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Attention changes in epilepsy patients following 3-month topiramate or valproate treatment revealed by event-related potential

Wei Sun [a], Yuping Wang [a,*], Weiwei Wang [b], Xun Wu [b]

[a] Department of Neurology, Capital Medical University Xuanwu Hospital, Beijing, 100053, People's Republic of China
[b] Department of Neurology, Peking University First Hospital, Beijing, 100034, People's Republic of China

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Abstract

The present study was designed to reveal changes of cognitive processes in epilepsy (EP) patients with Topiramate (TPM) or Valproate (VPA) treatment using Wechsler Adult Intelligence Scale (WAIS-CR) and event-related potential (ERP). Thirty untreated epilepsy patients were randomly divided into two groups receiving TPM or VPA, respectively. Fifteen healthy volunteers were included as controls. All the patients were examined by WAIS-CR and ERP before and 3 months after drug treatment. Controls were examined by ERP at the time recruited into the study and 3 months later. Unfamiliar grey-scale photographs of faces (front view) were used as stimuli. ERP were recorded at the same time. Mean Intelligence Quotient (IQ) in TPM group decreased after the 3-month treatment (90.40 vs. 81.00, $P<0.05$). One component of ERP-P300 was smaller in epilepsy patients than controls ($P<0.05$), but remained unchanged after TPM or VPA treatment ($P>0.05$). A delayed and smaller N270 was detected in patients compared to controls ($P<0.05$). After 3 months TPM treatment, it decreased further compared to before treatment ($P<0.05$). N170 was lower in patient groups, and it became lower after TPM treatment than before. Our results demonstrate that in all epilepsy patients with mild cognitive impairment ERP changes were found. TPM affected the cognitive functions in epilepsy patients reflected by the decreased full-scale intelligence quotient (FIQ). The imperative effects of TPM on visual perception function reflected by N170 were more obvious than that of VPA. Attention reflected by N270 was impaired after TPM treatment.

Keywords: Epilepsy; Topiramate; Valproate; Event-related potential; N170; N270; Cognitive; Attention

1. Introduction

Cognition, defined as the ability to retain, process and react to information, depends on many factors in the mental and overall physical status (Brunbech and Sabers, 2002). Cognitive impairment in epilepsy patients can be contributed by several factors including epileptic syndromes themselves, the etiology of epilepsy, seizure type, age of seizure onset, seizure frequency, anti-epileptic drugs (AEDs) and others (Aldenkamp et al., 2005). Among these factors, AEDs have been paid increasing attention because they are the major therapeutic modality for control of seizures. The ideal AEDs should have no unfavorable effects on cognition. However, most of them can suppress neuronal excitability or enhance inhibitory neuronal transmission, which might indirectly affect the cognitive processes including attention, short-term or working memory, long-term memory, and executive function in the central nervous system, thereby may worsen the mental status function (Perrine and Kiolbasa, 1999). In general, AEDs mono-therapy has less effect on cognition when the drug blood concentration is within therapeutic range (Meador, 2002). As a new AED, Topiramate (TPM) can be used in mono- or poly-therapy in various types of epilepsy patients especially those with intractable epilepsy. But it also has raised increased concerns about its relationship with cognitive difficulties. 31% of TPM-treated patients have been reported to possess many side effects in central nervous system such as attention deficit, dizziness and poor performance on verbal tests, and 5.8% of them had terminated treatment due to these problems (e.g., Privitera et al., 1996; Crawford, 1998; Tatum et al., 2001). On the other hand, the cognitive effects of classical AEDs, such as phenytoin, carbamazepine and valproate, seem to be similar and relatively

* Corresponding author. Tel.: +86 10 83198814; fax: +86 10 83157841.
E-mail address: wangyupi@hotmail.com (Y. Wang).

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Table 1
Summary of descriptive characteristics of the three groups

Patient characteristics	Control (n=15)	TPM (n=15)	VPA (n=15)
Sex (male/female)	8/7	9/6	7/8
Age (years) (mean±SD)	30.0±9.3	29.0±10.2	28.9±11.2
Education (years) (mean±SD)	12±4.1	13.4±3.1	11.1±3.4

modest, with only valproate having effects on attention (e.g., Forsythe et al., 1991; Gallassi et al., 1992; Brunbech and Sabers, 2002; Meador, 2002; Sun et al., 2007). Studies of cognitive abnormalities especially attention deficit related to TPM and VPA are mostly confined to retrospective studies, which make these results difficult to be evaluated.

Event-related potential (ERP) is an important method to evaluate the cognitive status of epilepsy patients (e.g., Sunaga et al., 1994; Soysal et al., 1999; Rodin et al., 1999; Tendon and Duban, 2000; Trinka et al., 2000; Sun et al., 2007). Differences in timing and scalp topography of particular ERP components allow inferences about the timing and spatial characteristics of brain activity involved in cognitive processing (Rugg and Coles, 1995). ERPs could be measured punctually with time-locked processing to external events in evaluating the cognitive function of patients.

In the field of ERP research, face perception has developed rapidly recently. Faces, as special objects, are a unique type of stimuli which contain rich social information, such as gender, age, expression, race and so on and can be well recognized even by newborns (Johnson et al., 1991). Electrophysiological studies on face perception have been focused on the N170 (N1). A confirmative neural potential related to face processing is the lateral-posterior temporal N170 component, which consistently shows greater amplitudes in response to faces than to stimuli from other categories (Bentin et al., 1996; George et al., 2005). Therefore, N170 is usually referred to as the N1 "special face negative potential" (Bentin et al., 1996; Eimer, 2000).

In recent studies, a prominent negative component of ERP with latency of around 270 ms (N270) was recorded from frontal, central and parietal areas and it can be evoked by the S1-S2 paradigm when the second stimulus (S2) of a pair differed from the first one (S1) in some attributes. When S2 was compared with S1, the inconsistency between the two stimuli caused stimulus-related perceptual conflict. N270 was only evoked by the stimulus pairs with conflicts, it was thus considered as a constant component of ERPs reflecting the conflict processing in the human brain (e.g., Cui et al., 2000; Kong et al., 2000; Wang et al., 2000; Wang et al., 2001, 2002; Zhang et al., 2002, 2003; Mao et al., 2005) Based on these studies, we found that ERP N270 is an important and sensitive method for the evaluation of the cognitive status of patients with obstructive sleep apnea syndrome, Parkinson's disease, depression, transient ischemic attack (TIA) and epilepsy (e.g., Zhang et al., 2002; Wang et al., 2002; Mao et al., 2005, Mao et al., 2006; Sun et al., 2007).

In this study, we employed the S1–S2 paradigm to elicit potentials in epilepsy patients and normal controls without any clinical dementia. We tried to find out the changes of N170, N270 and P300 in epilepsy patients before and three months after AED treatment and to verify the value of face perception ERP as an index for detecting multiple cognitive domains, including attention, short-term or working memory, and executive function.

2. Materials and methods

2.1. Subjects

Thirty-eight untreated epilepsy patients (17–40 years old with normal vision or corrected-to-normal vision) recruited from the Xuanwu Hospital of Capital Medical University and the First Hospital of Peking University were randomly divided into two groups according to AEDs to be used: topiramate treatment (TPM, N=21) and valproate acid treatment (VPA, N=17). Patients were organized in sequence number according to their visiting time and stratified according to age, gender and frequency of seizure and then divided into two groups by stratified randomization. Fifteen patients from each group were included in the final statistics. Three patients in the TPM group (14%) gave up treatment because of memory decreasing or dyslogia within the first two week, one patient gave up treatment because of limb numbness. The other four patients (2 of each group) terminated study due to personal reasons (such as work).

All patients had secondary generalized tonic-clonic seizures or complex partial seizures classified by the International League Against Epilepsy (ILAE) originated in 1981. Same number of patients with unifocal vs. multifocal seizures was included into both treatment groups. They all fulfilled the inclusion criteria: less than three seizures each month; no evidence of progressive brain or systemic diseases; normal results of neurological examination and CT/MRI scan; no alcohol abuse history; right-handed.

Fifteen age, gender and education-matched normal subjects (Control, N=15) were recruited from the community. None of them reported any history of neurological or psychiatric diseases. All subjects were right-handed.

All patients were evaluated by Wechsler Adult Intelligence Scale (WAIS-CR) (Gong and Wechsler, 1992) examination and ERP before and three months after the initiation of drug treatment. No patients had a seizure occurring within 24 h before the first or the second ERP recording. Control subjects received ERP examination when they were recruited and 3 months later. Independent t-tests and analysis of variance (ANOVA) revealed no significant difference between the two patient groups in their ages, education, duration of epilepsy, seizure onset age and seizure frequency. The summary of statistics describing the subjects in each group is presented in Tables 1 and 2.

Table 2
Clinical comparison of patients with epilepsy

Patient characteristics	TPM (n=15)	VPA (n=15)
Ages at onset of epilepsy (year)/(range)	25.8/16–38	19.3/16–40
Duration of epilepsy (year)/(range)	2.8/0.5–24	2.4/1–15
Seizure frequency at first assessment (per month)/(range)	1.5/0.2–2	1.8/0.5–3
Seizure frequency at second assessment (per month)/(range)	0.5/0–1	0.7/0–2
Blood anticonvulsant levels at second assessment (mean±SD) (μg/ml)	5.84±6.7 (n=11)	73±8.4 (n=15)

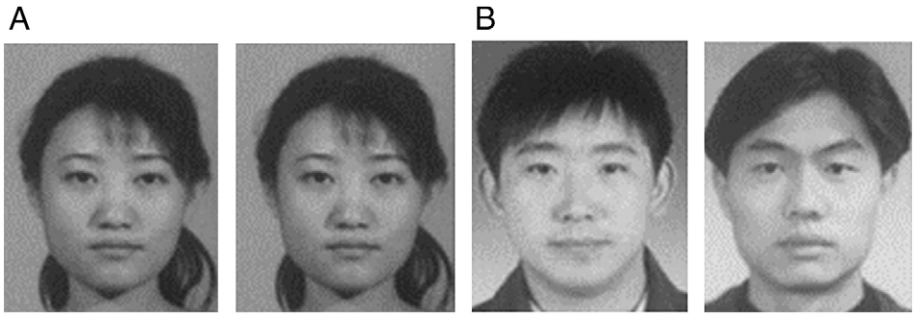

Fig. 1. A stimulus trial consists of unfamiliar grey-scale photographs of faces (front view). The stimulus pairs included two series (1) match: identical face picture S1 and S2 (condition 1, A); (2) conflict: different S1and S2 (condition 2, B).

The mode of prescription: TPM was given 25 mg/ day in the first week and increased by 25 mg/day each week (morning and evening, twice per day). The end dosage was 100 mg/day and hold for two months. VPA was given 200 mg/day in the first day and increased by 200 mg/day each day (morning and evening, twice per day). The end dosage was 800 mg/day. The average blood anticonvulsant levels of VPA ($n=15$) and TPM ($n=11$) after three months drug administration were presented in Table 2.

Informed written consent was obtained from all subjects. The protocol was approved by the Ethics Committee of Capital Medical University Xuanwu Hospital and Peking University Health Science Center.

2.2. Stimuli and task

Visual stimuli were presented on a monitor, 1 m in front of the subjects. A stimulus system (STIM, Neurosoft, Inc. Sterling, USA) was used for controlling the presentation of the stimuli. S1 and S2 in stimulus pairs were grey-scale photographs of faces flashing 300 ms in sequence and separated by an interval of 1000 ms. The interval between the end of the previous S2 and the onset of the following S1 was 3000 ms. The stimuli consisted of unfamiliar grey-scale photographs of faces (front view) obtained from college yearbooks. Females and clean-shaven males aged from 20 to 28 with natural facial expression were equally presented, and none had extraneous features such as spectacles or jewelry (Fig. 1). Each stimulus picture occupied a visual angle of approximately 2.74°×2.28°. The stimulus pairs were divided into two conditions of equal probability: (1) S2 had the same picture as S1 (match condition), and (2) S2 exhibited a different picture from S1 (conflict condition).

Table 3
WAIS-CR examination comparison of two groups (mean±SD)

	IQ	Examination 1	Examination 2	P value (based on χ^2)
TPM Group	VIQ	89.53±7.10	79.07±9.01 [a]	0.001
	PIQ	93.27±6.25	86.73±8.41 [a]	0.023
	FIQ	90.40±4.84	81.00±6.61 [a]	0.000
VPA Group	VIQ	87.73±4.88	86.93±5.19	0.667
	PIQ	90.67±9.28	89.80±10.53	0.813
	FIQ	88.33±4.70	87.40±5.34	0.615

[a] Significantly different from examination 1 ($P<0.05$).

Each subject was comfortably seated in a dimly lit, electrically shielded room with response buttons under his or her hands. In order to emphasize the "conflict" and "match" congruity effect in the task, subjects were asked to press a button to indicate if S2 was identical to or different from S1. After the onset of S2, subjects pressed the left button as fast and accurate as possible when S2 matched S1 and pressed the right button when S2 differed from S1. The left or right hand used for the response was counter-balanced in each subject.

2.3. Recordings

All subjects received two tests separated by a three-month interval. The electroencephalogram (EEG) was recorded from 10 scalp electrodes (F3, F4, C3, C4, P3, P4, O1, O2, T5, T6) according to the international 10–20 system, using Ag/AgCl electrodes with impedance less than 5 KΩ. The nose tip was used as the reference. Vertical electro-oculogram (EOG) and horizontal EOG were recorded by electrodes situated above and below the left eye and at points 2 cm outside of the outer canthi of both eyes, respectively. EEG was amplified with a band pass of 0.05–100 Hz, sampled at 500 Hz, and stored on a hard disk for off-line analysis. The averaging epoch was 1200 ms including a 200 ms baseline prior to the onset of the S1 presentation. Trials with EOG artifacts, incorrect behavioral responses or EEG

Table 4
Accuracy scores (%) and reaction times (RTs) (mean±SD) (ms)

	Group	Condition	Match	Conflict
Accuracy	Control	Recording 1	94±3	92±4
		Recording 2	95±3	93±3
	TPM	Recording 1	90±2	90±4
		Recording 2	93±3	91±5
	VPA	Recording 1	89±5	88±4
		Recording 2	90±5	89±4
Reaction time	Control	Recording 1	556±92	602±124 [a]
		Recording 2	521±113	588±133 [a]
	TPM	Recording 1	661±149 [b]	716±114 [a, b]
		Recording 2	768±137 [b, c]	815±132 [a, b, c]
	VPA	Recording 1	676±183 [b]	735±163 [a, b]
		Recording 2	638±173 [b]	730±164 [a, b]

[a] Significantly different from match condition ($P<0.05$).
[b] Significantly different from the control group ($P<0.05$).
[c] Significantly different from the first recording ($P<0.05$).

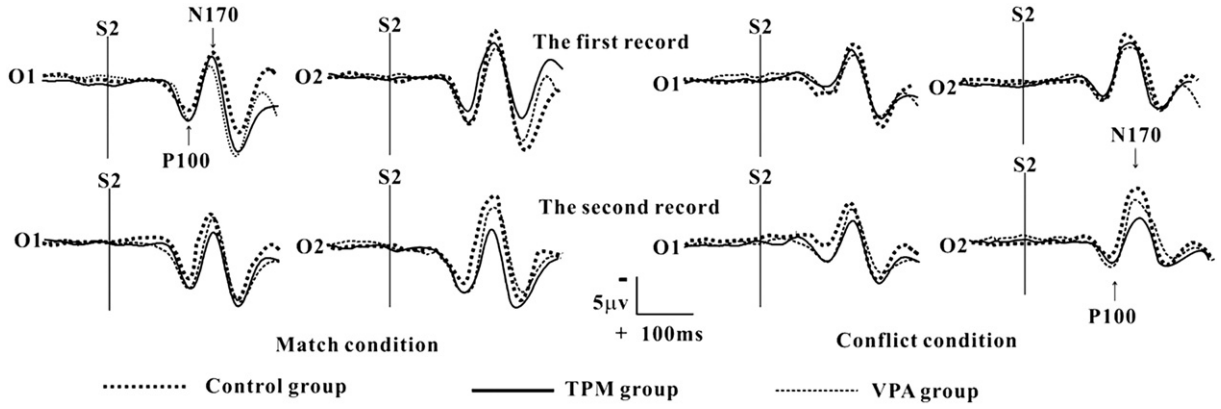

Fig. 2. The ERP consists of P100 and N170 in the match and conflict conditions on the occipital scalp (O1, O2) in the three groups.

exceeding ±70 μV were excluded from the average. More than 30 trials were averaged in each condition for each patient and control subject. The number of rejected trials did not differ between patients and control subjects.

2.4. Statistical data analysis

Statistical analyses were limited to artifact-free trials on which participants correctly identified a photo as required. A between-group and repeated measure ANOVA was employed to analyze the behavioral data of the three groups. In this study, N170 component was robust at O1 and O2 electrodes, whereas N270, P300 were the most prominent and steady at C3, P3, C4 and P4 electrodes. Therefore, the amplitude and latency data of these two potentials were measured at these areas. The P300 data were measured in the facial picture match condition in order to avoid the superimposing of N270 in the picture conflict condition. The amplitude of N270 was measured on the difference waveform derived by subtracting the ERPs elicited by the match condition from those by the conflict condition (Tian et al., 2001). The peak amplitude and peak latency data of N170, P300 as well as N270 were compared among the three groups in two recordings using a between-group, repeated measure ANOVA with Greenhouse–Geisser correction. When no N270 or P300 was present at one of the four electrodes, the component was considered absent and the data of the subject were excluded. Post-hoc Newman–Keuls test was also performed. The significance level for all statistical tests was $P<0.05$.

3. Results

3.1. WAIS-CR data

FIQ in TPM group decreased after three-month treatment (90.40 vs. 81.00, $P<0.05$) mainly due to distinct decrease of Verbal Intelligence Quotient (VIQ). Among the six-subentry indexes, digit span and vocabulary descended after the three months' treatment ($P<0.05$). Average Intelligence Quotient (PIQ) did not change in VPA group (before 88.33 vs. after 87.40, $P>0.05$) (Table 3).

3.2. Behavioral data

Behavioral accuracy and reaction time (RT) data were summarized in Table 4. The between-group, repeated-measures ANOVA revealed that there was no difference in correction rates among the three groups in the two recordings and two conditions. The ANOVA for RTs revealed significant effects

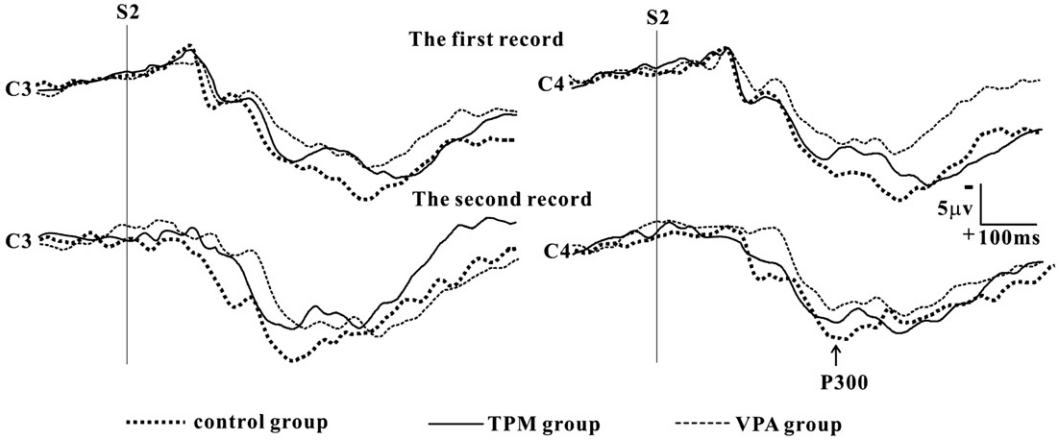

Fig. 3. The grand-averaged ERP waveforms evoked by S2 in the match condition in the three groups.

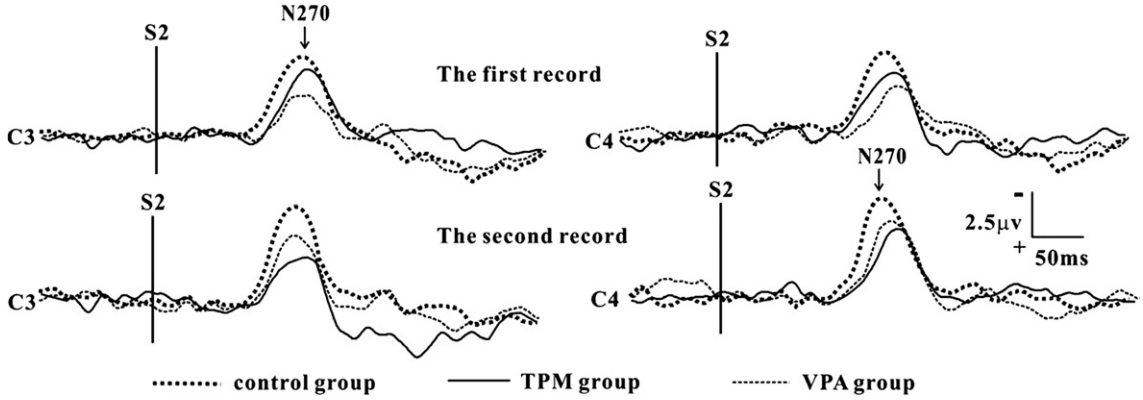

Fig. 4. The difference waveforms derived by subtracting the ERPs evoked in the match condition from those evoked in the conflict condition.

among three groups (F (2,42)=11.19, P<0.05). Post-hoc analysis showed RTs was longer in each patient group than the control group (P<0.05). Both patients and control subjects responded faster in the match condition than in the conflict condition (F (1, 42)=83.61, P<0.05). Only TPM group showed longer RTs after the 3-month treatment (P<0.05).

3.3. ERP data

Grand-averaged ERP waveforms of the three groups were shown in Figs. 2–4. In the match condition, P100, N170 (N1) and P300 were evoked by S2. In the conflict condition, the potentials formed another component, N270, before P300.

A between-group, repeated-measures ANOVA indicated that the peak amplitude of N170 was different among the three groups (F (2, 42)=6.50, P<0.01). A significant interaction, F (2, 42)=12.55, P<0.01, between group (TPM group, VPA group or control group) and electrode site (O1 or O2) was found. Post-hoc tests showed that the peak amplitudes of N170 in the TPM group and VPA group were both significantly smaller than that in the control group at O2 electrode site (P<0.05). The peak amplitude of N1 did not differ between the two patient groups. Only in TPM group the peak amplitude of N1 significantly decreased in the second recording compared to the first time (P<0.05). The peak latency of N1 was not significantly different among the three groups, or between two recordings in each group (Table 5, Fig. 2).

Each subject in the three groups exhibited a P300 component. A between-group, repeated-measures ANOVA indicated that the peak amplitude of P300 was different among the three groups (F (2, 42)=4.52, P<0.05). There is significant interaction between group (TPM group, VPA group or control group) and electrode site (C3, P3, C4 or P4) (F (2, 42)=3.55, P<0.05). Post-hoc tests revealed the peak amplitude of P300 in each patient group was significantly smaller than that in the control group at C3 and C4 electrodes (P<0.05). The peak latency of P300 did not differ significantly among the three groups, or between two recordings in each group (Table 6, Fig. 3).

All subjects in the control group exhibited a prominent N270, while the potential disappeared at separate sites in four patients, one from TPM group at P4 site (first recording), one from VPA group at C3 site (first recording), and two from VPA group at P3, P4 site (the second recording). However, there was no significant difference in the absence rate of the component among the control and the two patient groups (χ^2=0.58, P>0.05).

On the difference waveforms derived by subtracting the picture match potentials from the conflict potentials, the peak amplitudes of N270 were different among the three groups revealed by between groups ANOVA (F (2, 41)=5.20, P<0.01). A significant interaction between group and electrode site (C3,

Table 5
The peak latencies and the amplitudes of N170 (mean±SD)

		Site	Control		TPM		VPA	
			Recording 1	Recording 2	Recording 1	Recording 2	Recording 1	Recording 2
Latencies (ms)	Match	O1	157±18	153±12	158±14	158±14	157±19	160±15
		O2	159±17	154±14	157±12	159±14	161±17	163±14
	Conflict	O1	164±16	159±10	158±12	161±12	164±15	166±16
		O2	162±17	157±12	157±11	162±13	163±14	164±14
Amplitude (μV)	Match	O1	−4.1±3.1	−4.3±2.5	−3.3±2.6	−1.6±3.0[a, b]	−2.9±5.1	−2.8±4.2
		O2	−5.1±3.2	−5.6±3.3	−3.3±3.0[a]	−2.0±2.5[a, b]	−3.0±2.1[a]	−3.4±2.4[a]
	Conflict	O1	−4.0±3.6	−4.4±3.5	−3.2±3.5	−1.5±2.0[a, b]	−2.8±5.3	−2.2±3.3
		O2	−5.0±3.7	−5.9±5.0	−3.5±2.0[a]	−2.1±3.5[a, b]	−3.2±2.4[a]	−4.0±2.4[a]

[a] Significantly different from the control group (P<0.05).
[b] Significantly different from recording 1 (P<0.05).

Table 6
The peak latencies and the amplitudes of P300 (mean±SD)

	Site	Control		TPM		VPA	
		Recording 1	Recording 2	Recording 1	Recording 2	Recording 1	Recording 2
Latencies (ms)	C3	359±50	356±42	370±67	385±72	395±110	391±95
	C4	359±38	356±39	396±80	401±74	400±90	390±107
	P3	356±51	357±45	374±71	385±65	394±97	380±108
	P4	365±40	356±43	382±69	387±67	400±103	390±94
Amplitude (μV)	C3	12.6±4.2	12.9±4.3	7.9±3.3[a]	7.5±4.8[a]	7.6±2.5[a]	7.9±4.8[a]
	C4	11.6±4.8	11.3±3.9	7.6±4.1[a]	7.9±5.7[a]	7.8±2.8[a]	7.9±4.1[a]
	P3	10.1±5.1	10.6±4.5	7.9±4.2	8.1±4.0	7.8±2.8	8.6±4.3
	P4	9.5±5.6	9.6±4.9	7.6±4.8	7.9±5.4	8.1±3.1	8.2±4.5

[a] Significantly different from the control group ($P<0.05$).

C4, P3 or P4) was found (F (2, 41)=16. 08, $P<0.01$). The peak amplitude was significantly smaller in each patient group than that in control group at C3, C4, P3 and P4 electrode ($P<0.05$). No significant difference in the peak latency or amplitude of N270 was shown between TPM group and VPA group (Table 7, Fig. 4).

The significant interaction between group and recording times are shown (F (2, 41)=24.23, $P<0.05$). Only in the TPM group the amplitude of N270 was significantly decreased after the three months' treatment ($P<0.05$).

Epilepsy patients in each group exhibited a delayed N270 in comparison with the control group. There was a significant main effect among groups (F (2, 41)=21.09, $P<0.01$) or interaction between group and electrode site (C3, C4, P3 or P4) (F (2, 41)= 4.21, $P<0.05$). The peak latencies of N270 in each patient group on the difference-waveform were significantly longer than the control group at the four electrode sites ($P<0.05$).

4. Discussion

The result of WAIS-CR examination showed that FIQ decreased in the TPM group after three months' drug treatment. The value of FIQ in VPA group had no difference after three months' treatment. The result was the same as our clinical observation that TPM can cause memory loss and aphasia in epilepsy patients. This was consistent with other studies concerning TPM (Privitera et al., 1996; Crawford, 1998).

The epilepsy patients performed worse than the normal controls especially after TPM administration. The possible cause for the prolonged RTs indicated the slow reaction due to cognitive impairment including attention deficit. This cognitive decline caused the patient group to make much more errors and further delayed their RTs even before treatment. TPM made the cognitive processes, decision-making and reactive speed of epilepsy patients even worse.

ERP waveforms differ depending upon the modality and cognitive processes utilized. Faces represent highly meaningful non-linguistic stimuli and are related to the structural analysis of face (e.g., Botzel et al., 1995; George et al., 1996, 2005). The N170 with coding faces recorded over posterior occipito-temporal brain areas can index early processing of visual spatial attention (e.g., Bentin et al., 1996; Näätänen et al., 1993; Näätänen, 1995; Mangun, 1995; Luo et al., 2001). In our study, the peak amplitude of N1 decreased in patient groups, indicating that the epilepsy patients had damage in facial coding. Decreased N1 amplitude after the three months' TPM treatment suggested that TPM might aggravate the processing.

P300 has been widely used for investigating the cognitive functions and is thought to reflect the neurophysiological activities related to cognitive processes, such as attention, discrimination and working memory (Mecklinger and Ullsperger, 1993). It is suggested that P300 latency is correlated with composite score on cognitive tests. The amplitude of P300 reflects the degree of brain activity or the extent of cortical functioning area recruited in the tasks. The reduction of the amplitude in the two patient groups may indicate the declined brain activity or cortical functioning area in the epilepsy patients.

Table 7
The peak latencies and the amplitude of difference waveforms (mean±SD)

	Site	Control		TPM		VPA	
		Recording 1	Recording 2	Recording 1	Recording 2	Recording 1	Recording 2
Latencies (ms)	C3	287±31	286±31	315±34[a]	324±41[a]	330±30[a]	328±35[a]
	C4	290±28	284±25	320±36[a]	319±34[a]	324±31[a]	320±33[a]
	P3	278±36	286±39	317±41[a]	327±45[a]	305±37[a]	329±37[a]
	P4	282±33	282±31	305±42[a]	304±41[a]	317±40[a]	305±38[a]
Amplitude (μv)	C3	−6.7±2.8	−7.8±3.9	−5.0±2.5[a]	−2.3±2.2[a, b]	−3.0±3.8[a]	−4.3±3.8[a]
	C4	−6.5±2.9	−6.9±4.1	−4.6±3.0[a]	−2.8±4.5[a]	−2.9±3.3[a]	−3.9±3.3[a]
	P3	−6.5±2.4	−7.5±3.0	−4.6±2.3[a]	−2.1±2.7[a, b]	−2.9±4.1[a]	−4.1±3.2[a]
	P4	−6.3±2.3	−7.0±3.9	−4.3±2.1[a]	−2.0±2.3[a, b]	−2.5±3.0[a]	−3.9±2.5[a]

[a] Significantly different from the control group ($P<0.05$).
[b] Significantly different from recording 1 ($P<0.05$).

The delay of the N270 component in those epilepsy patients with normal IQ data indicated that in this subgroup of patients, cognitive slowing in identifying the conflict information was present even in the absence of clinical dementia. Meanwhile the decreased N270 amplitude in the two patient groups might be due to the decreased amount of neurons, which can be recruited into the same cognitive task. Further severe changes of N270 were found after the three-month TPM treatment. Previous studies (e.g., Tian et al., 2001; Zhang et al., 2002; Wang et al., 2002; Mao et al., 2005, 2006) showed that the conflict processing system might be modulated by attention, although information conflict can be automatically detected by the on-line monitoring function (Wang et al., 2001). It is suggested that the function of attention system in TPM group might be impaired at clinically effective dosage.

In conclusion, epilepsy patients showed some minor cognitive impairment as reflected in their reaction speed, visual perception, and attention adjustment. TPM may cause the deterioration of the above functions.

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