±8.71</td>
</tr>
</tbody>
</table>

Compared with control group, $P < 0.05$

Discussion

Adequate sleep is essential for children to reach optimal functional state. Rapid development of the nervous system in children makes them sensitive to hypoxia. Long-term sleep apnea and hypopnea can severely affect a child’s growth, and sometimes result in serious complications. As a part of the nervous system, the auditory system can also be affected by hypoxia related to sleep apnea and hypopnea.

Fischer et al. demonstrate that during sleep apnea, blood flow velocity in the middle cerebral artery is significantly decreased, with altered blood rheology, increased blood viscosity, and decreased oxygen saturation. These changes can affect blood– and oxygen–supply to hypermetabolic outer hair cells, resulting in decline in inner ear function, delay of neurotransmission in the auditory system and amblyacousia.

ABRs were used in this study to comprehend the influence of hypoxia from upper respiratory tract obstruction in children with OSAHS. The results showed little or no change in ABRs in children with mild OSAHS (AHI≥5/h), but delayed ABR wave latencies and increased interwave intervals in those with, moderate/severe OSAHS (AHI≥10/h). Adult PSG criteria are generally not applicable to children. Some researchers consider AHIs>10/h as representing serious problems in children. After reviewing studies by both Chinese and overseas researchers, we found the following children OSAHS criteria were appropriate for this study: “mild”=AHI≥5/h, “moderate”=AHI≥10/h and “severe”=AHI≥20/h. Our results indicated that cochlear function was affected when AHI≥10/h, as evidenced by delayed wave I latency when compared was normal control but no significant change in wave III, and V latencies and wave I–V interval. It seems that wave I latency is more sensitive to hypoxia than later waves. From the peripheral organs to the central centers, structures along the auditory system show variable sensitivity to hypoxia. The cochlea appears to be more sensitive than central structures to hypoxia. Waves III and V reflect electric activities in the brain stem nerve corpuscle, and inter–wave time probably represents the transmit time along the acoustic nerve. Pathological changes in the inner ear in OSAHS patients likely represent an early stage change. We feel that prolongation of wave I latency in the absence of the wave interval changes indicates some cochlear damage with intact central functions. This may be related to the blood supply and electrophysiological characteristics of the cochlea. The cochlear artery is an end branch of the anterior inferior
cerebellar artery and the sole blood supply to the cochlea with no collateral circulation. This makes the cochlear susceptible to hypoxia. In contrast, central auditory structures are likely supplied by branches from the internal carotid artery and vertebra basilar artery with affluent collateral circulation, and therefore less likely to suffer hypoxia than the cochlea. Wave I represents action potentials of the cochlear nerve. Cazals finds that the impact of hypoxia on acoustic function mainly happens in the cochlea. Hypoxia results in decrease of the endolymphatic potential and microphonics, which affect neural transmission in the cochlea. In ABR tests, these can lead to prolonged wave I latency and elevated wave V threshold.

DPOAE recording in OSAHS patients during sleep can be challenging due to the snoring noise. Yet children can be quite active when awake, presenting another challenge for DPOAE testing. Lower frequency DPOAEs were not included in this study to avoid interference by ambient noise (typically between 0.5 and 0.7 kHz). When high frequency DPOAEs (6 kHz and/or 8 kHz) were compared, decreased response amplitudes were noticed in OSAHS children. All factors adverse to cochlear function can cause changes in DPOAEs. Ototoxic medications, hypoxia and overstimulation can lead to decreased DPOAE amplitudes. Decreased SaO2 can stimulate formation of erythropoietin and synthesis of hemoglobin, which can lead to increase of the blood viscosity. The changes in hemodynamics can result in circulatory disorders and tissue ischemia and hypoxia, leading to deteriorated cochlear function. Mon et al found that DPOAE amplitude and cochlear blood flow completely recovered when discontinuation of blood flow through the internal auditory artery was less than 7 seconds; but recovered only partially and slowly in the presence of continuous partial or intermittent blood flow disruption. Telichi et al reported prolonged wave I latency at 18.3 seconds following discontinuation of blood flow through the internal auditory artery, and decreased wave I amplitude at 28.3 seconds. Delayed DPOAE phase was noticed at 4.8 seconds; decreased DPOAE amplitude at 14.8 seconds.

The decreased DPOAE amplitudes at 8 kHz and normal ABR results seen in children with mild OSAHS in this study suggested that OAEs can reflect changes in cochlear function at an earlier time than ABR. The cochlear stria vascularis tissue is rich of Na⁺−K⁺−ATP enzymes. Their activity seems to decrease progressively from the base to the top of the cochlea. Na⁺−K⁺−ATP enzymes are essential to the creation and maintenance of cochlear electric potentials. Factors that affect the ATP enzyme can reverse the endolymphatic potential. Therefore, although the stria vascularis is not directly involved in energy transition and information transmission, it provides the bioelectric energy source for hair cells. There is a close relationship among the stria vascularis, endolymphatic potential and auditory function. The effect of hypoxia is likely more intense on basal cochlea, where higher Na⁺−K⁺−ATP enzyme activity is observed, compared with the rest of the cochlea. This, combined with the relative low number of hair cells (i.e., low cellular reserve) in the basal area, may explain the early high frequency hearing damage ensuing hypoxia.

OAEs and ABRs are both used in detecting cochlear function changes. ABRs reflect integrated electroneurographic signals of the lower auditory pathway, while OAEs mainly evaluate outer hair cell function. OAEs seem to be more sensitive in judging the influence of hypoxia on cochlear function than ABRs. Based upon our results, we conclude that OAE and ABR should be performed in children with moderate/severe OSAHS as early as possible in order to discover compromised auditory function.

References
3 Praud JP. Snoring in children: still many questions, only a few

(Received July 30, 2008)