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ORIGINAL ARTICLE

Auditory brainstem response after electrolytic lesions in the unilateral medial geniculate body of tree shrews

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Abstract

OBJECTIVES: This study aimed to assess the processing of clicks and tone pips in the auditory brainstem of tree shrews and analyze the long-term evolution of postlesion plasticity in the auditory system and its ability to self-repair.
METHODS: The auditory brainstem response (ABR) was measured in the normal control group (n=10) and the electrolytic damage group (n=10) before and 0 h, 24 h, 48 h, 72 h, and 25 d after electrolytic damage. Recordings were performed under closed-field conditions using clicks and tone pips, followed by statistical analysis of the ABR threshold, amplitude and latency.
RESULTS: The results were as follows: (1) After electrolytic damage to the tree shrew medial geniculate body (MGB), the latency and amplitude of ABR waveforms from the left ear changed from 0 h to 25 d. All parameters were lower at 25 d than they were preoperatively. The amplitude of ABR wave VI (using click sound stimulation) decreased or disappeared in both ears. (2) The ABR threshold was significantly different in both ears at 72 h postoperatively compared with preoperatively (0 h) ($P < 0.05$) but recovered by 25 d.
CONCLUSION: Based on these results, we conclude the following: (1) The origin of wave VI in tree shrews may be associated with the MGB. After electrolytic damage to the MGB, the changes in the ABR waveforms at different frequencies indicated that the MGB nucleus had a certain characteristic frequency. (2) Unilateral injury to the MGB can lead to similar levels of hearing impairment in both ears.

Abbreviations:

ABR	- auditory brainstem response	MGBv	- ventral MGB
MGB	- medial geniculate body	MGBd	- dorsal MGB
AC	- auditory cortex	BAEP	- brainstem auditory evoked potential
TC	- thalamocortical		

INTRODUCTION

Miller's research states that sound information is transmitted from the thalamus to the auditory cortex (AC) through thalamocortical (TC) projections(Miller, Escabi, Read, & Schreiner, 2001). This transmission is critical for auditory plasticity, which involves descending projections from the cortex to subcortical structures, including the ability of central neurons to adjust their frequency tuning to relevant and meaningful stimuli.

Physiological research has shown the significance of corticofugal projections for a variety of different types of auditory plasticity. For example, these descending pathways can modify midbrain coding for sound localization (Bajo, Nodal, Moore, & King, 2010; Nakamoto, Jones, & Palmer, 2008).

A group of auditory thalamic nuclei, collectively referred to as the medial geniculate body (MGB), primarily receives, modifies, and transmits sensory information to specific areas of the cortex. There are two major MGB subdivisions in which cells often respond differently to acoustic stimuli: the ventral or lemniscal (MGBv) and the dorsal or extralemniscal (MGBd) divisions.

Tree shrews are squirrel-like animals that live in tropical shrubs in South and Southeast Asia. These animals have the highest brain-to-body mass ratio of any known mammal. Tree shrews have been suggested as a substitute for primates in biomedical research experiments because they have characteristics similar to those of primates. The recent release of a publicly available annotated genome sequence of the Chinese tree shrew and its genome database (www.treeshrewdb.org) has offered a solid base from which it is possible to elucidate the basic biological properties and create animal models using this species. The extensive characterization of key factors and signaling pathways in the immune and nervous systems has shown that tree shrews possess both conserved and unique features relative to primates (Bajo *et al.* 2010; Pan *et al.* 2014; Yu *et al.* 2014). Oliver and Hall (Oliver, 1982; Oliver & Hall, 1975, 1978) studied the temporal cortex of tree shrews, subdivided this structure according to cytoarchitectonic criteria, and analyzed the relationship between each subdivision of the thalamus and midbrain using retrograde and anterograde techniques. In the ventral division, the researchers identified two subdivisions: the ventral nucleus and the caudomarginal nucleus. The difference between the dorsal division and ventral division is that the cells on the dorsal side are slightly larger; additionally, the dorsal side has fewer densely packed cells and contains at least four distinct subdivisions. Two subdivisions of the medial division were combined, constituting a large cell division.

Melcher and Kiang verified the connection between diverse brainstem cell populations and brainstem auditory evoked potentials (BAEPs). First, they proposed a mathematical model that correlated BAEPs with underlying cellular activity. Furthermore, by combining insights derived from the model with key experimental data, these authors identified specific cell generators that triggered BAEPs in the cat. These results involved the correspondence between a specific brainstem

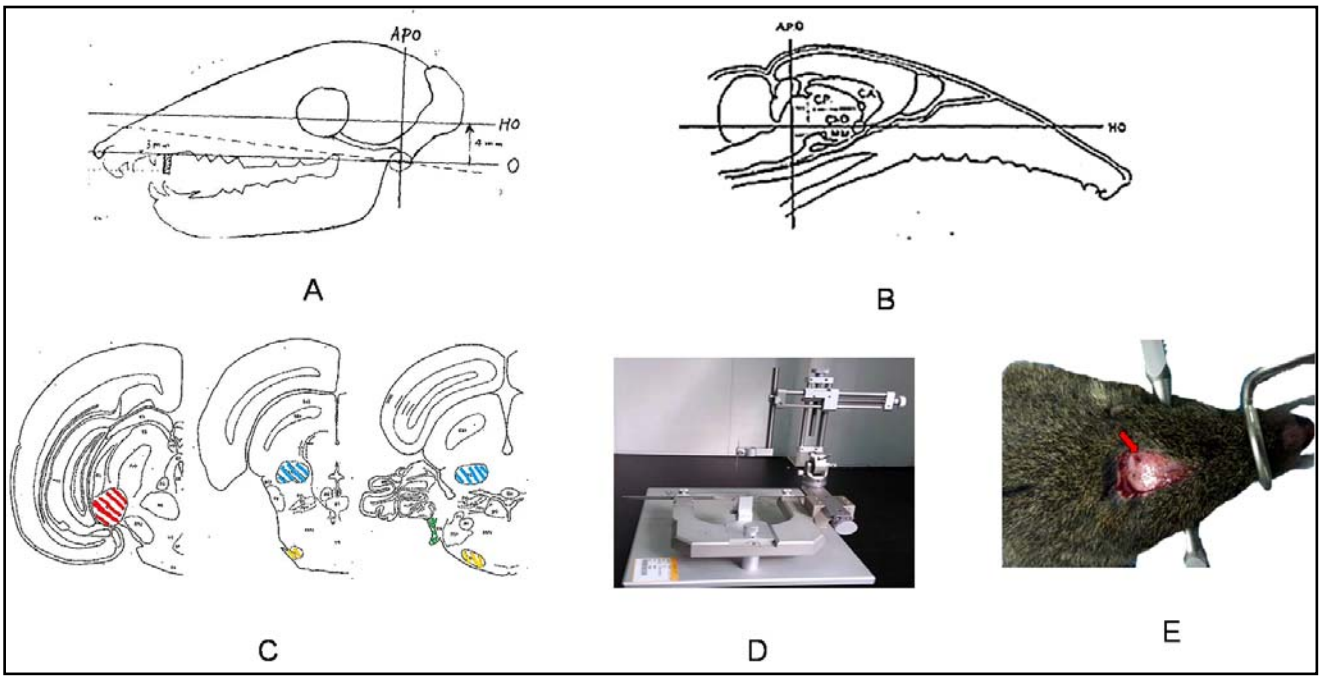

Fig. 1. A. HO plane (O 'plane 4 m m plane) and APO plane design **B.** Head cut the median sagittal profile in APO and HO plane by the brain structure **C.** Atlas of tree shrews brain (red for medial geniculate body (MGB), blue for the hypothalamic nucleus (NCI), yellow for the olive nuclear (OS), green for the cochlear nerve dorsal nucleus (CD), cochlear nerve abdomen (CV)) **D.** Stereotaxic apparatus **E.** Electrical lesion into the needle position

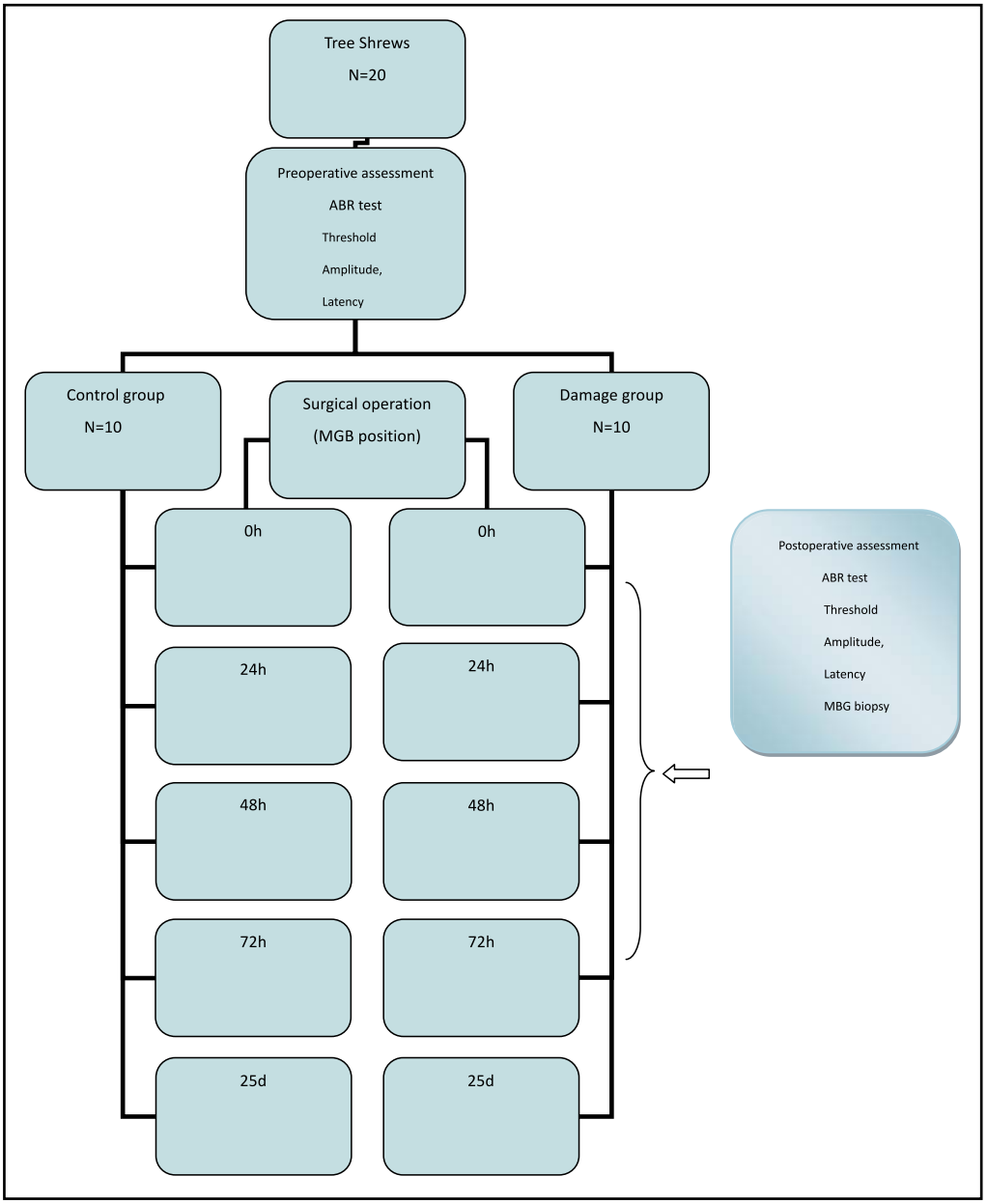

Fig. 2. Study design and flow diagram.

region and specific extrema in the BAEP waveform as determined by a lesion experiment; moreover, the values of the model parameters were derived from previously published physiological anatomical information (Melcher & Kiang, 1996).

Auditory electrophysiological responses have been recorded in animal models of central nervous system mass lesions (Burghaus *et al.* 2013; Nagao, Roccaforte, & Moody, 1979a, 1979b, 1980). Clinical research on hearing results in patients with different central auditory nuclear lesions has revealed important hearing loss using auditory brainstem response (ABR) testing (Burghaus *et al.* 2013).

This research aimed to clarify the role of the lower auditory pathway by assessing the ABR after unilateral MGB injury. We found that central lesions in tree shrews caused changes in the characteristics of auditory pathway lesions. We analyzed the pathogenesis and characteristics of central deafness by ABR testing and discuss the reasons for deafness at different time points. We hope that this animal model will play a role in future research on the auditory system.

METHODS

Materials

Twenty healthy adult tree shrews (age, 12-18 months; weight, 130-170 g; sex, both males and females) were provided by Kunming Medical University in China and randomly divided into two groups: there were 10 in the normal control group and 10 in the electrolytic damage group. All animal experiments were carried out in accordance with the protocol approved by the Institutional Animal Care and Use Committee

Tab. 1. Mean and standard deviation values of absolute and interwave latencies of control group tree shrew ABRs

Parameter	Normal latency data	
	Mean(ms)/(μV)	SD(ms)/(μV)
Absolute latency wave I	1.16	0.07
Absolute latency wave II	1.62	0.18
Absolute latency wave III	1.96	0.07
Absolute latency wave IV	2.66	0.13
Absolute latency wave V	3.60	0.12
Absolute latency wave VI	4.62	0.11
Interwave latency I-III	0.79	0.11
Interwave latency III-V	1.59	0.05
Interwave latency I-V	2.38	0.13
Amplitude wave I	0.31	0.21
Amplitude wave II	0.71	1.23
Amplitude wave III	1.97	0.94
Amplitude wave IV	1.56	0.96
Amplitude wave V	2.04	1.10
Amplitude wave VI	1.12	0.86

Stimuli:80dB SPL click

of Guangxi Medical University in China. The study was approved by the Institutional Animal Care and Use Committee of Guangxi Medical University in China. Animals were treated according to the Guide for the Care and Use of Laboratory Animals (eighth edition, National Academy Press).

Framework of the experimental design

The ABR of the tree shrews was examined preoperatively. To induce electrolytic damage, the position of the MGB was determined, and the dura mater was exposed with an electric drill; then, a stainless-steel electrode was inserted in the MGB. This electrode continuously emitted current for 20-30 s. In the control group, the electrode was inserted, but no current was applied. ABRs were recorded at 0 h, 24 h, 48 h, 72 h, and 25 d after surgery. Following exposure, tree shrews were fixed by cardiac perfusion for 1 h with phosphate buffer (pH 7.4, 4 °C) containing 4% paraformaldehyde. Coronal brain tissue cryosections were subjected to Nissl staining to observe changes at the site of electrolytic injury and in neurons.

Surgical operation

Tree shrews were anesthetized via an intraperitoneal injection of 1% pentobarbital sodium (0.4 mL/100 g). The animal was placed in the prone position after anesthesia. The head was fixed using an RWD stereo positioner (RWD, Shenzhen, China), and the limbs were fixed. Then, the dura mater was exposed with an electric drill, and a 0.2-mm-diameter stainless steel electrode was inserted into the MGB. Beyond the 0.5-mm tip, a stereotactic handle insulated the remainder of the electrode. The positive charge was on the electrode inserted in the MGB, and the negative charge was on the electrode inserted in the head incision. The incision was sutured by the continuous administration of 5-8 mA for 20-30 s. In the control group, the electrode was inserted, but no electricity was applied.

The stereotactic method (Y, 1990) was applied based on a three-dimensional coordinate system with three critical planes at right angles, according to a previous experiment (Y, 1990; Zhu *et al.* 2017).(Fig.1)

Hearing evaluation

Hearing was assessed according to the ABR preoperatively and postoperatively in each animal (TDT, Tucker-Davis Technologies, USA). The ABR recording electrode and the acoustic stimulator were produced by TDT (Tucker-Davis Technologies, USA). The system output was calibrated using a quarter-inch microphone prior to recording to confirm that the increase in voltage exactly corresponded to an increase of 6 decibel (dB) sound pressure level (SPL), with a maximum of 100 dB SPL. ABR recordings never exceeded this value.

The sound waves were transmitted in a closed field, and the probe was carefully placed in the ear canal. The ABR was recorded at a presentation rate of 21.0 per s using a click lasting 0.1 ms. A total of 1024 replicates were collected over a 10-ms time window and averaged. Tone-pip stimulation was presented at a rate of 21.0 times per s, and 512 repetitions were collected over a 10-ms time window and averaged. The click stimulus was used to provide a measure of neuronal

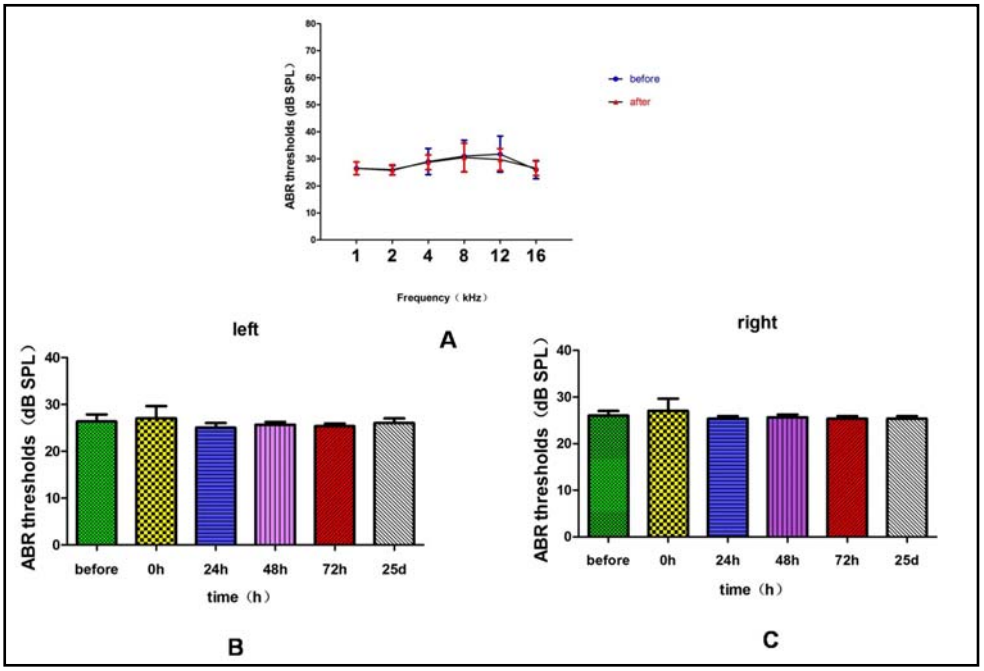

Fig. 3. A. ABR thresholds at different frequencies before and after surgery in control group. (P >0.05).
B. ABR thresholds before and after surgery in the left ear in control group.
C. ABR thresholds before and after surgery in the right ear in control group.

response time, as latencies recorded using this broadband measure are less susceptible than tone response latencies to variation with stimulus rise time and are therefore more useful for cross-study comparisons. Neurons were considered to be responsive to the click if a poststimulus time histogram (PSTH, compiled from 100 repetitions of the click using a bin width of 0.5 ms) showed a peak in firing following the click presentation that exceeded two times the standard deviation of the neuron's spontaneous rate. We defined the first-spike latency for the responsive neuron as the median latency of the spike over 100 click presentations, calculated from the PSTH using a bin width of 0.5 ms.

The threshold corresponding to the minimum intensity at which a given frequency could elicit an ABR was manually obtained for both ears. The absolute wave I latency was defined as the time in milliseconds (ms) from the onset to the positive peak of the wave. The interpeak latency was defined as the time in ms between the positive peaks of different ABRs.

Finally, the signal was filtered by a 500-Hertz (Hz) high-pass filter and a 3000-Hz low-pass filter. The

Tab. 2. The reference values of the interpeak latencies during ABR recordings from experimental group tree shrew ears ($\overline{X}$±s).

Time Point	Interpeak latencies (ms)		
	I–III	III–V	I–V
Left			
Preoperatively	0.82 ± 0.33	1.85 ± 0.45	2.47 ± 0.31
0 h	0.90 ± 0.10	2.02 ± 0.05	2.92 ± 0.12
24 h	0.82 ± 0.11	2.02 ± 0.05	2.84 ± 0.13
48 h	0.82 ± 0.13	1.89 ± 0.04	2.71 ± 0.13
72 h	0.66 ± 0.14	1.52 ± 0.08	2.18 ± 0.16
25 d	0.74 ± 0.15	1.73 ± 0.11	2.43 ± 0.15
Right			
Preoperatively	0.99 ± 0.35	1.97 ± 0.42	2.88 ± 0.33
0 h	1.11 ± 0.11	2.14 ± 0.08	2.96 ± 0.25
24 h	0.70 ± 0.17	1.73 ± 0.09	2.43 ± 0.76
48 h	0.82 ± 0.18	1.89 ± 0.02	2.67 ± 0.98
72 h	0.70 ± 0.19	1.60 ± 0.07	2.30 ± 0.71
25 d	0.75 ± 0.16	1.72 ± 0.18	2.47 ± 0.54

optimal frequency for the induced waveform in tree shrews is 4 kHz. The positive and negative peaks and corresponding latency values for each wave were evaluated at 80 dB SPL. The tone-pip test was performed at six different frequencies (1, 2, 4, 8, 12, and 16 kHz) to manually obtain the minimum intensity threshold of binaural hearing at a certain frequency. The absolute wave I delay was defined as the time in ms from the start to the positive peak of the wave. The interpeak delay was defined as the time between the positive peaks of different ABRs in ms.(Fig.2)

Data analysis

The ABR thresholds and wave latencies obtained for each group are reported as averages. Differences between the groups were analyzed by one-way analysis of variance (ANOVA). The least significant difference (LSD) test was used for multiple comparisons between groups. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS 20, Chicago, IL, USA).

RESULTS

Comparison of ABR findings in the control group at different time points

ABRs were measured in control animals (n=10) with a click stimulus at 80 dB SPL. The latency of ABR wave I in the control group was 1.34 ± 0.34 ms. Wave II rarely appeared, but when it did, the average latency was 1.62 ± 0.02 ms. Wave III was relatively stable, with a high peak and a latency of 2.57 ± 0.03 ms. The latency of waves IV and V was 3.28 ± 0.07 ms and 4.37 ± 0.14 ms, respectively. The latency of wave VI was 5.93 ± 0.04 ms. No significant differences were observed among postoperative time points (0 h, 24 h, 48 h, 72 h, and 25 d) in the control group in terms of the ABR threshold ($P > 0.05$), latency ($P > 0.05$) or amplitude ($P > 0.05$) in response to click stimuli. (Table 1, Fig. 3)

Comparison of ABR findings in the experimental group at different time points

(1) Wave latency:

After MGB injury, the latency at 0 h of wave I was 1.73±0.04 ms; wave II, 2.25±0.01 ms; wave III, 2.66±0.03 ms; wave IV, 3.30±0.01 ms; wave V, 4.21±0.01 ms; and wave VI, 5.57±0.03 ms. At 0 h after electrolytic damage to the left MGB, the latency of waves I, II, III, and IV in the left ear was lengthened, while the latency of waves V and VI was shortened (Table 2, Fig. 4A). The latency of each wave in the left ear shortened from 24 h to 25 d.

At 0 h after electrolytic damage to the left MGB, the latency of ABR waves I, II, III, and IV in the right ear was lengthened. Between 24 h and 25 d, the latency of waves I, II, III, and IV was sometimes lengthened and sometimes shortened. Prolonged latency was observed in waves V and VI at 0 h. Between 48 h and 25 d, the ABR latency was sometimes lengthened and sometimes shortened, exhibiting a lower overall value than that observed preoperatively (Fig. 4 B).

(2) Wave interpeak latency:

ABR measurements from both ears from 0 h to 25 d showed that the interpeak latency of waves I-III, III-V, and I-V was sometimes lengthened and sometimes shortened, exhibiting a lower overall value than that observed preoperatively (Fig. 4 F-G). Among the various wave latencies, those observed at 0 h were obviously lengthened, and those observed at 72 h were shortened.

(3) Wave amplitude:

Between 0 h and 72 h, the wave amplitude in both ears decreased. However, the wave amplitude increased between 72 h and 25 d, and the amplitude of waves V and VI was variable. At 0 h, the amplitude of each wave from both ears in response to 80-dB tone-pip stimuli at 1, 2, 4, 8, 12 and 16 kHz was significantly lower than that before injury. The amplitude of wave VI was markedly reduced or absent, while that of wave V was reduced; thus, the generation of wave VI may be associated with the MGB. Waves V and VI at 72 h after surgery showed the greatest reductions in amplitude; wave VI was significantly decreased to the point of disappearance. Between 72 h and 25 d, the amplitude increased, and at 25 d, the amplitude of waves V and VI was significantly lower than that preoperatively (Fig. 4 C-G).

(4) Wave threshold:

ABR wave III was used as the auditory response threshold decision criterion. Both waves III and V were relatively stable in the tree shrew ABR; however, the amplitude of wave V was lower than that of wave III. As the stimulus intensity was reduced in 10-dB steps, the ABR wave amplitude gradually decreased, and the wave occurrence rate was reduced. Wave III was the largest and most stable wave, followed by waves V, IV, I and VI. Thus, wave III was the primary wave of the tree shrew ABR and was set as the standard for measuring thresholds.

Comparison of the pre- and postoperative ABR thresholds in the left ear indicated a significant difference ($P < 0.05$) between the preoperative ABR and the ABR at 0 h, 24 h, 48 h, and 72 h. There was no difference in the ABR threshold between preoperatively and 25 d postoperatively ($P > 0.05$). The ABR threshold measured in the left ear preoperatively and at 0 h, 24 h, 48 h, 72 h, and 25 d postoperatively was 26.33 ± 1.53, 42.33 ± 2.52, 42.67 ± 2.52, 46.33 ± 3.22, 55.00 ± 5.00, and 25.76 ± 2.13 dB SPL, respectively.

There was a significant difference ($P < 0.05$) in the ABR in the right ear between preoperatively and 0 h, 24 h, 48 h, and 72 h postoperatively. There was no

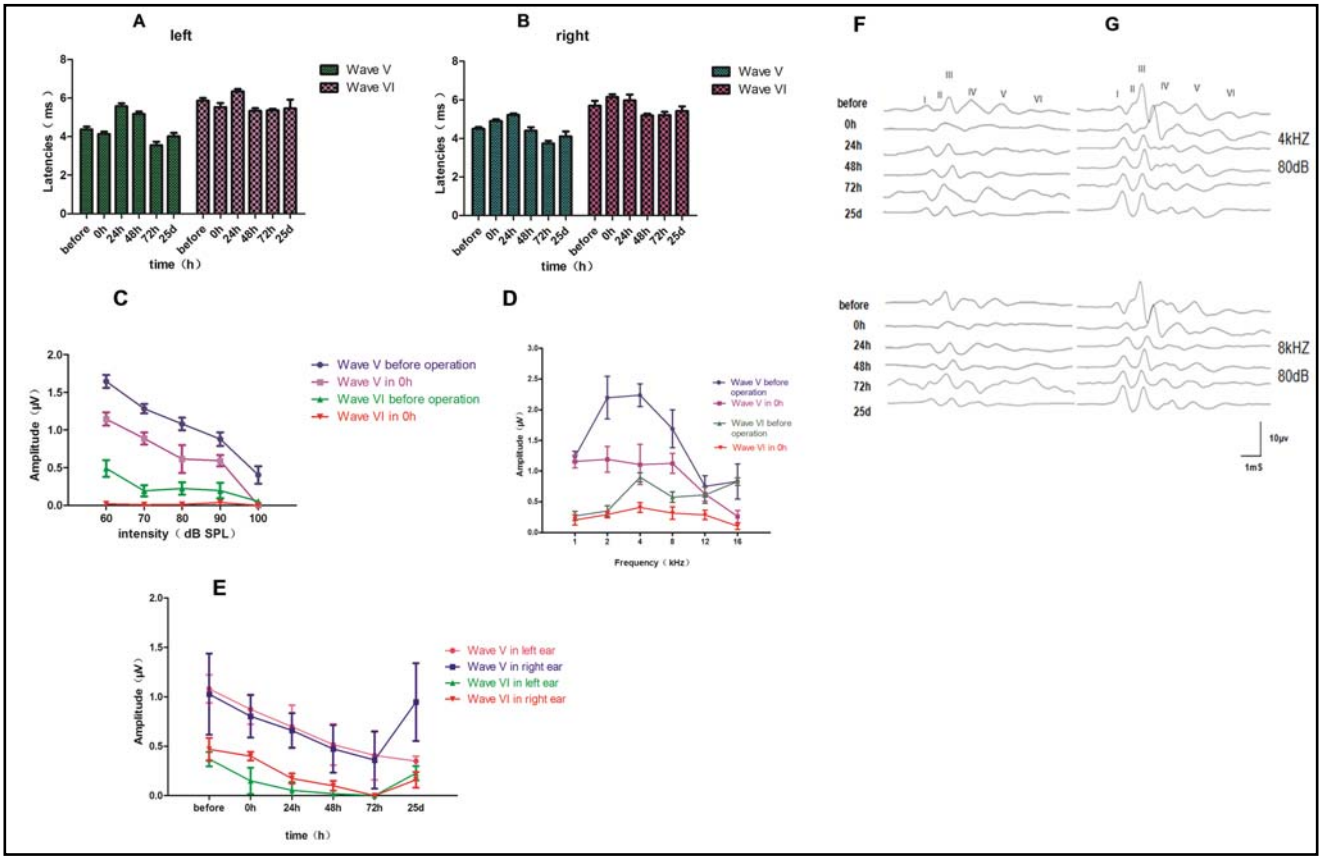

Fig. 4. A. ABR latency of waves V and VI before and after surgery in tree shrews using an 80-dB click stimulus in the left ear.
B. ABR latency of waves V and VI before and after surgery in tree shrews using an 80-dB click stimulus in the right ear.
C. ABR amplitude of waves V and VI with various intensities before surgery and at 0 h after surgery in both ears.
D. ABR amplitude of waves V and VI with various frequency levels before surgery and at 0 h after surgery in both ears.
E. Comparison of the ABR amplitude of waves V and VI in both ears.
F. ABR of the left ear of a tree shrew following damage to the left MGB. Top: ABR of the left ear before and after electrolytic damage using a 4-kHz, 80-dB sound (tone-pip stimulation). Bottom: ABR of the left ear before and after electrolytic damage using an 8-kHz, 80-dB sound (tone-pip stimulation).
G. ABR of the right ear of a tree shrew following damage to the left MGB. Top: ABR of the right ear before and after electrolytic damage using a 4-kHz, 80-dB sound (tone-pip stimulation). Bottom: ABR of the right ear before and after electrolytic damage using an 8-kHz, 80-dB sound (tone-pip stimulation).

difference in the ABR threshold between preoperatively and 25 d postoperatively ($P > 0.05$). The ABR threshold measured in the right ear preoperatively and at 0 h, 24 h, 48 h, 72 h, and 25 d postoperatively was 26.00 ± 1.00, 43.00 ± 2.65, 43.00 ± 3.00, 45.33 ± 1.53, 52.67 ± 2.52, and 26.33 ± 1.53 dB SPL, respectively (Fig. 5 A-C).

(5) Biopsies revealed necrosis of the left MGB, abnormalities in cell morphology and ischemic necrosis (Fig. 5 D).

DISCUSSION

ABR examination is a commonly used method for detecting hearing loss in the clinic and is a reliable and sensitive method for diagnosing various central nervous system diseases (Brantberg, Fransson, Hansson, & Rosenhall, 1999; Hecox & Galambos, 1974). High serum bilirubin levels can cause acute damage to the neonatal auditory pathway and changes in the ABR (Zhuang *et al.* 2013). Electrolytic injury to the cranial nerve nucleus can also be applied to injure the auditory nucleus. This method of auditory nucleus injury can be used to establish an animal model of hearing impairment with which to study the process of electrophysiological changes and understand the effects of MGB injury on the morphological features and mechanisms of hearing impairment. The ABR test revealed the level of hearing loss at different times, as well as the mechanisms and characteristics of central deafness. These findings can help to determine the relationship between ABR waves and MGB function because we observed changes in auditory electrophysiology after acute injury to the MGB.

Following damage to the left MGB, the shortened latency of waves V and VI at 0 h may be explained by the potential high excitability of central neurons following the loss of some afferent input. Additionally, the activity of nonparticipating auditory neurons, which are not active (i.e., are dormant) under normal

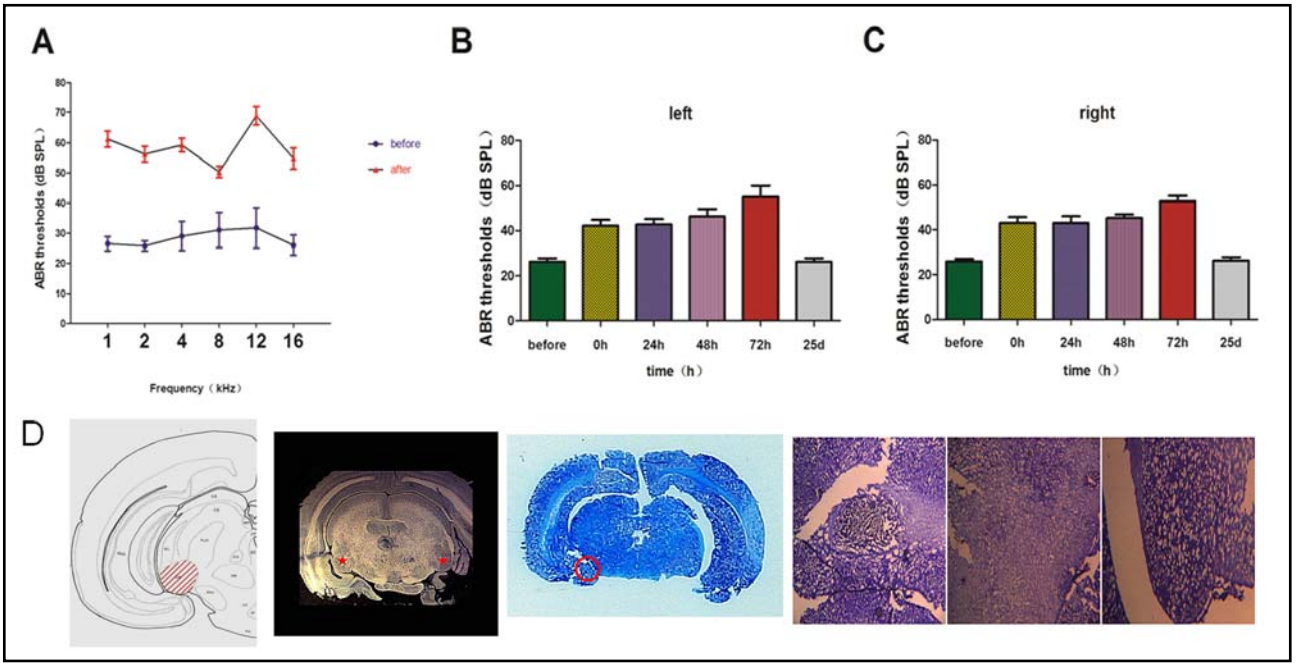

Fig. 5. A. ABR thresholds at different frequencies before and after surgery were significantly different, with elevated thresholds observed postoperatively ($P < 0.05$).
B. ABR thresholds before and after surgery in the left ear.
C. ABR thresholds before and after surgery in the right ear.
D. Lesion position on the atlas (red shadow). General view of the MGB (red star, MGB). General view of a section of the MGB group. Microscopic view of a section of the MGB group (10X).

conditions, may play a role in this mechanism and increase the speed of nerve activity. The latencies of waves V and VI were the longest within 24 h; in the left ear, nerve conduction was highly blocked 24 h after injury. Following electrolytic damage, the latency of each ABR wave from the opposite side (right) at 0 h postoperatively was lengthened. Between 0 h and 25 d, these latencies exhibited varying degrees of lengthening and shortening. The latencies of waves V and VI were the longest at 0 h. Moreover, the changes in latency were not synchronized across both ears. Although each side of the MGB is innervated by bilateral auditory nerve fibers, the direction of bilateral hearing damage and the effect on conduction are different, indicating early nerve conduction dysfunction in the ears. Following electrolytic damage, the latent phases of each ABR wave from both ears changed between 0 h and 25 d postoperatively. The interphase time of waves I-III, III-V, and I-V variably increased and decreased, with the longest latency period at 0 h after surgery and the shortest at 72 h after surgery. The latencies of waves V and VI at 0 h in the left ear were shortened, although the I-V latency was lengthened. Therefore, evidence from the left ear showed that the universal evaluation of wave I-V latencies after pathological changes to the cochlear nerve is a reliable measure. In both ears, the latency between waves showed similar trends of gradual reduction between 72 h and 25 d. A potential reason for this decline is that nerve function is unstable or in recovery during the period of convalescence from acute injuries. A longer observation time may be necessary to determine the final trend in wave latencies.

The amplitude of waves V and VI changed over time postoperatively, and that of wave VI almost disappeared in both ears at 72 h. The amplitude of wave V decreased similarly in both ears, but that of wave VI decreased more in the left ear than in the right ear. Because injury to the left MGB impacted the bilateral auditory pathway, as time progressed, the injury affected the degree of nerve dysfunction more heavily on the damaged side than on the undamaged side. The amplitude of wave VI at 72 h showed a decrease, and the degree of damage to the MGB was considered highest at this time. Changes in wave latency could predict early postcochlear lesions. The evoked response may have returned to a normal amplitude, but without behavioral testing, whether the animals could hear to a normal degree is unknown. This shortcoming is the main deficiency of our experiment. In a previous experiment, the latencies and amplitudes of responses in the MGB following bilateral electrolytic damage were restored to preoperative levels after 15-30 d, suggesting that a portion of the central nucleus lesion was reversible. Nonetheless, further studies will be conducted.

ABR wave III was used as the auditory response threshold decision criterion, and the threshold increase at 0 h postoperatively was significant at 12 kHz, indicating potential specific frequency characteristics in the damaged tree shrew MGB. Following surgery, the ABR threshold in both ears recovered from 0 h to 25 d with

a downward trend, and there was no difference in the ABR threshold between preoperatively and 25 d postoperatively ($P > 0.05$). These findings indicate that tree shrew brain tissue or nerve fibers have a certain self-healing capability such that the function of the auditory nerve fibers can be restored. Deafness after MGB injury results in an increase in the entire frequency threshold. The amplitude decreased, but the latency changed variably on both sides. Over time, hearing could be restored to some degree, and the magnitude of the difference may be related to the area and degree of damage.

After bilateral MGB damage in a previous study (Pan *et al.* 2014) the ABR threshold increased by 5-10 dB and did not recover 15-30 d after the surgery. The ABR threshold in the present study increased by 25-30 dB over 0-72 h after unilateral MGB damage and recovered by 25 d after MGB damage. Regardless, the mechanism of hearing loss is not clear. This may be due to MGB lesions and may reinforce the hypothesis that descending control acts as an enhancer of the auditory response. The ABR amplitude after bilateral MGB damage did not change, whereas the ABR amplitude after unilateral MGB damage in the present study decreased over 0-72 h and recovered by 25 d after surgery. The most distinct implication of the direct projection from the cochlear nucleus (CN) to the MGB, bypassing the upper olive, is that myriad other auditory nuclei of the outer lemniscus and lower thalamus provide fast signals to the auditory thalamus. This hypothesis is supported by physiological studies, proving that cells in the medial division of the MGB (MGBm) respond to acoustic stimulation with the shortest latency of all MGB cells (Anderson & Linden, 2011). The MGBm is clearly the main target of CN-MGB projections. The conventional view of the MGBm is that the neurons are relatively nonselective to acoustic stimulation. They are extensively adapted to characteristics such as stimulus frequency and have a lower response probability and longer response latency than neurons in the MGBv and lemniscal pathways. Therefore, the ABR changes with changes in latency, amplitude and threshold, which may be related to the position of the MGB, the size of the MGB and the current intensity.

CONCLUSIONS

Based on our findings, we conclude the following: (1) The origin of wave VI in tree shrews may be associated with the MGB. After electrolytic damage to the MGB, the changes in the ABR waveforms at different frequencies indicated that the MGB nucleus had a certain characteristic frequency. (2) Unilateral injury to the MGB can lead to similar levels of hearing impairment in both ears. Both changes in evoked electrical activity and their reversal over time depend on the number of connections lost after MGB damage and reinforce the hypothesis that descending control acts as an enhancer of the auditory response.

ACKNOWLEDGEMENTS

None.

COMPETING INTERESTS

The authors declare that they have no competing interests.

AVAILABILITY OF DATA AND MATERIALS

During the current study, the datasets used and/or analyzed are available from the corresponding author upon reasonable request.

CONSENT FOR PUBLICATION

Not applicable.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All experimental procedures were performed in accordance with the CHN Animal Protection Act and approved by the Guangxi Medical University Animal Care and Use Committee.

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REFERENCES

1 Anderson LA, & Linden JF (2011). Physiological differences between histologically defined subdivisions in the mouse auditory thalamus. Hear Res. **274**(1–2): 48–60. doi: 10.1016/j.heares.2010.12.016

2 Bajo VM, Nodal FR, Moore DR, King AJ. (2010). The descending corticocollicular pathway mediates learning-induced auditory plasticity. Nat Neurosci. **13**(2): 253–260. doi: 10.1038/nn.2466

3 Brantberg K, Fransson PA, Hansson H, Rosenhall U. (1999). Measures of the binaural interaction component in human auditory brainstem response using objective detection criteria. Scand Audiol. **28**(1): 15–26.

4 Burghaus L, Liu WC, Dohmen C, Haupt WF, Fink GR, Eggers, C (2013). Prognostic value of electroencephalography and evoked potentials in the early course of malignant middle cerebral artery infarction. Neurol Sci. **34**(5): 671–678. doi: 10.1007/s10072-012-1102-1

5 Hecox K & Galambos R (1974). Brain stem auditory evoked responses in human infants and adults. Arch Otolaryngol. **99**(1): 30–33.

6 Melcher JR, & Kiang NY (1996). Generators of the brainstem auditory evoked potential in cat. Iii: Identified cell populations. Hear Res. **93**(1–2): 52–71.

7 Miller LM, Escabi MA, Read HL, Schreiner CE (2001). Functional convergence of response properties in the auditory thalamocortical system. Neuron. **32**(1): 151–160.

8 Nagao S, Roccaforte P, Moody RA (1979a). Acute intracranial hypertension and auditory brain-stem responses. Part 1: Changes in the aduitory brain-stem and somatosensory evoked responses in intracranial hypertension in cats. J Neurosurg. **51**(5): 669–676. doi: 10.3171/jns.1979.51.5.0669

9 Nagao S, Roccaforte P, Moody RA (1979b). Acute intracranial hypertension and auditory brain-stem responses. Part 2: The effects of brain-stem movement on the auditory brain-stem responses due to transtentorial herniation. J Neurosurg. **51**(6): 846–851. doi: 10.3171/jns.1979.51.6.0846
10 Nagao S, Roccaforte P, Moody RA (1980). Acute intracranial hypertension and auditory brain-stem responses. Part 3: The effects of posterior fossa mass lesions on brain-stem function. J Neurosurg. **52**(3): 351–358. doi: 10.3171/jns.1980.52.3.0351
11 Nakamoto KT, Jones SJ, Palmer AR (2008). Descending projections from auditory cortex modulate sensitivity in the midbrain to cues for spatial position. J Neurophysiol. **99**(5): 2347–2356. doi: 10.1152/jn.01326.2007
12 Oliver DL (1982). A golgi study of the medial geniculate body in the tree shrew (tupaia glis). J Comp Neurol. **209**(1): 1–16. doi: 10.1002/cne.902090102
13 Oliver DL & Hall WC (1975). Subdivisions of the medial geniculate body in the tree shrew (tupaia glis). Brain Research. **86**(2): 217–227.
14 Oliver DL, & Hall WC (1978). The medial geniculate body of the tree shrew, tupaia glis. Ii. Connections with the neocortex. J Comp Neurol: **182**(3): 459–493. doi: 10.1002/cne.901820306
15 Pan XH, Yang XY, Yao X, Sun XM, Zhu L, Wang JX, et al. (2014). Bone-marrow mesenchymal stem cell transplantation to treat diabetic nephropathy in tree shrews. Cell Biochem Funct. doi: 10.1002/cbf.3037
16 Yang WG, Liu J, Luo YQ, Chen PL, Zhang CR, Wan XC, et al. (1990). A Stereotaxic Atlas of the Brain of Tupaia Belangeri and Macaque Monkey Living in Guangxi. Guangxi. China: Guangxi Science & Technology Publishing House.
17 Yu D, Xu L, Liu XH, Fan Y, Lu LB, Yao YG (2014). Diverse interleukin-7 mrna transcripts in chinese tree shrew (tupaia belangeri chinensis). PLoS One. **9**(6): e99859. doi: 10.1371/journal.pone.0099859
18 Zhu M, Li H, Gyanwali B, He G, Qi C, Yang X, et al. (2017). Auditory brainstem responses after electrolytic lesions in bilateral subdivisions of the medial geniculate body of tree shrews. Neurol Sci. **38**(9): 1617–1628. doi: 10.1007/s10072-017-3013-7
19 Zhuang Y, Li GN, Zhou Y, Hu YY, Li J, Zhan CX (2013). [relationship of b/a ratio and acidosis with abnormal brainstem auditory evoked potentials in neonates with severe hyperbilirubinemia]. Zhongguo Dang Dai Er Ke Za Zhi. **15**(5): 332–334.