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Original Article

The correlations of speech-evoked auditory brainstem responses and cognitive function in patients with obstructive sleep apnea hypopnea syndrome

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Abstract: Objective: Patients with obstructive sleep apnea hypopnea syndrome (OSAHS) are at high risk of cognitive impairment, which has been investigated mainly by event-related potentials (ERPs) P300 and cognitive scale in previous study. Recently, it was reported that abnormal speech-evoked auditory brainstem responses (speech-ABRs) might reflect the disorders at the level of cortex as well as reveal auditory processing disorders at the brainstem level. The aim of this study was to investigate the relationship between speech-ABRs test results and cognitive impairment in patients with OSAHS. Methods: 60 patients with OSAHS (patient group) and 25 age matched healthy subjects (control group) were enrolled in this study. The patients were then divided into three groups (mild group, n=19, moderate group, n=20 and severe group, n=21) according to the severity of the syndrome (minimum oxygen saturation and Apnea Hypopnea Index). Speech-ABRs and auditory P300 were recorded by professional audiologist in shielded room. Cognitive function was evaluated by Montreal Cognitive Assessment (MoCA). SPSS17.0 software was used for statistical analysis. Results: Delayed latency and decreased amplitude of response onset peaks in speech-ABRs were detected in patients compared with control group (both $P < 0.05$). The V-A slope was decreased with increased disease severity. Prolonged P300 latency and reduced amplitude occurred concomitant to an increase of disease severity as well. However, there were no differences for the interpeak latency either by speech-ABRs or P300. Total MoCA scores decreased progressively, with significant differences between the control group and the mild, moderate and severe groups (all $P < 0.05$). Correlation and bivariate linear regression analysis revealed that the absolute value of amplitudes of waves V and A were negatively correlated with the latency of P300, and positively correlated with Montreal Cognitive Assessment scores. It implies that abnormal changes in amplitudes of waves V and A may reflect the degree of cognitive impairment indirectly in patients with OSAHS. Conclusion: These results suggest that there are deficits in the auditory brainstem pathway encoding speech sounds in patients with OSAHS, and that such deficits might affect and reflect the cognitive function in patients with OSAHS.

Keywords: Obstructive sleep apnea hypopnea syndrome, speech evoked auditory brainstem response, cognitive function, montreal cognitive assessment, event-related potentials

Introduction

Obstructive sleep apnea hypopnea syndrome (OSAHS) is a condition characterized by repeated episodes of sleep apnea (cessation of breathing for 10 s or longer) or hypopnea (significant reduction in breathing), associated with intermittent hypoxemia and frequent arousal, which are significant nocturnal consequences of the disorder [1, 2]. Many studies have reported a wide range of neurocognitive impairments in OSAHS patients, including selective and sustained attention [3, 4], information processing speed [5], short-term memory, and executive functioning [6-8]. The conclusions of all these studies are based on various types of neuropsychological scale test. It is increasingly recognized that the neurocognitive deficits experienced by OSAHS patients are largely mild cognitive impairments, as confirmed by neuropsychological tests such as the Mini-Mental State Examination. However, some studies have revealed that this measure is inadequate for detecting some neurocognitive deficits, includ-

ing primarily test memory and language acquisition abilities [9]. Other familiar tests use aspects of the Wechsler test; these are mostly used to measure attention/memory function in individuals with cognitive impairment [10]. The Montreal Cognitive Assessment (MoCA) is a convenient, stand-alone cognitive assessment instrument that covers various important domains of neurocognitive functions and can be quickly administered to patients [11]. In the present study, we used this scale as a tool to screen cognitive function in OSAHS patients.

It is well-known that event-related potentials can be used to achieve greater precision and sensitivity during cognitive evaluation. In the early 1960s, Sutton identified event-related potentials (ERPs) and showed their relationship to cognitive processes [12]. Since the 1980s, some scholars [13] have studied cognitive function in patients with OSAHS using ERPs. The main ERP component associated with attention and information processing during the Oddball paradigm task is the P300 [14]. Some studies have reported that patients with OSAHS exhibit sustained and delayed P300 latencies and a reduction in amplitude [3, 15-17], which indicated that ERP responses could be used to identify cognitive dysfunction as an objective marker.

Speech represents the sound combination of certain significance, certain tones and certain loudness features. In conversational speech, there are some delicate markers that imply a listener to begin and end the meaningful segments. How complex sound stimuli get transformed into meaningful unit signals in the nervous system is very important for their cognitive function. The auditory brainstem response (ABR) to speech sound stimuli simulates the acoustic characteristics of the speech signal with high similarity in temporal changes and spectral distributions. After decades of research, the use of speech-evoked auditory brainstem response has been widely applied [18].

Auditory processing disorders are characterized by a reduced ability to perceive information contained in auditory stimuli despite intact auditory pathways. Abnormal speech-evoked ABRs may reflect the disorders at the brainstem level, but may imply cortical-level disorders simultaneously, which are intimately linked [18, 19]. Some researchers have investigated the neural processing of simple acoustic signals, such as a click, at the brainstem level in individuals with OSAHS [20]. But no studies have examined the brainstem response to complex auditory signals like speech in OSAHS patients. Several studies have revealed that analysis of speech-ABR is an objective and non-invasive electrophysiological test that is useful for examining auditory brainstem function during the processing of complex stimuli like speech in a broad range of developmental and educational disorders [21-23]. These studies showed that poor cortical sensitivity to acoustic change was related to asynchronous onset timing in the auditory brainstem in children with learning disabilities. Therefore, in the present study, we focused specifically on patients with OSAHS and investigated their auditory brainstem responses to /da/ synthetic syllable stimuli. We expected that the speech-ABR would show evidence of hypoxemia-related differences in amplitude and latency because of a reduced ability to accurately encode rapidly temporal changes in speech.

Materials and methods

Patient group

Sixty male subjects between the ages of 18 and 40 were recruited from Chaoyang hospital, Beijing, China. Since the decline of SaO_2 is the main cause for damage of speech and cognitive function, sixty participants were divided into three subgroups based on their SaO_2: the mild group (n=19; 85% ≤ minimum SaO_2 ≤ 90%), the moderate group (n=20; 80% ≤ minimum SaO_2 < 85%), and the severe group (n=21; minimum SaO_2 < 80%) [24].

Inclusion criteria: Subjects are male, diagnosed with OSAHS on the basis of complaints, physical examination, and polysomnography monitoring; without previous treatment of OSAHS; Educational attainment is at least high school (primary school (6 years), middle school (3 years), high school (3 years) in China); normal hearing and no treatment experience, no visual disorders.

Exclusion criteria: Patients were with any neurological or psychiatric diseases (including depression); recent use of drugs known to affect

sleep or daytime sleepiness, a history of brain traumatic injury or unstable high blood pressure and other diseases (e.g., asthma, hypothyroidism, periodic leg-movement) causing daytime hypoxemia (SaO_2 < 90%).

Control group

Twenty-five healthy and age matched male controls (normal: AHI < 5, SaO_2 > 90%) were recruited. All controls exhibited good sleeping habits, normal hearing, no visual disorders, no psychiatric or nervous system diseases, and no recent use of drugs known to affect sleep or daytime sleepiness.

Each participant was written informed of the purpose of the experiment, and were cooperative. The protocol complied with the Declaration of Helsinki and was approved by the Ethics Committee/IRBs with No.12-83.

Polysomnography (PSG)

All subjects underwent overnight PSG using standard techniques and scoring criteria for sleep stages (EEG and submentalis EMG), leg movements (anterior tibialis EMG), and arousals from sleep. Arterial oxyhemoglobin saturation was measured by pulse oximetry and airflow was measured by nasal pressure cannula. Respiratory effort was assessed using thoracoabdominal movements (respiratory inductance plethysmography). All PSG studies were scored by licensed and registered PSG technologists, and reviewed by experienced sleep medicine specialists.

P300 test

To assess the auditory P300, we used the Biologic Navigator Pro System (VER 7.0.0, Biologic Systems Corporation, Natus Medical Inc., Mundelein, IL). Testing was carried out between 8:00 a.m. and 10:00 a.m., in a sound proof chamber. The sound was presented through a headset. Electroencephalographic recordings were obtained from silver-plate electrodes at Fz midline scalp sites. Reference electrodes were attached to the right earlobe and ground electrodes were attached to the left earlobe, according to international 10-20 system. Equal to or lower than 2 kΩ was allowed for impedance. EEG data were recorded with a 0.1- to 100 Hz band-pass filter at a sampling rate of 1000 Hz. The test technique was the target stimulus model. The target stimulus was the tone burst at a frequency of 2 kHz, randomly presented 30 times, with a probability of presentation in 20% of the stimuli; the frequent stimulus consisted of a tone burst at a frequency of 1 kHz, with 80% probability of presentation. The rate of stimulus presentation was 1.10 per second and the stimuli were presented binaurally with intensity of 70 dB SPL. The response triggered by the perception of the stimuli was a motor response, requiring individuals to identify and silently count the number of occurrences of target stimuli when they perceived rare stimuli. If the difference between the number of silent counts and actual target stimuli was > 10%, the test was deemed invalid. The data was processed as followed: First, the gross artifacts were rejected by visual inspection, and then eye blinking artifacts were removed using standard blink-correction algorithms [25]. After artifact rejection, the data were band-pass filtered at 0.1- to 30 Hz. Each subject was tested twice, and mean values for latencies and amplitudes were calculated.

Speech-ABR test

The BioMARK (Biological Marker of Auditory Processing) module of Biologic Navigator Pro System was used to collect /da/-evoked responses. The 40 ms /da/ stimuli were delivered to the right ear through insert earphones (Biologic) at an intensity of 80 dB SPL and at a stimulus rate of 10.9 Hz. A band-pass filter of 100-2000 Hz was applied and impedance was equal to or lower than 2 kΩ. Impedance values were optimized at the beginning of each test session and checked periodically throughout the session to ensure that values remained stable. Record period was over 60-ms post-stimulus time and trials with artifacts that measured in excess of ±35 μV were rejected from the averaged response. Three blocks of 2000 artifact-free responses were collected. Responses to each polarity of the /da/ stimulus were averaged separately and added together. For each subject, peak latency and amplitude were determined for the brainstem onset responses (positive peaks V and negative peak A), offset response (negative peak O), and the frequency-following responses (negative peaks D, E, F). Latency (ms) and magnitude (μV) values were calculated in the BioMAP™ software for each

Table 1. Demographic information (M ± SD)

Groups	Age (year)	Body mass index (kg/m^2)	Pathogenesis (year)	Minimum SaO_2 (%)	AHI	Educational Level (year)
Mild (n=19)	32.1±4.5	28.2±3.4[a]	3.8±0.8	87.3±1.2	9.1±2.6	≥ 12
Moderate (n=20)	33.5±4.3	29.4±3.5[a]	4.8±1.3	82.1±2.1	21.9±4.3	≥ 12
Severe (n=21)	34.8±4.9	30.8±3.7[a]	5.9±1.7	71.3±6.6	54.4±17.9	≥ 12
Control (n=25)	31.2±4.9	25.2±2.3	-	> 90	< 5	≥ 12
F value	2.546	12.344	-	-	-	-
P value	0.062	0.000	-	-	-	-

Note: [a]*P < 0.05*, vs. control group. (mild vs. Control, *P*=0.003; moderate vs. Control, *P*=0.000; severe vs. Control, *P*=0.000) (one-way analysis of variance).

Table 2. Different Speech-ABR waves latencies, amplitudes and V-A slope in patients and control (M ± SD)

Groups		Mild	Moderate	Severe	Control	*F* value	*P* value
Latency (ms)	V	6.82±0.39[a]	6.80±0.36[a]	6.83±0.29[a]	6.59±0.28	2.902	0.040
	A	7.92±0.28[a]	7.91±0.26[a]	7.95±0.26[a]	7.73±0.25	3.323	0.024
	D	23.15±0.56	23.27±0.57	23.38±0.76	23.03±0.64	1.258	0.294
	E	31.57±0.82	31.93±0.87	32.11±1.04	31.63±1.05	1.476	0.227
	F	40.45±0.68	40.80±1.09	40.65±0.97	40.71±1.05	0.459	0.712
	O	48.39±0.43	48.36±0.48	48.37±0.45	48.44±0.42	0.128	0.943
Slope (μV/ms)	V/A	0.20±0.25[a,b]	0.18±0.01[a]	0.15±0.06[a]	0.26±0.17	11.427	0.000
Amplitude (μV)	V	0.06±0.03[a,b]	0.06±0.02[a,b]	0.04±0.02[a]	0.09±0.02	16.215	0.000
	A	-0.16±0.04[a,b]	-0.15±0.05[a,b]	-0.12±0.03[a]	-0.19±0.03	14.266	0.000
	D	-0.11±0.07	-0.09±0.06	-0.09±0.05	-0.10±0.04	0.332	0.802
	E	-0.18±0.03	-0.20±0.04	-0.18±0.04	-0.20±0.03	1.630	0.189
	F	-0.10±0.03	-0.10±0.03	-0.10±0.02	-0.11±0.03	0.611	0.610
	O	-0.11±0.03	-0.12±0.05	-0.12±0.04	-0.13±0.04	0.577	0.632

Note: [a]*P < 0.05,* vs. Control group; [b]*P < 0.05,* vs. Severe group (one-way analysis of variance).

wave. The VA onset complex was further analyzed by computing slope, which is a measure of neural synchrony for onset responders.

MoCA scale

The MoCA scale is typically used to screen mild cognitive impairment quickly and conveniently, in patients exhibiting normal Mini-Mental State Examination scores [11]. Scores < 26 are considered to indicate mild neurocognitive impairment. Each correct answer is equal to one point, while an incorrect answer or no answer is equal to zero points. At the end of the test, we calculated scores for each subdomain, and for the total scale. To certify the reliability and accuracy of the MoCA, subjects underwent the test between 9:00 a.m. and 9:30 a.m., and the test was conducted by the same physician trained in psychology.

Statistical analysis

Data analysis was performed using SPSS 17.0 software (SPSS, Chicago, IL, USA). All data are presented as means ± SD. A normal distribution of the data was assessed using the Kolmogorove-Smirnov test. One-way analysis of variance followed by the least significant difference (LSD) test was used to compare P300 latency and amplitude and Speech-ABR results separately, as well as MoCA scores among the groups of subjects. Pearson correlation coefficients (r) and linear regression were used to evaluate the correlations among P300, speech-ABR and MoCA scores. Values of $P < 0.05$ were considered statistically significant. Comparisons were performed using rank sum tests followed by the Kruskal Wallis test, to analyze the scores in each MoCA subdomain. On the basis of the repeated hypothesis test, adjusted val-

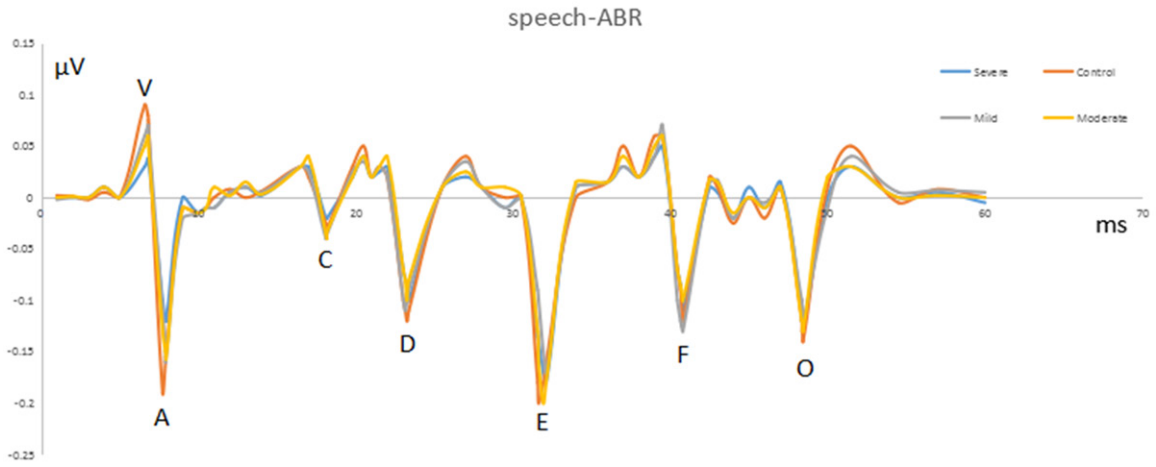

Figure 1. A typical speech ABR with 6 characteristic peaks (V, A, D, E, F, O) elicited by the speech stimulus /da/ and show the grand average waveform for the patients group (severe, blue line; moderate, yellow line; mild, gray line) and the control group (red line). Waves V and A represent the response to the onset of sound. Waves D, E, and F indicate the frequency-following response (FFR). Wave O represents the offset response. The stimulus of the /da/ was time-shifted by ~6.8 ms to account for the time delay between the presentation of the stimulus and the generation of the response. The latency and the amplitude of wave V and A in the patient groups was longer than that in the control group.

ues of $P < 0.008$ were considered statistically significant. The initial data can be found in Supplementary Data.

Results

Demographic and clinical data

The illness duration of OSAHS patients ranged from 4 to 6 years. Patients and controls were matched by age, gender (male) and educational level (years of education ≥ 12, above high-school education), with no significant differences between the two groups ($P > 0.05$). All subjects exhibited normal hearing (the pure tone test and acoustic immittance were normal). However, OSAHS patients exhibited significantly greater body mass indexes than control subjects ($P < 0.05$; **Table 1**).

Patterns of wave change in speech-ABR of patient groups

The patient groups showed delayed latency and decreased amplitude of response onset peaks compared with control group counterparts (both $P < 0.05$). There was no significant difference in the sustained response (waves D, E and F), waves O and interpeak latency of speech-ABRs among groups. The differences in speech-ABR amplitudes of wave V and A between controls and the mild, moderate and severe groups of OSAHS patients were statistically significant (all $P < 0.01$). The differences in speech-ABR amplitudes of wave V and A between the severe group and the control, mild and moderate groups were also statistically significant (all $P < 0.05$). The V-A slope decreased with increased disease severity (**Table 2**, **Figures 1**, **2**).

Patterns of wave change of P300 in patient groups

Prolonged P300 latency and reduced amplitude occurred concomitant to an increase of disease severity. The differences in P300 latency between controls and the mild, moderate and severe groups of OSAHS patients were statistically significant (P=0.034, 0.001, 0.000, respectively). The differences between the severe group and the control, mild and moderate groups were also statistically significant (P=0.001, 0.035, 0.000, respectively). The amplitude in the severe group appeared to be lower than that in three other groups (P=0.031, 0.030, 0.001 for the mild, moderate, and control groups, respectively), but we found no significant differences among the mild, moderate and control groups ($P > 0.05$) (**Table 3**, **Figure 3**).

MoCA scores and correlations between P300 and speech-ABRs

Total MoCA scores decreased progressively as the disease severity increased, with significant

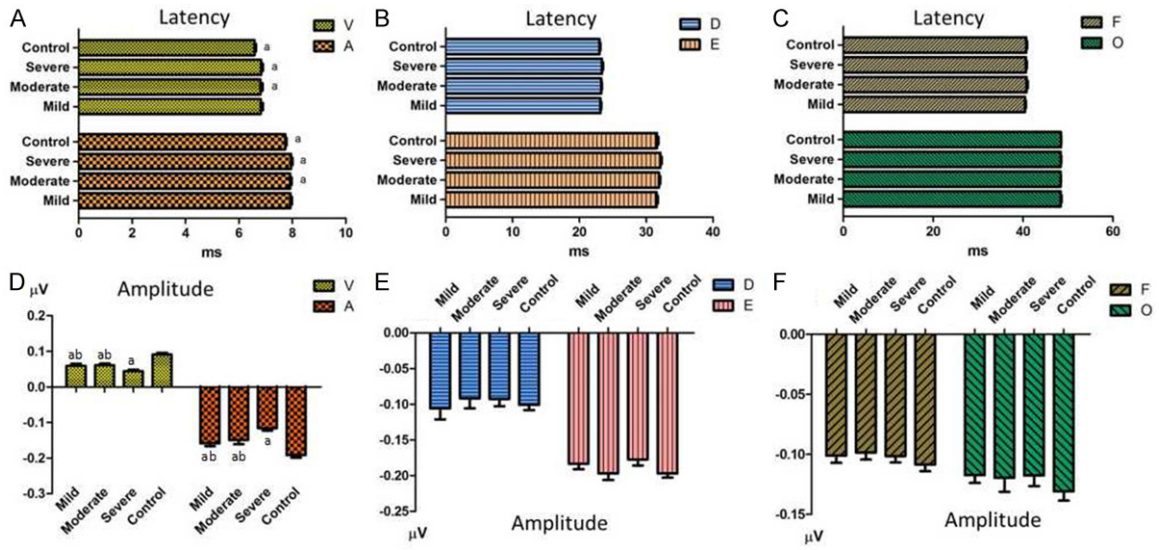

Figure 2. The mean latency and amplitude of 6 peaks of the speech-ABR are shown, with error bars representing +1 standard deviation of the mean.

Table 3. Comparison of P300 latency and amplitude in patient groups and control group (M ± SD)

Groups	Mild (n=19)	Moderate (n=20)	Severe (n=21)	Control (n=25)	*F* value	*P* value
Latency (ms)	317.43±9.58[a,b]	322.05±12.48[a,b]	330.16±13.90[a]	309.48±11.83[b]	11.647	0.000
Amplitude (μV)	5.49±1.50[a]	5.48±1.56[a]	4.29±1.80[a]	5.97±1.93	3.809	0.013

Note: [a]*P < 0.05*, vs. Control group; [b]*P < 0.05*, vs. Severe group (one-way analysis of variance).

differences between the control group and the mild, moderate and severe groups of OSAHS patients (F=38.669, P=0.000 < 0.05), as well as within mild, moderate and severe groups (mild vs. control P=0.004; mild vs. moderate P=0.001; mild vs. severe P=0.000; moderate vs. control P=0.000; moderate vs. severe P=0.002; severe vs. control P=0.000). The subdomain scores revealed a significant reduction in aspects of memory/delayed recall, attention, language and abstraction in severe OSAHS patients compared with the control group (all P < 0.008). In particular, only the differences in language scores between the control group and the mild, moderate and severe groups were statistically significant (P < 0.008 respectively) (**Table 4**).

As speech-ABR amplitudes for waves V and A increased, the MoCA scores also progressively increased. Linear regression analysis revealed a positively correlate between these two as the P300 latency became prolonged and the amplitude decreased, the MoCA scores decreased progressively. Linear regression analysis revealed statistically significant correlations between the P300 latency and amplitude and MoCA scores. Furthermore, as speech-ABR amplitudes of waves V and A decreased, the P300 latency became progressively prolonged. Amplitude V and amplitude A were negatively correlated with Latency P300 (**Table 5** and **Figure 3**).

Discussion

OSAHS patients with mild cognitive impairment commonly exhibit excessive daytime sleepiness and hypoxemia induced by nocturnal sleep-disordered breathing and apnea episodes [26]. These symptoms have been represented most commonly in terms of attention and memory processing. Cortical and subcortical structures form an integrated neural network that interact with each other through afferent and efferent neural pathway [27]. The brainstem is an important structure to them and can both influence and be influenced by this network's processes. And in this regard, speech encoding in the brainstem auditory

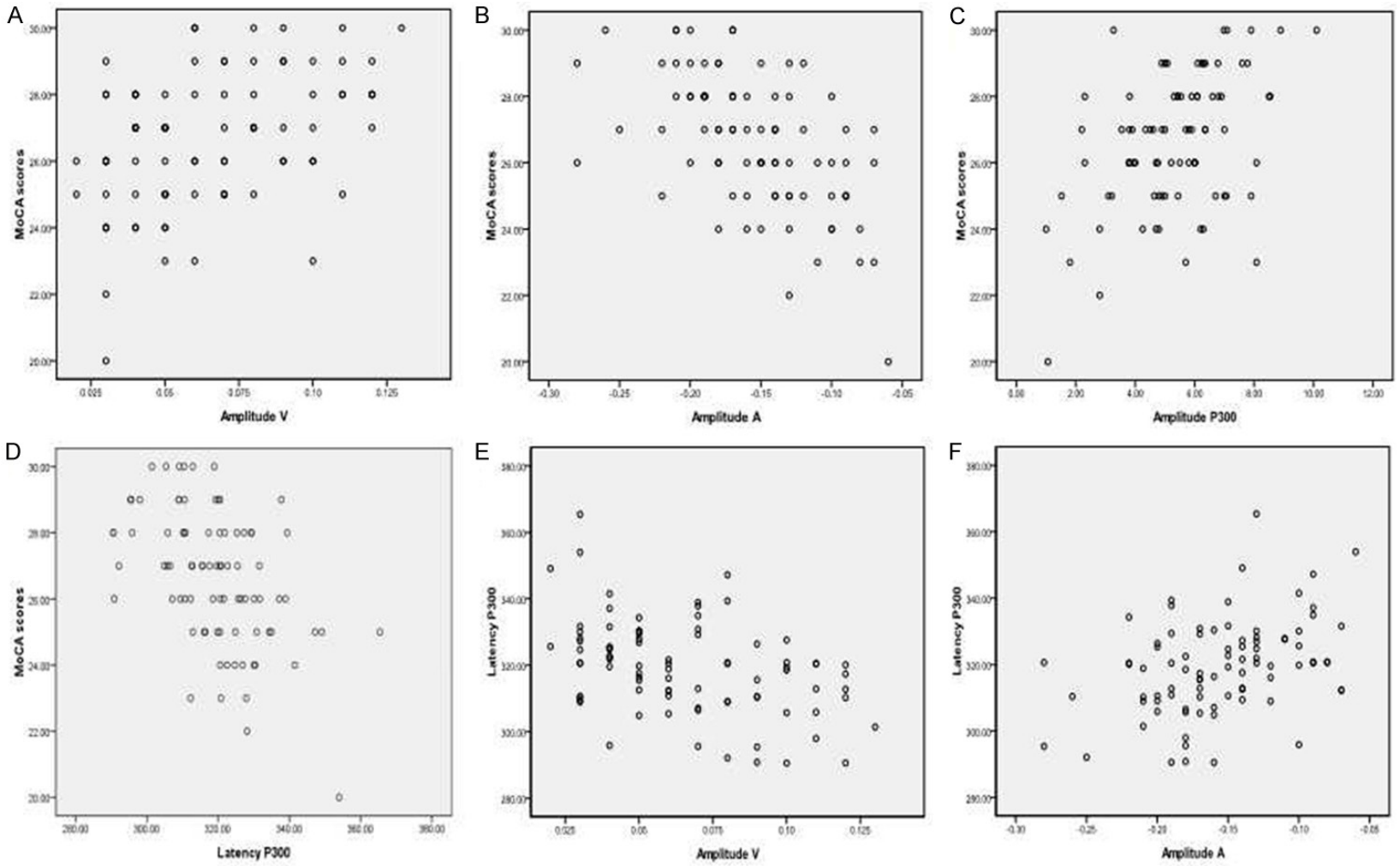

Figure 3. Correlation scatter diagram about linear regression analysis within amplitude V, amplitude A, amplitude P300, Latency P300 and MoCA scores. Specific value refers to **Table 5**.

Table 4. MoCA total scores and subdomain scores among all groups (M ± SD)

Groups		Mild (n=19)	Moderate (n=20)	Severe (n=21)	Control (n=25)
Total scores		27.32±1.16[a,c,d]	25.85±1.23[a,b,d]	24.52±1.69[a,b,c]	28.52±1.16[b,c,d]
Subdomain scores	Visuospatial & executive	4,84±0.37	4.65±0.49	4.57±0.6	4.92±0.28
	Naming	3.00±0.00	3.00±0.00	2.95±0.22	3.00±0.00
	Memory & delayed recall	4.37±0.60	4.25±0.64	3.90±0.70[a]	4.56±0.51
	Attention	5.79±0.54	5.40±0.68	5.24±0.54[a,b]	5.76±0.44
	Language	1.79±0.71[a]	1.55±0.60[a]	0.95±0.80[a,b]	2.48±0.65
	Abstraction	1.63±0.50	1.25±0.64[a]	1.19±0.60[a]	1.76±0.44
	Orientation	5.95±0.23	5.85±0.37	5.71±0.46	5.96±0.20

Note: 1. MoCA total scores: F=38.669, *P=0.000 < 0.05.* [a]*P < 0.05*, vs. Control group; [b]*P < 0.05,* vs. Mild group; [c]*P <0.05,* vs. Moderate group; [d]*P < 0.05,* vs. Severe group. (one-way analysis of variance). 2. MoCA subdomain scores: [a]*P < 0.008*, vs. Control group; [b]*P < 0.008,* vs. Mild group. (Kruskal Wallis test of rank sum tests, adjusted *P* values 0.008 is approximate calculation with Chi-square test).

Table 5. Bivariate correlations and regression within amplitude V, amplitude A, latency P300 and MoCA scores

	r	Linear regression equation	*F* value	*P* value
Amplitude V and MoCA	0.42	Y=24.732+29.091X	17.793	0.000
Amplitude A and MoCA	-0.562	Y=22.939-23.784X	38.404	0.000
Amplitude P300 and MoCA	0.455	Y=23.922+0.509X	21.689	0.000
Latency P300 and MoCA	-0.486	Y=48.818-0.069X	25.704	0.000
Amplitude V and Latency P300	-0.418	Y=332.587-202.754X	17.606	0.000
Amplitude A and Latency P300	0.387	Y=337.133+114.593X	14.631	0.000

Note: Pearson correlation coefficients are represented by r.

pathway can be influenced by hypoxemia-related inputs from peripheral auditory nervous systems or abnormal orders from more cortical ones via efferent neural fibers [28]. Thus, the disorder of sensory and regulation of the cortex has been associated with hypoxemia-related brainstem neural dysfunction, such as language impairment [27]. A previous study reported that chronic nocturnal intermittent hypoxemia during sleep resulted in dysfunction of the frontal executive cortex, which is particularly vulnerable to hypoxemia, and is proposed to constitute the pathological basis of memory impairment in OSAHS patients [8]. This effect may operate through the forehead and rear head area, generating electrophysiological activity patterns that lead to ERP abnormalities [29]. Previous research has shown that the cortex and hippocampus, P300 generation structures, are particularly sensitive to hypoxemia [30]. Moreover, hypoxemia may induce neuronal lesions and atrophy of the hippocampus, which restricts neurocognitive performance [31].

In our study, the P300 amplitude was significantly lower in the three OSAHS groups than in the control group which is similar to Martins et al. [32]. The amplitude reflects brain activity in the parietal-temporal and pre-frontal areas, associated with auditory memory [33, 34], which would be reduced in patients with OSAHS. The P300 latency is a sensitive parameter in OSAHS patients. Latency is associated with the interstimuli frequency to the individual's attention and concentration [3, 33]. It reflects the velocity of brainstem neurons in response to a stimulus. The latency of the P300 in the OSAHS group was significantly delayed. As shown in **Table 3**, this difference exists not only between the patient groups and control group, but also among mild, moderate, and severe groups of OSAHS patients. This suggests that the changes in latency in response to hypoxemia are more sensitive than those in amplitude [15].

The MoCA is typically considered as the gold standard for examining mild cognitive impairment in OSAHS patients. To further examine the role of the P300 in the evaluation of cognitive impairment, we analyzed the correlation between the P300 and MoCA. We found that the latency of the P300 was negatively correlated with MoCA scores and the amplitude of the P300 was positively correlated with MoCA

scores. Thus, we believe that the P300 is an objective means of evaluating the cognitive function of patients with OSAHS, and is an effective supplement to the MoCA scale.

MoCA is a brief and sensitive tool for assessing cognitive impairment in OSAHS patients. We found that MoCA scores decreased progressively as hypoxemia worsened. Evaluation of MoCA subdomains further revealed selective impairment of memory/delayed recall, attention, language and abstraction in the moderate-to-severe groups. These findings are in accordance with the majority of complaints of OSAHS patients. More remarkably, a Kruskal Wallis test analysis of mild, moderate and severe groups showed that only the subdomains of language scores were significantly different from those in the control group. Based on this finding, we analyzed the composition of this subdomain. It includes two tests, sentence repeats (2 sentences, 2 scores) and word expression fluency (1 score). In the three groups of patients, the average error rates of the three terms were 53%, 40% and 35%, but in control group they were only 8%, 5% and 4%, respectively. This shows that the subdomain of language is sensitive and reliable for cognitive function testing of speech responses. How listeners encode such rapid, brief, and complex stimuli into meaningful units and send that information to the cortex is very important for their cognitive function [35].

In Speech-ABR, waves V and A reflect highly synchronized neural responses to the onset of the stimulus. When comparing the latency values of all patients to those of healthy controls, only Peak V and Peak A were significantly different. These findings indicate that patients with OSAHS have abnormalities in the acoustic representation of a speech sound as low as the auditory brainstem. Thus, the acoustic characteristics of the speech /da/ used to measure speech-ABRs may be challenging to the auditory system. The amplitudes of Peak V and Peak A in the OSAHS group were significantly lower than those in the control group. Amplitude reflects the quantity and intensity of brainstem neurons in response to the onset of the stimulus. As shown in **Table 2**, this difference exists not only between patient groups and the control group, but also among the mild, moderate, and severe groups of OSAHS patients, which suggests that the changes in amplitude are more sensitive to hypoxemia than latency. V/A slope reflects the ratio of interpeak amplitude and interpeak latency of Peak V and Peak A. The smaller the value, the lower the interpeak amplitude and the longer the interpeak latency. The value of the V/A slope is more comprehensive and objective than simple measurement of Peak V and Peak A. Moreover, the frequency-following responses (waves D, E, and F) were not significantly different from those in the control group. This might be explained from two aspects, the first, source-class responses representing steady-state aspects of the stimulus are rate and noise resistant and are not easy to be disrupted in the brainstem auditory pathway; the second, there are distinct neural mechanisms relative to the onset peaks representing acoustic transients in the stimulus (peaks V, A).

Wave O (the offset response) was insignificantly different between the study and control groups. This suggests that the timing of responses from onset to offset in brainstem was shortened to stimulate, the compression of reaction time may be the cause of the missing and disorder of speech information coding. However, wave C was not analyzed because of its unreliability [36].

Our results reveal that the quantity and intensity of the brainstem neurons in response to onset of the stimulus are decreased, and that the encoding of speech sounds in the subcortical auditory pathway can be lagged locally at the level of the response generator. Some researchers suggested that at the levels of the cochlear nucleus and inferior colliculus, there are many types of brain stem cells and the synchronous response of them is likely relative to the onset response of the speech-ABR [37]. Because of the existence of the theory of neural synchrony in the central auditory system, which may be independent of changes at the periphery, these brain stem cells are likely to be affected by hypoxemia-related loss in cortical structures [38].

Overall, there exist apparent difference between normal subjects and patients with OSAHS at the onset synchrony of auditory brainstem neurons. The speech coding defects of the brainstem have a deleterious effect on cortical responses to the same stimulus. As a result, certain cognitive impairments may originate

from a disorder in auditory neural system at the level of the brainstem. The deficits in the auditory brainstem pathway encoding speech are more obvious when hypoxemia was aggravated. Combined with the results of previous studies, our findings suggest that hypoxemia is a leading factor in the correlation between encoding of speech and cognitive dysfunction [39].

In this study, the interindividual variability to the response in patient group and control group may lead to the lack of significant differences for lots of the speech-ABR variables. Some researchers found that when recording speech-ABRs, even in normal-hearing subjects using insert earphone, there was possible stimulus artifact disturbance [40]. Because of the similarity in temporal changes and spectral distributions between the stimulus and response, it is difficult for us to identify this stimulus artifact.

The reason of using alternating polarities is to extract the neural response from the cochlear and eliminate stimulus artifact [40]. Shielded transducers may be helpful in removing the stimulus artifact. The fast Fourier transform (FFT) is the most common algorithm for performing spectral analysis [35]. Unfortunately, in our study, we could not perform MATLAB tests to measure spectral analysis of FFR owing to a lack of resources.

Conclusion

In conclusion, the emergence and application of speech-ABR reinforce the viewpoint that the auditory system must include its cognitive function and sensory function. In other words, subcortical function reflects the inherent confluence of sensory and cognitive function; that they may co-exist in an interactive way. There are deficits in the auditory brainstem pathway encoding speech sounds in patients with OSAHS, and that such deficits be an important risk factor for cognitive disorders in the cortex. In future, Speech-ABR can not only provide objective diagnostic tests and techniques to determine appropriate intervention strategies, but also examine the effectiveness of interventions in the OSAHS population.

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Disclosure of conflict of interest

None.

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