Mismatch negativity is abnormal but not lateralizing in temporal lobe epilepsy

Lili Zhao^a, Dongmei An^a, Limei Mao^b, Xiangdong Tang^b, Li He^a, Dong Zhou^{a*}

a Department of Neurology, West China Hospital, Sichuan University,
Chengdu, Sichuan, China

b Department of Electroneurophysiology, West China Hospital, Sichuan
University, Chengdu, Sichuan, China

* Correspondence to: Dr. Dong Zhou, Department of Neurology, West China
Hospital, Sichuan University, 37th Guoxuexiang Road, Chengdu, Sichuan
610041, China. Tel.: +86 28 85422549; fax: +86 28 85422549. Email:
zhoudong66@yahoo.de

Abstract

The purpose of the research was to investigate the changes of mismatch negativity (MMN) in temporal lobe epilepsy (TLE) patients and to explore the possible role of MMN in lateralizing the epileptic focus of TLE. Thirty TLE patients and thirty healthy controls were included. MMN was elicited in each subject. TLE patients were divided into three subgroups: unilateral left TLE; unilateral right TLE and bilateral TLE. MMN amplitudes and latencies were compared between the TLE and the control group, and also among the three subgroups of TLE, using repeated measures analyses of variance (ANOVA). To assess the lateralizing value of MMN, MMN latencies and amplitudes at the mastoid sites between the ipsilateral and contralateral sides of epileptic focus in unilateral TLE patients were compared using T-test. Compared with controls, each subgroup of TLE patients had longer latencies of MMN at both front-central and mastoid sites, but the amplitudes of MMN were not significantly different. The amplitudes and latencies of MMN were not significantly different between the ipsilateral and contralateral sides of epileptic focus at mastoid sites. The present findings suggest prolonged latencies of MMN indicate cognitive impairment in TLE. Both the mastoid sites and the front-central sites are involved which reflect widespread cortical abnormalities in TLE. However, the changes of MMN during the interictal phase are not useful for lateralizing the epileptic focus in TLE patients.

Keywords:

Temporal lobe epilepsy; Event-related potential; Mismatch negativity;

Cognitive impairment

1. Introduction

Cognitive dysfunction is one of the most common comorbidities of epilepsy, which may even exist prior to the seizure onset [1-3]. As the most common focal epileptic syndrome in adults, temporal lobe epilepsy (TLE) is associated with a wide range of cognitive impairments in various severity, depending on the specific syndrome and its associated underlying characteristics [4, 5]. Due to the damage of mesial temporal structures or the limbic system, memory decline is considered as the most significant cognitive deficit in TLE [2, 6].

Mismatch negativity (MMN) is an early auditory event-related potential (ERP) which is the result of an automatic memory-based comparison process that detects a discrepancy between the neural representation of the regularity of recent stimulation and the representation of the deviant sound. MMN is believed to reflect the earliest cortical event in the cognitive process of auditory information and be a part of auditory pre-attentive memory [7].

The major MMN generators are considered to be located in the superior temporal cortex near the primary auditory cortex [8], and the frontal cortex is the additional generator [9]. Therefore, MMN has been extensively applied in neurological disorders affecting the temporal lobe including TLE [10-12]. In TLE studies, MMN is often recorded both at front-central sites and mastoid sites. Many studies have indicated that the frontally recorded MMN is

composed of contributions from both the auditory and frontal cortices, whereas the mastoid 'MMN' gets a contribution from the auditory- cortex MMN generator only [13]. However, we find that the existing literature evaluating MMN response in TLE patients is limited and discrepant. Delayed latencies of MMN[14, 15] and its magnetic equivalent[16] were observed in patients with intractable epilepsy compared to healthy controls. However, studies reported differences in the amplitude changes at the front-central and the mastoid sites. Miyajima et al reported an increase of MMN amplitude at front-central sites in patients with TLE, but no significant changes at mastoid sites[14]. On the other hand, Hara et al found that the MMN was diminished at mastoid sites but not at the frontal-central sites[15]. In Lin's study, the amplitudes had no significant changes at all sites[16]. Given that the source of MMN is closer to the presumed epileptogenic zone in TLE, we hypothesize that MMN at the mastoid sites is more prone to be abnormal. TLE has been well acknowledged as a network disease involving different structures in the temporal lobe and also in regions remote from the epileptogenic zone [17]. Therefore, this study aims to investigate the MMN in TLE, and also to explore whether the MMN at the front-central sites is affected.

MMN is often elicited at bilateral mastoid sites, which are considered to reflect temporal lobe activity only. Previous researches analyzed both patients with left and right temporal lobe epilepsy together[14, 16]. It might preclude the possibility of assessing the lateralizing value of MMN. It is interesting to

explore whether the alteration of MMN, especially the mastoid mismatch component, has a possible role of lateralizing the epileptic focus in TLE.

Therefore, the current study aims to investigate the changes of MMN at both front-central sites and bilateral mastoid sites and explore whether the alteration of MMN at the mastoid sites has a possible role of lateralizing the epileptic focus in TLE patients.

2. Methods

2.1 Subjects

Consecutive TLE patients were recruited from the Epilepsy monitoring unit, West China Hospital, Sichuan University from 2014 to 2016. Age and sex matched healthy controls were also recruited during the same period.

The inclusion criteria of the TLE patients were: 1. Ictal semiology strongly suggests a temporal origin, including epigastric rising sensation, experiential phenomena (most commonly fear) and gustatory or olfactory sensations, decreased responsiveness, oro-alimentary and/or motor automatisms [18]. 2. All TLE patients underwent long-term video electroencephalogram (EEG) recording. At least two seizures were recorded during the video-EEG monitoring. Interictal EEG demonstrated temporal epileptiform discharges, and ictal EEG suggested temporal onset. 3. All patients underwent a structural MRI scan with 3.0T MRI scanner. Patients with significant structural lesions in the temporal lobe except those with mesial temporal sclerosis were excluded. 4. Patients were seizure-free for at least three months.

The exclusion criteria were: 1. Subjects who had hearing loss were excluded. Basic audiological screening (pure tone test and acoustic immittance) had been done before the MMN testing. 2. Each subject had been evaluated by an experienced psychiatrist. Subjects with history of psychiatric disorders were excluded, since abnormal MMN were commonly observed in many psychiatric disorders [7]. 3. Subjects with other neuropathies (including drug or poison intoxication, other metabolic diseases or genetic diseases), or trauma that might affect the cognitive function were also excluded.

Based on a combination of clinical symptoms, EEG, and structural MRI, TLE patients were further divided into subgroups: unilateral left TLE, unilateral right TLE and bilateral TLE with seizures arising from bilateral temporal lobe independently or simultaneously on scalp EEG.

All subjects gave a written informed consent. This study was approved by the Ethical Committee of West China Hospital.

2.2 Neuropsychological test

Cognitive status was evaluated by the Mini Mental State Examination (MMSE) which was widely used for the assessment of cognitive status for clinical or research purpose. MMSE was administered in a separate room by a trained physician. The scale ranges from 0 to 30, a higher score indicating better cognitive performance.

2.3 Mismatch negativity (MMN)

The odd-ball model was used in MMN testing, with brief pure tones used as the stimulus. The deviation frequency was 750 Hz with a rate of 20%, and the

standard frequency was 1000 Hz with a rate of 80%. Stimuli were delivered binaurally via earphones at 70 dB SPL as subjects were seated reading a book meanwhile they were instructed to ignore auditory stimuli. Subjects were instructed to avoid unnecessary eye movement and eye blinking during the session. Stimuli consisted of pure tones presented for 100 ms each, with a rise/fall time of 5ms and a stimulus onset asynchrony (SOA) of 500 ms.

The MMN was recorded from the front-central sites (Fz, Cz) and bilateral mastoid sites. The tip of the nose served as the reference for all electrodes. A ground electrode was attached to the forehead. Impedance between the electrodes and skin was kept below 5 kilo-ohms. MMN difference waveforms were derived from point-by-point subtraction of the standard stimulus values from those elicited by the deviant stimuli, and MMN difference waveforms were assessed within a custom-tailored window (100–250 ms). Because MMN was known to show inverted polarity at mastoid locations, our study adopted the term ‘mismatch positivity’ (MMP) to describe the mismatch component at this location[19]. The average waveforms for the electrode sites with negative polarity (MMN; Fz and Cz) and positive polarity (MMP; left and right mastoids) were evaluated separately. (Figure 1)

2.4 Statistical analyses

All statistical analyses were conducted using SPSS Version 19.0. MMN/MMP peak latencies and amplitudes were examined using two-way repeated measures analyses of variance (ANOVA) with one between subject factor GROUP (TLE and control), and one within subject factor SITE (front-central sites: Fz and Cz; mastoid sites: left and right mastoid). Using the

same statistical methods, the MMN/MMP amplitudes and latencies were compared between the subgroups monotherapy and polytherapy, and also among the controls, subgroup left TLE, right TLE and bilateral TLE. MMSE scores were compared using univariate analysis of variance (ANOVA) procedures among the three subgroups and the control group.

To assess the lateralizing value of MMN, the MMP peak latencies and amplitudes over the mastoid sites between the ipsilateral and contralateral sides of epileptic focus in unilateral TLE patients were compared using T-test. $P\text{-value} < 0.05$ was considered as statistically significant.

3. Results

3.1 Demographic and clinical information

Thirty TLE patients, with an average age of 37.74 ± 13.74 yrs old (ranging from 16 to 59) and thirty age and sex matched healthy controls were included. All participants were right-handed. There were 11 unilateral left TLE patients, 10 unilateral right TLE patients and 9 bilateral TLE patients. One-third of the TLE patients (10/30) demonstrated mesial temporal sclerosis. There were no demographic differences between the TLE group and control group. (Detailed information sees Table 1 and Table 2). The MMSE score of the patient groups as a whole was significantly lower than that of control group (25.75 ± 2.38 vs 28.22 ± 1.54 ; $p < 0.001$). Each subgroup had the significantly lower MMSE score than control group. However, the difference of the MMSE score among the three TLE subgroups was not significant.

3.2 MMN/MMP changes in TLE patients

Compared with controls, TLE patients had longer latencies of MMN/MMP at

both front-central sites and mastoid sites [front-central sites: $F(1,58)=9.51$, $p < 0.05$; mastoid sites: $F(1,58)=12.43$, $p = 0.001$], but the amplitudes of MMN/MMP were not significantly different [front-central sites: $F(1,58)=0.655$, $p > 0.05$; mastoid sites $F(1,58)=0.218$, $p > 0.05$]. No significant main effect of SITE or interaction between GROUP and SITE was observed. (MMN/MMP peak latencies and amplitudes in patients with TLE and controls see Table 3)

In the TLE group, thirteen patients were under monotherapy and seventeen patients were under polytherapy. The two-way repeated measures ANOVA analysis revealed no significant main effect of GROUP, SITE or interaction between GROUP and SITE. (MMN/MMP peak latencies and amplitudes in patients with monotherapy and polytherapy of antiepileptic drugs see Table 4)

Compared with controls, each subgroup of the patients had longer latencies of MMN/MMP both at front-central sites and mastoid sites, but the amplitudes of MMN/MMP were not significantly different. However, neither the amplitude nor the latency of MMN/MMP was significantly different between the three subgroups. (Figure 2)

3.3 The lateralizing value of MMP.

Only the unilateral left (11 patients) and right (10 patients) TLE patients were included in this analysis. At mastoid sites, the amplitudes and latencies of MMP were not significantly different between the ipsilateral and contralateral sides of epileptic focus, $p > 0.05$ (table 5)

4. Discussion

The current study investigated the MMN/MMP at the front-central sites and mastoid sites in patients with TLE. Compared to controls, patients with TLE had longer latencies of MMN/MMP at both front-central sites and mastoid sites,

but the amplitudes of MMN/MMP were not significantly different. However, neither the amplitude nor the latency of MMN/MMP was significantly different among the three subgroups. At mastoid sites, the amplitudes and latencies of MMP were not significantly different between the ipsilateral and contralateral sides of epileptic focus in unilateral TLE patients.

The latencies of MMN/MMP in patients with TLE were prolonged at both front-central sites and mastoid sites, which was in line with the conclusions from other authors [11, 14, 16]. MMN latency is thought to support heterogeneity in auditory stimuli processing speed [13, 20]. TLE is related to various transient and chronic brain electric and neurochemical disturbances [21]. Cognitive abnormalities are observed in patients with TLE [4]. In our study, the significantly lower MMSE score in the patient groups indicated the cognitive impairment in them. MMN being the initial memory comparator[7], its delayed latency further supported the cognitive abnormality. Longer latencies of MMN/MMP in the TLE group indicate that TLE patients may spend more time finding the switch of attention from one stimulus to another. In addition, the primary auditory cortex located in the temporal lobe, therefore, the increase MMN latencies in TLE patients may be the result of an early slowing in auditory information processing speed, which could be related to attention difficulties observed in TLE patients[14, 22].

Studies have shown MMN and MMP have different generators, exhibiting different patterns. In our study both MMN and MMP are equally affected by TLE. These findings suggest that not only the temporal lobe but also the frontal

lobe is affected in TLE and demonstrate that epilepsy reflects network-level instability which is a widely distributed yet highly integrates cortical network supporting cognitive activities[23, 24]. Therefore, while epileptic focus itself may play an important role in the cognitive dysfunctions, it is likely to be subsumed by a complex network of regions. Seizure could result in the neuronal alterations in ictal location and distant area [25].

In the current study, the amplitudes of MMN/MMP in TLE patients were not significantly different from the controls at all sites. These results were not consistent with the previous studies in which the MMN amplitudes were diminished at mastoid sites or enhanced at front-central sites in TLE.[14, 15]. In previous studies, different lesions involving more diverse areas within the temporal lobe had different effects on MMN amplitude [26] .For instance, lesions in superior temporal lobe might reduce the amplitude of MMN, while lesions in the medial part of temporal lobe led to pathological increase of MMN amplitude[27]. However, majority of our patients were MRI negative, only 10 patients showed mesial temporal sclerosis, which might interpret the different findings from previous studies. In addition, Hirose et al compared MMNs related to deviant stimuli with different durations and frequencies in patients with TLE and found that MMN and MMP related to frequency deviant did not differ between TLE and controls at the midline sites or at the mastoid sites. Our study used frequency deviant to evoke MMN/MMP and came to the same conclusion [28].

In the subgroup with bilateral TLE, it was not surprising that the alteration of latencies of MMN/MMP occurred bilaterally. It was also interesting to note that in the two subgroups with unilateral TLE, the alteration of MMN/MMP did not only confine to the side of the epileptic focus, but also involved the contralateral side as well. In addition, there was no difference of either latency or amplitude of MMN/MMP among the three subgroups of TLE. These results suggested that there was not clear relationship between the changes of MMN/MMP and the laterality of epileptic focus. The interictal MMN/MMP may not use as a lateralizing tool in pre-surgical evaluation. As discussed above, complex networks involving various brain regions are often involved in TLE. Contralateral temporal lobe is one of the most important structures in the epileptic network of TLE. The medial temporal region is not the only region active at seizure onset, but the contralateral temporal lobe also is rapidly activated[25, 29]. A number of PET studies have also reached the same conclusion [30, 31]. In our study, regardless of the laterality of the epileptic focus, MMN/MMP was equally affected at all sites on both sides. But it was important to take into account the following factors when interpreting the results. Firstly, all of our patients were free of seizures for at least three months prior to the test. The decline in the value of ERP recordings for the delineation of the epileptogenic focus may occur during the interictal phase[32]. The time span between seizure onset and ERP recording needs to be further investigated. Secondly, the effect of antiepileptic drugs (AEDs) may not be

neglected [33-35]. There was not significant difference in MMN/MMP between the group with monotherapy and that with polytherapy, which was consistent with the previous finding[36]. However, the exact type and dosage of AEDs in each individual may still have impact on the results of MMN/MMP. Further association study or study on drug-naïve patients may help.

5. Conclusions

The prolonged latencies of MMN indicate cognitive impairment in TLE. Both the mastoid sites and the front-central sites are involved which reflect widespread cortical abnormalities in TLE. The changes of MMN/MMP during the interictal phase are not useful for evaluation of the laterality of epileptic focus.

Acknowledgments

This work was supported by the National Science Foundation of China [NSFC] 81401079, and the China Postdoctoral Science Foundation 2015M570787 and 2016T90854. The authors are thankful to the Electrophysiology Laboratory Staff, Department of Electroneurophysiology, West China Hospital, Sichuan University for their technical support.

Conflict of interest

None of the authors has any conflict of interest to disclose.

References

- [1] Hermann, B. and Seidenberg, M. Epilepsy and cognition. *Epilepsy Currents* 2007; 7:1-6.
- [2] Fisher, R.S., Vickrey, B.G., Gibson, P., Hermann, B., Penovich, P., Scherer, A., et al. The impact of epilepsy from the patient's perspective I. Descriptions and subjective perceptions. *Epilepsy research* 2000; 41:39-51.
- [3] Bell, B., Lin, J.J., Seidenberg, M. and Hermann, B. The neurobiology of cognitive disorders in temporal lobe epilepsy. *Nature Reviews Neurology* 2011; 7:154-164.
- [4] Baxendale, S. and Thompson, P. Beyond localization: the role of traditional neuropsychological tests in an age of imaging. *Epilepsia* 2010; 51:2225-2230.
- [5] Elger, C.E., Helmstaedter, C. and Kurthen, M. Chronic epilepsy and cognition. *The Lancet Neurology* 2004; 3:663-672.
- [6] Myatchin, I., Mennes, M., Wouters, H., Stiers, P. and Lagae, L. Working memory in children with epilepsy: an event-related potentials study. *Epilepsy research* 2009; 86:183-190.
- [7] Näätänen, R., Kujala, T., Kreegipuu, K., Carlson, S., Escera, C., Baldeweg, T., et al. The mismatch negativity: an index of cognitive decline in neuropsychiatric and neurological diseases and in ageing. *Brain* 2011; 134:3435-3453.
- [8] Giard, M.H., Perrin, F., Pernier, J. and Bouchet, P. Brain Generators Implicated in the Processing of Auditory Stimulus Deviance: A Topographic

Event- Related Potential Study. *Psychophysiology* 1990; 27:627-640.

[9] Rosburg, T., Trautner, P., Dietl, T., Korzyukov, O.A., Boutros, N.N., Schaller, C., et al. Subdural recordings of the mismatch negativity (MMN) in patients with focal epilepsy. *Brain* 2005; 128:819-828.

[10] Korostenskaja, M., Pardos, M., Fujiwara, H., Kujala, T., Horn, P., Rose, D., et al. Neuromagnetic evidence of impaired cortical auditory processing in pediatric intractable epilepsy. *Epilepsy research* 2010; 92:63-73.

[11] Gene-Cos, N., Pottinger, R., Barrett, G., Trimble, M.R. and Ring, H.A. A comparative study of mismatch negativity (MMN) in epilepsy and non-epileptic seizures. *Epileptic disorders* 2005; 7:363-372.

[12] Borghetti, D., Pizzanelli, C., Maritato, P., Fabbrini, M., Jensen, S., Iudice, A., et al. Mismatch negativity analysis in drug-resistant epileptic patients implanted with vagus nerve stimulator. *Brain research bulletin* 2007; 73:81-85.

[13] Näätänen, R., Kujala, T., Escera, C., Baldeweg, T., Kreegipuu, K., Carlson, S., et al. The mismatch negativity (MMN)—a unique window to disturbed central auditory processing in ageing and different clinical conditions. *Clinical Neurophysiology* 2012; 123:424-458.

[14] Miyajima, M., Ohta, K., Hara, K., Iino, H., Maehara, T., Hara, M., et al. Abnormal mismatch negativity for pure-tone sounds in temporal lobe epilepsy. *Epilepsy research* 2011; 94:149-157.

[15] Hara, K., Ohta, K., Miyajima, M., Hara, M., Iino, H., Matsuda, A., et al. Mismatch negativity for speech sounds in temporal lobe epilepsy. *Epilepsy &*

Behavior 2012; 23:335-341.

[16]Lin, Y.-Y., Hsiao, F.-J., Shih, Y.-H., Yiu, C.-H., Yen, D.-J., Kwan, S.-Y., et al. Plastic phase-locking and magnetic mismatch response to auditory deviants in temporal lobe epilepsy. *Cerebral Cortex* 2007; 17:2516-2525.

[17]Besson, P., Dinkelacker, V., Valabregue, R., Thivard, L., Leclerc, X., Baulac, M., et al. Structural connectivity differences in left and right temporal lobe epilepsy. *Neuroimage* 2014; 100:135-144.

[18]Bancaud, J., Henriksen, O., Rubio-Donnadieu, F., Seino, M., Dreifuss, F. and Penry, J. Commission on classification and terminology of the international league against epilepsy. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. *Epilepsia* 1981; 22:489-501.

[19]Baldeweg, T., Williams, J.D. and Gruzelier, J.H. Differential changes in frontal and sub-temporal components of mismatch negativity. *International Journal of Psychophysiology* 1999; 33:143-148.

[20]Paavilainen, P. The mismatch-negativity (MMN) component of the auditory event-related potential to violations of abstract regularities: a review. *Int J Psychophysiol* 2013; 88:109-123.

[21]Jokeit, H. and Ebner, A. Effects of chronic epilepsy on intellectual functions. *Progress in brain research* 2002; 135:455-463.

[22]Piazzini, A., Turner, K., Chifari, R., Morabito, A., Canger, R. and Canevini, M.P. Attention and psychomotor speed decline in patients with temporal lobe

epilepsy: a longitudinal study. *Epilepsy research* 2006; 72:89-96.

[23]Spencer, S.S. Neural networks in human epilepsy: evidence of and implications for treatment. *Epilepsia* 2002; 43:219-227.

[24]Bernhardt, B.C., Bernasconi, N., Concha, L. and Bernasconi, A. Cortical thickness analysis in temporal lobe epilepsy Reproducibility and relation to outcome. *Neurology* 2010; 74:1776-1784.

[25]Maccotta, L., He, B.J., Snyder, A.Z., Eisenman, L.N., Benzinger, T.L., Ances, B.M., et al. Impaired and facilitated functional networks in temporal lobe epilepsy. *NeuroImage: Clinical* 2013; 2:862-872.

[26]Alain, C., Woods, D.L. and Knight, R.T. A distributed cortical network for auditory sensory memory in humans. *Brain research* 1998; 812:23-37.

[27]Lopes, R., Simões, M.R., Ferraz, L. and Leal, A.J. The mismatch negativity (MMN) potential as a tool for the functional mapping of temporal lobe epilepsies. *Epilepsy & Behavior* 2014; 33:87-93.

[28]Hirose, Y., Hara, K., Miyajima, M., Matsuda, A., Maehara, T., Hara, M., et al. Changes in the duration and frequency of deviant stimuli engender different mismatch negativity patterns in temporal lobe epilepsy. *Epilepsy & Behavior* 2014; 31:136-142.

[29]Hogan, R.E., Kaiboriboon, K., Bertrand, M.E., Rao, V. and Acharya, J. Composite SISCOM perfusion patterns in right and left temporal seizures. *Archives of neurology* 2006; 63:1419-1426.

[30]Trotta, N., Goldman, S., Legros, B., Ligot, N., Guerrey, N., Baete, K., et al.

Metabolic evidence for episodic memory plasticity in the nonepileptic temporal lobe of patients with mesial temporal epilepsy. *Epilepsia* 2011; 52:2003-2012.

[31]Van Bogaert, P., Massager, N., Tugendhaft, P., Wikler, D., Damhaut, P., Levivier, M., et al. Statistical parametric mapping of regional glucose metabolism in mesial temporal lobe epilepsy. *Neuroimage* 2000; 12:129-138.

[32]Abubakr, A. and Wambacq, I. The localizing value of auditory event-related potentials (P300) in patients with medically intractable temporal lobe epilepsy. *Epilepsy & Behavior* 2003; 4:692-701.

[33]Chen, Y.-J., Chow, J.C. and Lee, I.-C. Comparison the cognitive effect of anti-epileptic drugs in seizure-free children with epilepsy before and after drug withdrawal. *Epilepsy research* 2001; 44:65-70.

[34]Rosburg, T., Marinou, V., Haueisen, J., Smesny, S. and Sauer, H. Effects of lorazepam on the neuromagnetic mismatch negativity (MMNm) and auditory evoked field component N100m. *Neuropsychopharmacology* 2004; 29.

[35]Panagopoulos, G., Thomaides, T., Tagaris, G. and Karageorgiou, C. Auditory event related potentials in patients with epilepsy on sodium valproate monotherapy. *Acta Neurologica Scandinavica* 1997; 96:62-64.

[36]Ozmenek, O.A., Nazliel, B., Leventoglu, A. and Bilir, E. The role of event related potentials in evaluation of subclinical cognitive dysfunction in epileptic patients. *Acta Neurologica Belgica* 2008; 108:58.

Figure captions

Figure 1

Grand-averaged MMN/MMP elicited by deviant stimuli (probability=0.20) and standard stimuli (probability=0.80) in the auditory oddball paradigm

MMN: Mismatch negativity at front-central sites

MMP: Mismatch negativity at mastoid locations

Figure 2: comparison of MMN/MMP latencies and amplitudes among the subgroup unilateral left TLE, unilateral right TLE, bilateral TLE and the controls.

Use absolute value to represent the amplitudes of MMN

MMN: Mismatch negativity at front-central sites

MMP: Mismatch negativity at mastoid locations

LMAS: left mastoid

RMAS: right mastoid

Table 1 Clinical information of TLE patients and healthy controls.

	controls		patients		
	N=30		N=30		
Variables	Mean	SD	Mean	SD	
Age(years)	44.27	9.61	37.74	13.74	NS
MMSE score	28.22	1.54	25.57 [*]	2.38	
Gender	16/14		14/16		
(male/female)					
Disease	NA	NA	8.18	4.61	
duration(years)					
Antiepileptic	NA	NA	13/17		
drug					
monotherapy/					
polytherapy					
hippocampal	NA	NA	10/20		
sclerosis					
/normal					

NA: not applicable.

NS: no significant difference

* : Significant difference compared with healthy controls.

Table 2 Clinical information of healthy controls and the subgroups of TLE patients

Variables	controls		patients						
	N=30		Left TLE		Right TLE		bilateral TLE		
			N=11		N=10		N=9		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age (years)	44.27	9.61	39.00	12.23	38.60	17.01	38.60	17.61	NS
Disease duration(y ears)	NA	NA	6.33	4.60	7.87	4.29	10.10	4.55	NS
MMSE score			25.57	2.07	25.75	2.60	25.88	2.66	NS
AED monotherapy/ polytherapy	NA	NA	5/6		4/6		4/5		
hippocampal sclerosis/normal	N/A	N/A	3/8		3/7		4/5		

AED: antiepileptic drug;

NS: no significant difference

Table 3 MMN/MMP peak latencies and amplitudes in patients with TLE and controls

Peak	Site	TLE		controls	
		Mean	SD	Mean	SD
Latencies(ms)	Fz	196.83 [*]	11.54	176.09	27.23
	Cz	196.29 [*]	13.14	177.40	26.44
	Lmas	196.95 [*]	16.27	174.36	24.37
	Rmas	198.58 [*]	15.77	174.90	23.67
Amplitudes(μV)	Fz	-1.94	-1.37	-1.93	-0.93
	Cz	-1.93	-1.35	-2.26	-1.07
	Lmas	2.27	1.34	2.04	1.30
	Rmas	2.28	1.07	2.14	1.48

* Significant difference compared with healthy controls.

Table 4 MMN/MMP peak latencies and amplitudes in patients with monotherapy and polytherapy of antiepileptic drugs

		monotherapy		polytherapy		
		N=13		N=17		
Peak	Site	Mean	SD	Mean	SD	
Latencies(ms)	Fz	193.40	9.91	199.28	12.33	NS
	Cz	192.10	13.32	199.27	12.63	NS
	Lmas	196.28	17.95	197.90	14.47	NS
	Rmas	198.78	17.42	198.30	14.03	NS
Amplitudes(μ v)	Fz	-1.83	-1.22	-2.10	-1.61	NS.
	Cz	-2.04	-1.37	-1.77	-1.37	NS
	Lmas	2.25	1.17	2.30	1.61	NS
	Rmas	2.22	0.87	2.37	1.35	NS

NS: no significant difference

Table 5 Comparison of latencies and amplitudes of MMP between ipsilateral and contralateral sides of epileptic focus

	Ipsilateral side of epileptic focus		Contralateral side of epileptic focus		t	P
	Mean	SD	Mean	SD		
Latencies(ms)	197.93	17.30	196.80	16.90	-0.181	0.857
Amplitudes(μ v)	2.08	1.15	2.28	0.94	0.513	0.612

— Deviant
— Standard