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Evaluating the feasibility of measures of motor threshold and cortical silent period as predictors of outcome after temporal lobe epilepsy surgery

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ABSTRACT

Introduction: Although it is well known that ES alters cortical excitability, little is known about the relationship between ES outcome and cortical excitability. Transcranial magnetic stimulation has been successfully used to evaluate cortical excitability in epilepsy patients. The present study aimed to assess the value of the motor threshold (MT) and cortical silent period (CSP) as predictors of the outcome of temporal lobe epilepsy surgery (TLES).

Materials and methods: Epileptic foci in the epilepsy patients were identified via video-electroencephalography (v-EEG) monitoring, brain magnetic resonance imaging (MRI), single-photon emission computed tomography (SPECT), and positron emission tomography (PET), and neurophysiological testing. MT, CSP-150, and CSP-max were measured in 10 epilepsy patients on both the ipsilateral and contralateral side of the epileptic focus 1 week before and 3 months after TLES. Pre- and post-operative MT and CSP measurements were compared, and the results were interpreted based on the clinical outcome of TLES.

Results: Mean follow-up period was 28.8 months. In all, 8 patients were seizure-free post TLES, whereas in 2 patients seizures persisted. No significant differences were observed in ipsilateral or contralateral hemisphere MT measurements before and after surgery. Both CSP-150 and CSP-max values in the non-focal hemispheres decreased in the 8 patients that were seizure-free post TLES, whereas no differences were observed in the 2 patients with seizures that persisted post TLES.

Conclusions: The present findings indicate that monitoring pre- and post-TLES CSP changes may be predictive of the early clinical outcome of TLES.

1. Introduction

Epileptic disorders are the clinical result of excitatory and inhibitory system imbalance within the central nervous system.[1] Surgical removal of the epileptic focus is widely accepted as an effective therapy for selected patients with medically refractory epilepsy; however, there is no consensus regarding accurate predictors of surgical outcome due to the use of heterogeneous study groups, differences in surgical procedures and duration of follow-up, and varying definitions of surgical success and failure.

The primary measure of the outcome of epilepsy surgery (ES) is the end of seizures, and secondary outcome measures are the frequency and severity of seizures, quality of life, level of disability, and mortality.[2–5] Transcranial magnetic stimulation (TMS) has been used to non-invasively and almost painlessly investigate the human cerebral cortex. The motor threshold (MT) and cortical silent period (CSP), and intracortical inhibition and intracortical facilitation have been used to evaluate motor cortex excitability.[6]

Cortical excitability is likely to change after surgical removal of the epileptic focus;[7,8] therefore, TMS parameters may be useful for predicting the outcome of ES. The present study aimed to assess the value of the MT and CSP as predictors of the outcome of temporal lobe epilepsy surgery (TLES).

2. Materials and methods

The study included 10 patients (8 female and 2 male) aged 25–39 years (mean age: 30.7 years) with drug-resistant temporal lobe epilepsy (Table 1). The patients underwent pre-surgical monitoring at Gülhane Military Medical Hospital, Department of Neurology, Epilepsy Monitoring Unit, Ankara, Turkey between January 2005 and May 2009. Epileptic foci were identified and surgical techniques were chosen based on the results of video-electroencephalography

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Table 1
Patient characteristics.

Patient	Age (years)	Gender	Family history	Handedness	Duration of disease (years)	Seizure type(s) before surgery	Seizures during sleep	Etiology	Seizure frequency before surgery	Surgical procedure	AEDs before and after surgery	Seizure frequency after surgery	Post-surgical follow-up period (months)
1	34	Female	No	Ambidextrous	33	CPS	Yes	Left MTS	2–3/month	Left AMTL	VPA, OXC, LEV	No seizure	15
2	25	Female	No	Right	19	CPS, SGTCS	No	Right MTS	1–2/month	Right AMTL + AHCT	CBZ, LEV	No seizure	51
3	38	Female	No	Right	14	CPS	No	Right MTS	1–2/week	Right AMTL + AHCT	CBZ, TP, LEV	No seizure	11
4	39	Female	No	Right	38	CPS, SGTCS	Yes	Right MTS	1–2/week	Right AMTL + AHCT	VPA, CBZ, LEV	1–2/week	24
5	28	Female	Aunt	Left	11	CPS, SGTCS	No	Right MTS	1–2/month	Right AMTL	VPA, CBZ	No seizure	53
6	28	Female	Sister	Right	26	CPS, SGTCS	Yes	Left MTS	1–2/month	Left AMTL + AHCT	VPA, CBZ, LEV	No seizure	57
7	29	Female	Father and brother	Right	17	CPS, SGTCS	No	Right MTS	2–3/month	Right AMTL + AHCT	CBZ, LEV, TP	2–3/month	23
8	29	Male	No	Right	27	CPS, SGTCS	No	Left MTS	1–2/month	Left AMTL + AHCT	CBZ, TP	No seizure	12
9	26	Male	No	Right	13	CPS, SGTCS	Yes	Right MTS	5–6/month	Right AMTL + AHCT	CBZ, LEV	No seizure	27
10	31	Female	Father	Right	25	CPS	No	Left MTS	1–2/week	Left AMTL + AHCT	VPA, CBZ	No seizure	15

CPS: complex partial seizure; SGTCS: secondary generalized tonic–clonic seizure; MTS: mesial temporal sclerosis; AMTL: anteromedial temporal lobectomy; AHCT: amygdalohippocampectomy; VPA: valproic acid; CBZ: carbamazepine; OXC: oxcarbazepine; LEV: levetiracetam; TP: topiramate.

(v-EEG) monitoring, brain magnetic resonance imaging (MRI), single-photon emission computed tomography (SPECT), and positron emission tomography (PET), and neurophysiological testing. All of the patients provided written informed consent to undergo TLES, and TMS testing before and after TLES. The Gülhane Military Medical Hospital Ethics Committee approved the study protocol.

Patients 1 and 5 underwent anteromedial temporal lobectomy (AMTL), and the others underwent AMTL and amygdalohippocampectomy (AHCT). During AMTL, 3.5 cm of the temporal pole (from the temporal tip) was removed, including half of the superior temporal gyrus, and the middle and inferior temporal gyri. During AHCT, the amygdala, anterior part of the tail of the hippocampus, and the entire head and body of the hippocampus and parahippocampal gyrus were surgically removed. Following surgery, the patients' antiepileptic drug (AED) regimens remained unchanged. Additionally, pre-surgical and post-surgical AED blood levels were identical and within therapeutic ranges. Patient characteristics are shown in Table 1.

TMS testing was performed 7 days prior to surgery by a neurologist blinded to the location of each patient's epileptic focus. TMS testing was repeated 3 months post surgery by another neurologist blinded to the pre-surgery measurements. TMS testing in patients 4 and 7 – whose seizures persisted post TLES – was performed at least 3 days after they had seizures. TMS was performed while the patients were in a seated position, using a 9-cm diameter circular coil (Dantec MC125) capable of generating a peak magnetic field of 1.0 T. Responses of the abductor pollicis brevis (APB) muscles were recorded bilaterally with a Dantec Evolution EMG apparatus, using Ag–Cl surface electrodes. The coil was placed over the scalp projecting the motor cortex area about 7 cm lateral of the vertex. The position of the coil was changed slightly and the stimulus was administered until the optimal position for APB muscle response was determined.[8–10]

2.1. MT measurement

MT was defined as the lowest intensity stimulus required to elicit an MEP 50 $\pm$ 10-μV in amplitude from the resting APB muscle, with $\geq$5 successful trials out of 10. Initial stimulus intensity was 30% of the maximum stimulus intensity and was increased by 1–5% until we obtained the MT. MT was measured for both APB muscles independently.

2.2. CSP measurement

CSP-150 and CSP-max measurements were obtained for each patient. During the procedure patients were requested to contract their APB muscles using 50% of their maximum contraction force. For CSP-150 measurement the stimulus intensity was adjusted to 1.5-fold that of the MT measurement for the same APB muscle and was administered from the contralateral side of the scalp during contraction of the ABP muscle. CSP-150 was defined as the mean value of 5 measurements and CSP-max was defined as the mean value of 5 CSP measurements obtained with the maximum stimulus intensity.[9–12]

Seizure-free was defined as no seizure during the follow-up period. Pre- and post-surgical MT and CSP measurements were compared, in terms of the side of epileptic focus and the contralateral side. Statistical evaluation of the data acquired before and after surgery was performed using the paired *t* test.

3. Results

None of the patients experienced complications during TMS testing. Mean pre-surgical MT (as a percentage of maximum stimulus intensity) was 52.7 $\pm$ 2.6% on the ipsilateral side and