研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
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International Congress Series 1278 (2005) 284–287

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A study of brain-evoked potential in 100 ms after transcranial magnetic stimulation

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Abstract. Transcranial magnetic stimulation (TMS)-evoked N100 component (TMS-N100) is a negative peak wave at about 100 ms after TMS to the motor cortex. To elucidate the contribution of somatosensory and auditory inputs to the generation of TMS-N100, and to determine the cognitive effect of this potential, we recorded TMS-N100 with the TMS-compatible whole-head 60-channel EEG system from 10 healthy subjects. The peak latencies and pattern of potential distributions were similar between TMS-N100 under the ignore condition and the potential evoked by SMT+AUD in 100 ms (SMT+AUD N1) under the ignore condition. The amplitude of TMS-N100 significantly increased under the cognitive condition, while the latency and the potential distribution of TMS-N100 were not changed. These cognitive effects were also observed on SMT+AUD N1 under the cognitive condition. Therefore, inputs of TMS-N100 are the magnetic stimulation to the cerebral cortex and somatosensory and auditory inputs accompanied with TMS. The amplitude of TMS-N100 is increased by performing the cognitive task, thus, the cognitive status should be considered when the amplitude of TMS-N100 is interpreted.

Keywords: Transcranial magnetic stimulation; TMS-N100; Input pathway; Cognitive effect

1. Introduction

Transcranial magnetic stimulation (TMS)-evoked N100 component (TMS-N100), which is a negative peak wave at about 100 ms after TMS to the motor cortex, has been

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0531-5131/
doi:10.1016/j.ics.2004.11.100

reported as a pronounced and reproducible cerebral potential [1–3]. It was reported that TMS-N100 contained the auditory N1 component [4,5] and that its amplitude was increased with an increase in stimulus intensity [3]. In addition to the auditory input generated by the coil, the somatosensory input to the generation of TMS-N100 should be considered because TMS stimulates not only the cerebral cortex but also the tissues below the coil, and this would generate the trigeminal somatosensory evoked potential and/or the trigeminal somatosensory event-related potential. On the other hand, the middle-latency event-related potentials, e.g., the auditory N1 [6] and the somatosensory N140 [7], are known to have cognitive effects. This implies that TMS-N100 also has cognitive effects.

The aim of this study is to elucidate the contribution of somatosensory and auditory inputs to the generation of TMS-N100 and to determine the cognitive effect of this potential.

2. Methods

The evoked potentials were recorded with the TMS-compatible whole-head 60-channel EEG system (Nexstim, Helsinki, Finland), which enabled recording from 2 ms after each TMS pulse [8] from 10 healthy subjects, who were 20- to 34-year-old men. We applied two types of stimulation—(i) TMS: TMS to the left motor cortex of the hand area at the intensity of 1.1 motor thresholds, and (ii) SMT+AUD: the combined stimulation of the electrical shock to the scalp and the click sound, under two different conditions, a condition in which the subjects were instructed to ignore the stimuli (the ignore condition) and a condition in which they had to count the number of stimuli mentally (the cognitive condition).

The EEG was obtained with eXimia EEG (Nexstim). This EEG system was composed of TMS-compatible EEG amplifiers. The EEG was recorded continuously using a TMS-compatible flexible electrode cap with specially shaped 60 Ag/AgCl electrodes (Electro-Cap International, Ohio, USA), using linked earlobes as a reference. The band-path was 0.1–500 Hz, and the sampling rate was 1450 Hz. The electrode impedance for all the recording sites was maintained at below 5 kΩ.

The 50–60 epochs were averaged from −50 to 500 ms. The baseline was set at the average of a 50 ms prestimulus period. The averaged responses were digitally filtered (1–45 Hz).

3. Results

(1) The peak latencies and pattern of potential distributions were similar between TMS-N100 under the ignore condition and a potential evoked by SMT+AUD in 100 ms (SMT+AUD N1) under the ignore condition.
(2) The amplitude of TMS-N100 significantly increased under the cognitive condition, while the latency and the potential distribution of TMS-N100 were not changed.
(3) These cognitive effects were also observed on SMT+AUD N1 under the cognitive condition (Table 1; Fig. 1).

The subtracted waveform, i.e., 'cognitive condition' minus the 'ignore condition', is also superimposed. The mean amplitude and peak latency of the subtracted waveform were 7.5 μV and 110.5 ms, respectively, for TMS-N100 and 3.8 μV and 109.8 ms,

Table 1
The amplitudes and latencies of TMS-N100 and SMT+AUD N1 in Cz

	Ignore condition		Cognitive condition	
	Amplitude (μV)	Latency (ms)	Amplitude (μV)	Latency (ms)
TMS-N100				
Mean	13.5	110.0	20.2*	108.7
S.E.	1.4	3.0	1.8	2.4
SMT+AUD N1				
Mean	4.2	112.9	7.2	108.5*
S.E.	0.4	1.7	0.6	1.5

* $p<0.05$, after cognitive vs. ignore conditions.

respectively, for SMT+AUD N1. The amplitude of the subtracted waveform of TMS-N100 was larger than that of the subtracted waveform of SMT+AUD N1, while the peak latencies showed no difference.

4. Discussions

4.1. Input pathway of TMS-N100

SMT+AUD evoked a cerebral potential having a latency and potential distribution similar to those of TMS-N100, but its amplitude was apparently smaller than that of TMS-N100, suggesting that the somatosensory and auditory inputs generated by TMS may produce TMS-N100, in part.

4.2. The effect of cognitive task on TMS-N100

The amplitude of TMS-N100 was increased by performing the cognitive task, thus, the TMS-N100 already includes an endogenous component. A recent report demonstrated that the amplitude of TMS-N100 is increased with an increase in stimulus intensity [3]. Therefore, it is concluded that TMS-N100 has dual properties of exogenous and endogenous components.

Finally, we considered that it would be interesting to ask the subjects how they directed their attention when performing the cognitive task. There has been no report of a phenomenon by which subjects directly perceive a stimulus to the motor cortex, such as

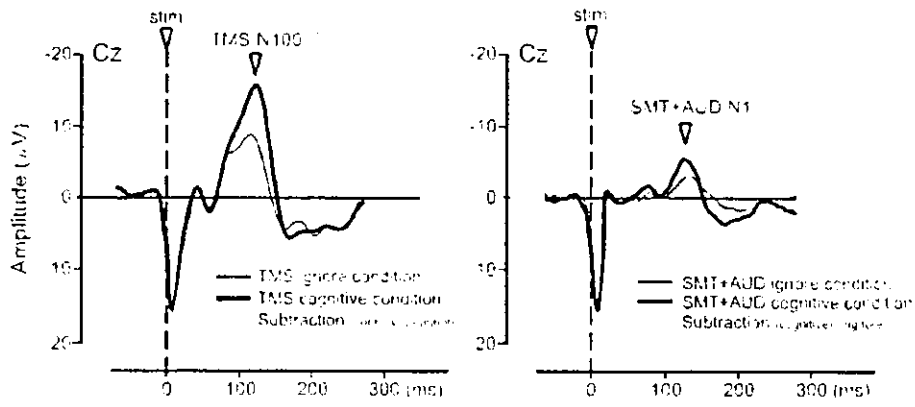

Fig. 1. The grand averaged waveforms of TMS-N100 and SMT+AUD N1 in Cz.

the case of phosphenes in the visual cortex. Moreover, the movement of the finger induced by TMS did not reveal any direct relation with the cerebral potentials around 100 ms discussed here. Thus, the subjects must have counted the click sounds and/or skin sensations generated by TMS to perform the cognitive task. This view is supported by the report from the subjects after performing the cognitive task sessions.

5. Conclusions

The inputs of TMS-N100 are the magnetic stimulation to the cerebral cortex and the somatosensory and auditory sensations accompanied with TMS. The amplitude of TMS-N100 is increased by performing the cognitive task, thus, the cognitive status should be considered when the amplitude of TMS-N100 is interpreted.

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Repetitive exercise training changes input–output property of the corticospinal pathway during lengthening and shortening contractions in human first dorsal interosseus muscle

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Abstract. We investigated the modulation of the corticospinal excitability during lengthening (LEN) and shortening (SHO) contractions in the first dorsal interosseus (FDI) muscle. The maximum slope of input–output property (the relationship between stimulus intensities vs. motor evoked potentials) during LEN contractions was significantly higher than that during SHO contractions. However, after repetitive exercise training of LEN and SHO contractions for 2 weeks, the maximum slope during LEN contractions was significantly reduced. This result suggests that the FDI muscle is inexperienced in a significant number of LEN contractions in daily life.

Keywords: Lengthening contraction; Transcranial magnetic stimulation; First dorsal interosseus muscle; Input output property

1. Introduction

Hitherto, we have investigated excitability of the corticospinal pathway during lengthening (LEN) and shortening (SHO) contractions in the elbow flexors and soleus muscle by using transcranial magnetic stimulation. The corticospinal excitability is characterized by input–output (I/O) property (i.e. the relationship between stimulus

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0531-5131/
doi:10.1016/j.ics.2004.11.095

intensities vs. area of motor evoked potentials). Using this technique, we demonstrated that the plateau value and maximum slope were significantly lower during LEN contractions than during SHO contractions [1,2]. The following question, however, arises here. Does this modulation of the corticospinal excitability hold in all skeletal muscles of our body? The elbow flexors and soleus muscle are often performing the LEN contractions in daily life. However, it is unlikely that the first dorsal interosseus (FDI) muscle experiences a significant number of LEN contractions in daily life.

Hence, the purpose of this study was to investigate how the corticospinal excitability during LEN and SHO contractions are modulated in the FDI muscle. Furthermore, we investigated whether the modulation is changed by training or not because the FDI muscle would be inexperienced in a significant number of LEN contractions in daily life.

2. Methods

2.1. Subjects

Sixteen healthy subjects participated in this study. Subjects were randomly assigned to one of two groups: Control group (n=8) and Training group (n=8). Subjects were seated in an armchair with their forearm and hand supported by a custom-built device.

2.2. General procedure

The training group participated in six training sessions over a 2-week training period. Before and after the training period, each subject participated in TMS measurement. The control group also participated in the same measurement.

2.3. Training program

The subjects trained three times per week for 2 weeks. Each training session comprised 10 sets of 12 repetitions, with each repetition comprising the entire range of motion (~40°) in the abduction–adduction plane. The loads which correspond to approximately 5% of MVC force were applied as the training loads. The training session was performed at a constant angular velocity (8°/s) by visual feedback.

2.4. EMG

EMG was obtained from the first dorsal interosseus (FDI) muscle.

2.5. Transcranial magnetic stimulation

TMS was applied over the scalp using a stimulator with a double 70 mm stimulating coil, and triggered at 10° of abduction of the index finger (the longitudinal axis of the hand=0°). At that time, the background EMG activity levels during LEN and SHO contractions were maintained to approximately 10% of MVC. The stimulus intensity was expressed as a percentage of the maximum stimulator output and was increased in steps of 5 or 10% of maximal output from below 10% of motor threshold to a plateau level of response. TMS was at least provided five times at each stimulus intensity.

3. Results

(1) In the pre-measurement in both groups, the maximum slope during LEN contractions was significantly higher than that during SHO contractions ($p<0.05$).
(2) The maximum slope during LEN contractions was significantly lower after the training compared with before the training ($p<0.05$).

4. Discussion

The higher maximum slope during LEN contractions in the pre-measurement might indicate the specificity of the modulation of the corticospinal excitability in the FDI muscle. However, the fact that the maximum slope was reduced by training suggests that the FDI muscle is inexperienced in a significant number of LEN contractions in daily life.

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Short communication

The effect of repetitive transcranial magnetic stimulation on long-term potentiation in rat hippocampus depends on stimulus intensity

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Accepted 8 September 2003

Abstract

We investigated the effect of repetitive transcranial magnetic stimulation (rTMS) on long-term potentiation (LTP) in the rat hippocampus. Rats were magnetically stimulated at a rate of 1000 pulses/day for 7 days by a round coil, in which the peak magnetic fields at the center of the coil were 0.75 and 1.00 T. LTP enhancement was observed only in the 0.75-T rTMS group, while no change was observed in the 1.00-T rTMS group. These results suggest that the effect of rTMS on LTP depends on the stimulus intensity.

Theme: Neural basis of behavior
Topic: Neural plasticity

Keywords: Repetitive transcranial magnetic stimulation (rTMS); Hippocampus; Long-term potentiation (LTP); Eddy current

Transcranial magnetic stimulation (TMS) is a non-invasive technique to stimulate the brain by magnetically induced eddy currents through a coil positioned on the surface of the head [2,25]. TMS has been widely used for functional brain mapping [8,26]. Recently, repetitive TMS (rTMS) has become an increasingly important therapeutic tool for the potential treatment of neurological and psychiatric disorders such as depression and Parkinson's disease [9,14]. Many studies have reported that gene expressions, such as c-*fos*, glial fibrillary acidic protein (GFAP), and brain derived neurotrophic factor (BDNF), were enhanced in the rat brain by rTMS [7,10,17]. The effect of rTMS on brain function must still be clarified.

Long-term potentiation (LTP) is a long-lasting increase in synaptic efficacy resulting from the high-frequency stimulation of afferent fibers [5]. LTP in the hippocampus is thought to be a typical model of synaptic plasticity related to learning and memory [15]. rTMS-related effects in the hippocampus have been previously investigated, e.g., monoamine release, neurogenesis, and memory function [6,12,21]. To clarify the mechanisms underlying the effects of rTMS on the hippocampus, an electrophysiological approach was adopted. Our previous study reported that LTP was not affected by 0.50 T rTMS (< motor threshold, same stimulus condition as this study), while LTP was significantly suppressed by 1.25 T rTMS (>motor threshold) [18], suggesting that rTMS affects hippocampal function. To maximize efficacy and reduce the risk of rTMS, the effect of rTMS on the synaptic plasticity in the hippocampus at different intensities must be clarified. In this study, we investigated the effects of 0.75 T (< motor threshold) and 1.00 T (>motor threshold) rTMS on the LTP in the rat hippocampal CA1, and clarified the dependence of the stimulus intensity in rTMS.

All experimental procedures performed in this study were approved by the Animal Ethics Committee of the University of Tokyo. Male Wistar rats (4 weeks old, 60–80 g, Saitama Experimental Animals Supply) were used. Pairs of rats (one stimulated and one sham control) were housed in individual cages with free access to food and water at room temperature. Rats were magnetically stimulated by a round coil (inner diameter = 15 mm, outer diameter = 75 mm, thickness = 10 mm) positioned over the rat's head (Fig. 1B). Rats were held by the nape of the neck beneath the coil in a wakeful state during the stimulation delivery. The stimulator (NIHON KOHDEN) delivered

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doi:10.1016/j.brainres.2003.09.009

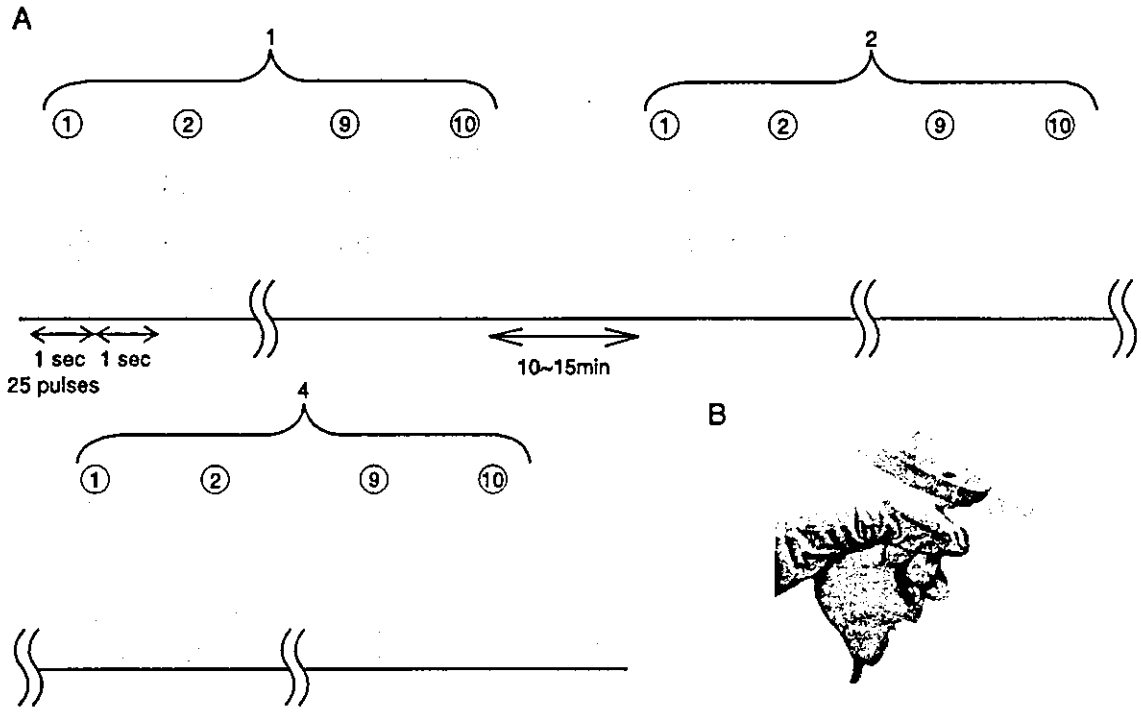

Fig. 1. (A) Stimulus pattern for one day. Ten 1-s trains of 25 pulses/s with a 1-s intertrain interval were applied to the rats four times per day for 7 days. (B) Magnetic stimulation of a rat.

biphasic cosine current pulses for 238 μs. The peak magnetic fields were set to 0.75 T (<motor threshold) and 1.00 T (>motor threshold) at the center of the coil. The motor threshold was determined based on previously reported methods [17]. The motor-evoked potentials (MEP) at the hindlimb biceps femoris muscle were measured in response to the TMS intensity. The motor threshold was determined as the TMS intensity when the MEP peak was greater than 5% of the maximum peak of the MEP. Since determining the motor threshold in each individual rat is a stressful and invasive procedure, six different rats of the same age, weight, and sex as the rats used in the rTMS experiment were used solely to determine the motor threshold to exclude any possible brain damage in the experimental rats. The average motor threshold was approximately 0.93 T.

Ten 1-s trains of 25 pulses/s with a 1-s intertrain interval were applied to the rats four times per day for 7 days (Fig. 1A). During the intervals between the four stimulations, the coil was cooled down. Rats of the sham control were treated with a sham coil (i.e., nonstimulated) and exposed to the same noise produced during the stimulation.

The eddy current induced in the rat brain was calculated using a rat head model constructed from the scalp, the skull and the brain based on MR images (Fig. 2A–C). The conductivities of the brain, the skull, and the scalp were set to 0.20, 0.015, and 0.43 S/m, respectively [19]. There is a strong spatial inhomogeneity of the electrical characteristics of brain tissue [12]. For simplicity, we adopted the previously reported method using a human head model constructed from the scalp, the skull and the brain [22]. Electric currents applied to the coil were 4.2 kHz continuous sinusoidal waves, and the current density applied to the coil in this calculation was 8.75×10^7 A/m^2, which produced a peak magnetic field of approximately 0.75 T at the center of the coil. The model was constructed and calculated using a computer program (PHOTO-Series). When the peak magnetic field at the center of the coil was 0.75 T, the maximum eddy current in the brain was approximately 9 A/m^2 (Fig. 2D). The eddy current density is proportional to the changing rate of the magnetic field or the peak magnetic field. Therefore, when the peak magnetic field at the center of the coil is 1.00 T, the eddy current in the brain is approximately 12 A/m^2.

Approximately 15 h after the final stimulation, the rats were anesthetized with diethyl ether and decapitated. The brain was quickly removed from the skull and placed on an ice-cold filter paper damped with artificial cerebrospinal fluid (ACSF) containing (in mM) NaCl 125, KCl 3, NaH_2PO_4 1.2, $NaHCO_3$ 26, $CaCl_2$ 2.0, $MgCl_2$ 1.0, and glucose 10. The hippocampus was dissected, and transverse slice sections (400 μm) were obtained with a microslicer. The slices were incubated and allowed to recover in ACSF bubbled with 95% O_2/5% CO_2 (pH 7.4) at room temperature for a minimum of 1 h before recording. The slices were then transferred to a recording chamber and continuously perfused (approximately 2 ml/min) with ACSF at 30 °C. Field excitatory postsynaptic potentials (fEPSP) were recorded using a tungsten electrode from the dendrites of CA1 pyramidal cells by stimulating Schaffer collaterals with a tungsten bipolar stimulating electrode. A single stimulus

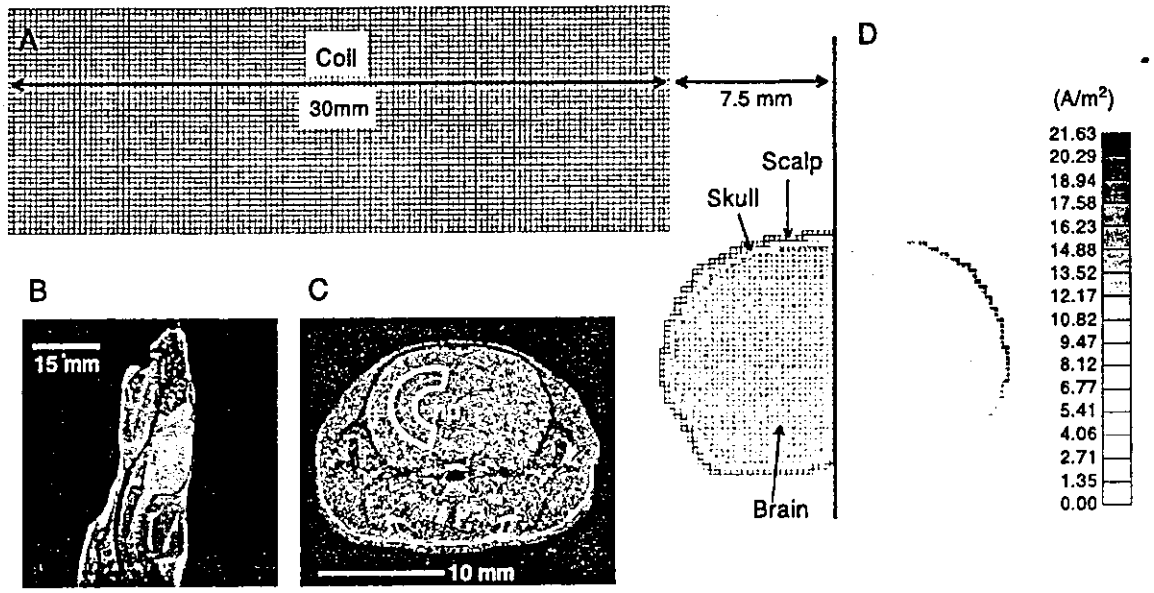

Fig. 2. Modeling of the rat head and calculation of the eddy current. (A) Positional relationship between the coil and the rat head. The rat head model was constructed from the scalp, skull and brain. (B) Sagittal MR image of a rat head. (C) Coronal MR image of a rat head. hp: area of hippocampus. (D) Estimated eddy current when the peak magnetic field was set to 0.75 T at the center of the coil.

was administered at 20-s intervals. The stimulus intensity was set to generate a fEPSP with a slope that was approximately 30% of the maximum determined from the input–output curve. After obtaining stable fEPSP recordings for 20 min, LTP was induced by tetanus stimulation (100 Hz for 1 s, 0.1-ms duration). fEPSP recordings were then continuously obtained for 60 min after tetanus stimulation and subsequently analyzed with pCLAMP software (Axon Instrument). Each slice was used for only one experiment and then discarded. LTP data were obtained from 10 sham rats (1–5 LTPs from each rat for a total of 26 LTPs) and 10 stimulated rats (1–4 LTPs from each rat for a total of 26 LTPs) of the 0.75-T rTMS group, and from 8 sham rats (1–4 LTPs from each rat for a total of 15 LTPs) and 8 stimulated rats (2–4 LTPs from each rat for a total of 21 LTPs) of the 1.00-T rTMS group. All the LTP data for each group were averaged and statistically analyzed by repeated measures of ANOVA. Data were expressed as the mean ± standard error (S.E.). A probability level of less than 0.05 was considered to be statistically significant.

LTPs were observed in both the 0.75-T stimulated and sham control groups, as shown in Fig. 3. The induction phase of LTP (first 10 min after tetanus stimulation) of the 0.75-T stimulated group was enhanced compared with that of the sham control group. The maintenance phases of LTP (from 10 min after tetanus stimulation to 60 min) of the stimulated group (267 ± 26%) was significantly enhanced compared with the sham control group (212 ± 10%) ($F_{1,50}=4.410, p=0.0408$). LTPs were also observed in both the 1.00-T stimulated and sham control groups, as shown in Fig. 4. The induction phase of LTP of the 1.00 T stimulated group was also enhanced compared with that of the sham control group. There were no significant differences ($F_{1,34}=1.749$, $p=0.1948$), however, between the maintenance phases of LTP of the 1.00-T stimulated group (223 ± 13%) and the sham control group (199 ± 13%).

According to our data, LTP is not significantly affected by 1.00 T rTMS, but enhanced by 0.75 T rTMS, suggesting that 0.75 T rTMS possibly activates hippocampal function. Two possible mechanisms for the enhancement of LTP by 0.75 T rTMS are as follows: (1) LTP induction is affected by rTMS directly. Previously reported studies revealed that the expression of c-*fos*, glial fibrillary acidic protein (GFAP) and brain derived neurotrophic factor (BDNF) were en-

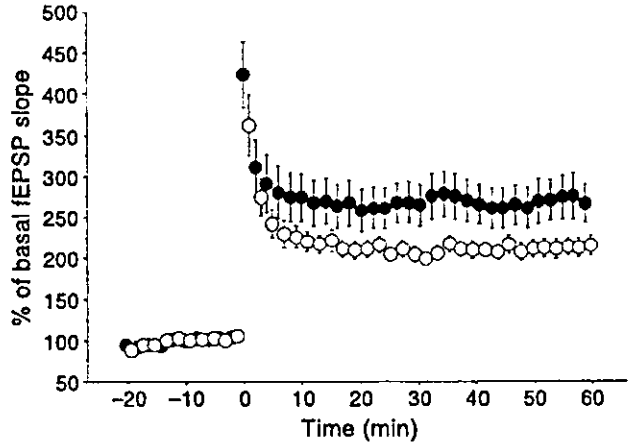

Fig. 3. LTPs of 0.75 T stimulated and sham control groups. LTPs were observed in both the stimulated and sham control groups. The maintenance phase of the LTP of the stimulated group (267 ± 26%) (black circle) was significantly enhanced compared with the sham control group (212 ± 10%) (white circle) ($p=0.0408$). Each circle represents the average of six successive responses (for 2 min). Rat $N=10$ for each group. Error bar = ± 1 S.E.

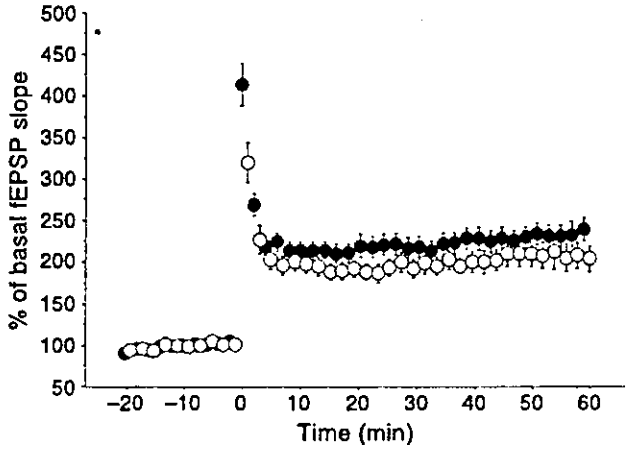

Fig. 4. LTPs of 1.00-T stimulated and sham control groups. LTPs were observed in both the stimulated and sham control groups. There was no significant difference ($p=0.1948$) between the maintenance phase of the LTP of the stimulated group (225 ± 14%) (black circle) and the sham control group (199 ± 13%) (white circle). Each circle represents the average of six successive responses (for 2 min). Rat $N=8$ for each group. Error bar = ± 1 S.E.

hanced in the dentate gyrus and hippocampal CA3 by TMS [7,10,17]. It is also reported that GFAP, which is intimately associated with LTP [16,27], is one of the genes that is strongly upregulated by intense neuronal activity in the hippocampal dentate gyrus [23,24]. There are many mechanisms associated with LTP induction, for example, the enhancement of transmitter release, the activation of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) and *N*-methyl-D-aspartate (NMDA) receptors, and changes in the number of synaptic-spine contacts and in the shape of the spine heads [3,4,13]. Therefore, 0.75 T rTMS possibly induces the gene expression in the hippocampus, and affects some of the mechanisms associated with LTP induction, resulting in LTP enhancement. (2) LTP in the hippocampus is indirectly affected by 0.75 T rTMS via gene expression in brain regions other than the hippocampus because the peripheral brain regions are exposed to stronger eddy currents than the hippocampus (Fig. 2D). It is reported that TMS induces the expression of c-*fos* in the cingulate gyrus, frontal cortex and parietal cortex [10,11]. In general, information is transferred from the cingulate cortex, temporal lobe cortex, amygdala, orbital cortex, and olfactory bulb to the hippocampus [1]. Therefore, there is a possibility that brain regions other than the hippocampus are affected by 0.75 T rTMS, and hippocampal function is activated indirectly. Further studies are needed to clarify these two mechanisms.

In our previous study, we reported that 0.50 T rTMS (<motor threshold) had no effect on LTP in the rat hippocampus, while 1.25 T rTMS (>motor threshold) suppressed LTP [18]. In summary, we conclude that rTMS of 0.50 T (<motor threshold) and 1.00 T (>motor threshold) have no effect on hippocampal function, rTMS of 0.75 T (<motor threshold) may potentially activate hippocampal function, and rTMS of 1.25 T (>motor threshold) may potentially impair hippocampal function. It is reported that the effect of rTMS depends on individual parameters (e.g., frequency, intensity) [20]. Our results suggest that the effect of rTMS depends on the stimulus intensity, and rTMS administered at the appropriate stimulus intensity may potentially activate hippocampal function.

Acknowledgements

This work was supported partly by a Grant-in-Aid for Specially Promoted Research (No. 12002002) from the Ministry of Education, Culture, Sports, Science and Technology of Japan (to S.U.), and partly by a grant in aid from the Magnetic Health Science Foundation (to M.O.). The authors would like to thank Dr. H. Funamizu, Mr. T. Tsurugizawa, Mr. N. Yasumatsu, Dr. N. Takata, and Ms. E. Rosenberg for their help.

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FEM-Based Determination of Optimum Current Distribution in Transcranial Magnetic Stimulation as an Alternative to Electroconvulsive Therapy

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***Abstract*—In this study, we investigated dependences of the current distribution in transcranial magnetic stimulation (TMS) on coil current intensity, coil diameter, and coil position, and compared the current distribution with that of electroconvulsive therapy (ECT). The head model consisted of 4-mm finite elements. In the ECT model, a voltage of 100 V was applied between a pair of electrodes place on the tempora. In the TMS model, eddy current distributions were obtained for figure-eight coils with diameters of 50, 75, and 100 mm, and coil positions varied from the vertex to the forehead. The difference in current distributions in ECT and TMS decreased with the coil position approaching to the forehead. The coil of 100-mm diameter gave the minimum difference at a coil current of 87 kA. The difference decreased with an increase in the coil diameter.**

***Index Terms*—Electroconvulsive therapy (ECT), finite element method (FEM), transcranial magnetic stimulation (TMS).**

I. Introduction

ELECTROCONVULSIVE therapy (ECT), in which electric currents are applied to the brain, improves severe mental illnesses such as depression [1]. Transcranial magnetic stimulation (TMS) is a method to stimulate neurons using eddy currents generated by pulsed magnetic fields [2]. Because TMS has a potential to give a comparable therapeutic effect to ECT with less invasiveness, TMS has been used for treatments of depression in numerous studies [3]. However, these trials have not necessarily given beneficial results.

Because the mechanisms of ECT largely remain to be understood, the optimum stimulus intensity and the desirable current distribution in ECT are still not clear. In many cases, however, ECT with a commonly used voltage (100 V) and an electrode position (electrodes attached to the tempora) has produced an improvement of depression. Thus, an appropriate approach for the initial attempt of TMS therapy is to find a stimulus condition which gives a similar current distribution in the brain to ECT. In a previous study, we calculated current distributions in ECT and TMS using the finite element method (FEM) [4]. Nadeem *et al.* performed an impedance method simulation for the same purpose [5]. However, these studies obtained results for only one condition of TMS.

Manuscript received October 19, 2003. This work was supported in part by Specially Promoted Research under Grant 12002002 and in part by JSPS Fellows, the Ministry of Education, Culture, Sports, Science and Technology, Japan.

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Digital Object Identifier 10.1109/TMAG.2004.828982

In the present study, we investigated dependences of the current distribution in TMS on coil current intensity, coil diameter, and coil position. Current distributions in ECT and TMS were compared under various conditions to find optimum conditions of TMS as an alternative to ECT.

II. Methods

We used a three-dimensional human head model obtained from the Brooks Air Force Laboratory (Brooks Air Force, TX) [6]. Conductivities of the tissues were calculated for a frequency of 4.2 kHz. It was assumed that the relative magnetic permeabilities of all the tissues were 1.0. Though the original model had a spatial resolution of 1 mm, we reconstructed the model with a resolution of 4 mm to reduce computation time. The numbers of nodes and elements were 81 192 and 74 369, respectively. All the results were obtained using commercial software (PHOTO-Series developed by PHOTON Co., Ltd.) based on the FEM.

As a typical condition of ECT, as shown in Fig. 1(a), a voltage of 100 V was applied between a pair of electrodes place on the tempora. Electric potentials were set to 77 nodes for each electrode. The equations for calculating current distributions in ECT were previously described [4].

The figure-eight coils used for the TMS model consisted of a pair of circular coils with diameters of 50, 75, and 100 mm. Fig. 1(b) shows the TMS model with the 75-mm coil. To investigate dependence of eddy current distributions on the coil position, the coil was moved around the center of the head O with an angle θ, from the vertex toward the forehead [$\theta = 30°$ in Fig. 1(b)]. Both of the coil elements were moved along the surface of the head. Fig. 1(c) presents waveform of the coil current $I(t)$ in TMS. From $t = 0$ to $t = T$, the waveform is given by $I(t) = I_0 \sin(2\pi t/T)$, where I_0 is the peak intensity and T is the pulse width. In this study, we used a constant pulse width of 240 μs. Magnetic field $\mathbf{B}$ was calculated using the Biot-Savart's low. The vector potential $\mathbf{P}$ of the eddy currents $\mathbf{j}_T$ was defined as

$$\mathbf{j}_T = \nabla \times \mathbf{P}. \tag{1}$$

The eddy current distribution was obtained by solving the following:

$$\nabla^2 \mathbf{P} = \sigma \frac{\partial \mathbf{B}(\mathbf{r}, t)}{\partial t}. \tag{2}$$

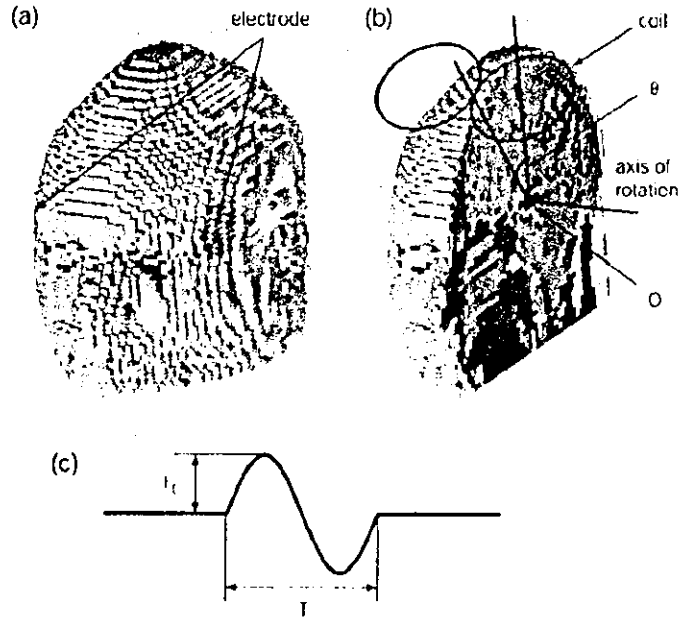

Fig. 1. (a) Numerical model of ECT. A voltage of 100 V was applied between a pair of electrodes located at the tempora. (b) Numerical model of TMS. Pulsed electric currents were applied to a coil placed on the scalp. (c) Waveform of the coil current in TMS.

The difference in current distributions between ECT and TMS was evaluated using the following two performance functions:

$$F_1 = \frac{1}{V_0}\int_{\text{brain}} (|\mathbf{j}_E| - |\mathbf{j}_T|)^2\, dV \tag{3}$$

$$F_2 = \frac{1}{V_0}\int_{\text{brain}} \Big(|j_{E,x} - j_{T,x}| + |j_{E,y} - j_{T,y}| + |j_{E,z} - j_{T,z}| \Big) dV \tag{4}$$

where V_0 is the volume of the brain and $\mathbf{j}_E$ is the current in ECT. Integration was performed over the elements included in the brain. Because these functions increase with the difference in current distributions between ECT and TMS, the optimum condition of TMS gives minimum values of the functions.

III. Results and Discussion

Fig. 2(a)–(c) shows current distributions in ECT on coronal, sagittal, and transversal slices. The scalp under the electrodes located on the tempora exhibited the maximum current density 876 A/m^2. Because the skull had a relatively low conductivity, a significant amount of the current flowed along the scalp and did not penetrate the skull. Because the electrodes were located on the opposite sides of the brain, the injected currents distributed among the brain and did not significantly attenuate at the deeper regions. Fig. 2(d) displays current distributions on the surface of the brain (the gray matter, the white matter, and the cerebellum). The frontal cortex exhibited higher current densities. The maximum current density within the brain was 69 A/m^2.

Fig. 3(a)–(c) shows current distributions in TMS on coronal, sagittal, and transversal slices calculated for coil position of $\theta = 30°$, coil diameter of 75 mm, and coil current of 150 kA.

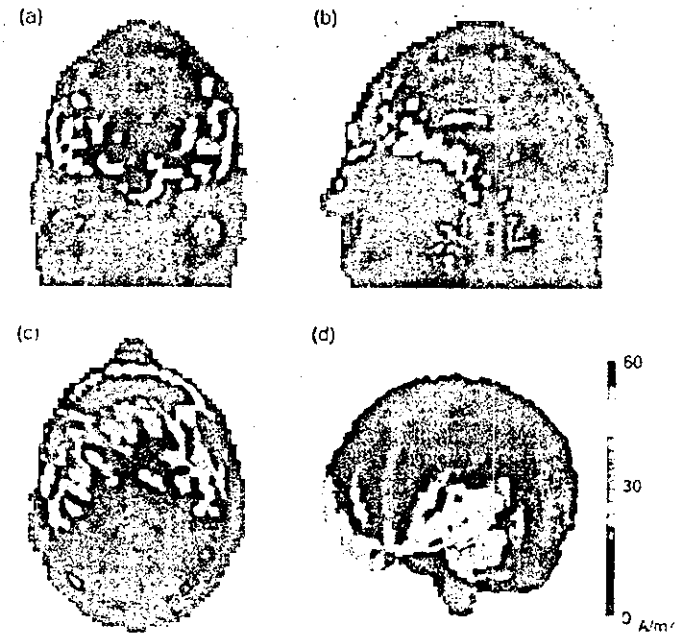

Fig. 2. Current distributions in ECT represented in (a) coronal, (b) sagittal, and (c) transversal slices, and (d) the brain surface.

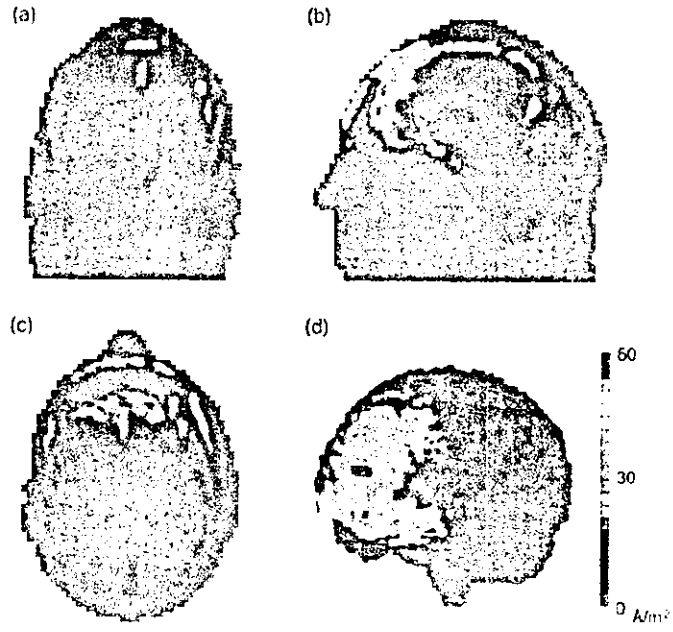

Fig. 3. Current distributions in TMS represented in (a) coronal, (b) sagittal, and (c) transversal slices, and (d) the brain surface.

Fig. 3(d) shows current distributions on the surface of the brain. The brain surface under the intersection of the coil exhibited high current density values. The maximum current density within the brain was 82 A/m^2, which was comparable to that of ECT. Because the model had a homogeneous magnetic permeability, the magnetic fields were not disturbed by tissues and efficiently induced eddy currents in the brain. Relatively weak currents flowed in the scalp. Because the pain during stimulation is perceived mainly on the scalp, TMS causes weaker pain than ECT. The scalp under the coil exhibited the maximum current density 158 A/m^2, which was much smaller compared to the case of ECT. Magnetic field generated by

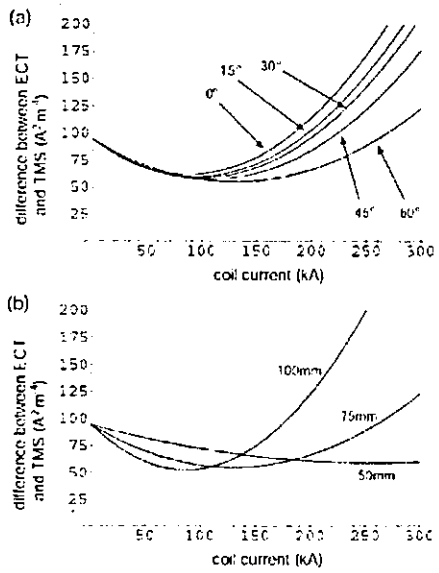

Fig. 4. Difference in current distributions between ECT and TMS evaluated by a performance function F_1 (3). (a) Dependence of the function on the coil current and the coil position. The coil position is represented by the angle θ from the vertex. (b) Dependence of the function on the coil current and the coil diameter.

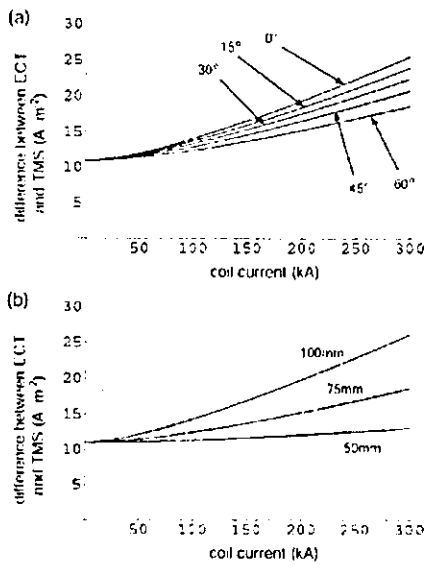

Fig. 5. Difference in current distributions between ECT and TMS evaluated by a performance function F_2 (4). (a) Dependence of the function on the coil current and the coil position. (b) Dependence of the function on the coil current and the coil diameter.

the coil attenuated with an increase of distance from the coil. Eddy current density exhibited higher values on the surface and gradually decreased with depth from the surface. Current densities at the center of the brain was below 10 A/m^2. Coils with smaller diameters induced more localized eddy currents and exhibited more significant attenuation in deep regions. A certain amount of current flowed in the side of the brain because the two coil elements were positioned in a horizontal orientation.

Fig. 4(a) shows dependence of the performance function F_1 on the coil current and the coil position. A coil of 75-mm diameter was used and the coil angle θ was varied from 0° to 60°. The minimum value of F_1 decreased with an increase of the coil angle. At larger coil angles, the coil approached to the electrode positions in ECT, and generated currents in the forehead. In our previous calculation, a coil was placed on the vertex ($\theta = 0$); however, the results above suggested that a larger coil angle could give a better result. The coil angle was limited to 60° in order to avoid interference between the coil and the nose. In the case of $\theta = 60°$, the performance function had a minimum value of 55 A^2/m^4 at a coil current of 130 kA which corresponded to a magnetic flux density of 2.2 T at the center of each coil element.

Fig. 4(b) shows dependence of the performance function F_1 on the coil current and the coil diameter. Data were presented for coil diameters of 50, 75, and 100 mm with a constant coil position of $\theta = 60°$. The minimum value of F_1 decreased with an increase in the coil diameter. This was because eddy currents induced by larger coils distributed in larger and deeper areas. Thus, the use of larger coils is desired to obtain similar current distributions to ECT. In the case of 100-mm diameter, the performance function had a minimum value of 53 A^2/m^4 at a coil current of 87 kA, which corresponded to a magnetic flux density of 1.1 T. In a previous study by Nadeem *et al.*, a current of 7.7 kA was applied to a ten-turn coil [5], while we obtained the optimum coil current of 87 kA for the single turn coil of 100-mm diameter. The optimum condition in our study is similar in the resulting magnetic field to the previous study because, in both cases, the product of the coil current and the number of turns is approximately 80-kA turn.

Fig. 5 shows difference in current distributions between ECT and TMS evaluated by the performance function F_2. In the case of this performance function, we could not obtain an optimum condition of TMS because the function had minimum values at approximately 0 kA for all coil positions and all coil diameters. The function F_2 was designed for comparing both the intensity and direction of currents, while the function F_1 was designed for comparing only the intensity of currents. ECT gives rise to electric currents in the direction perpendicular to the brain surface. TMS induces eddy currents in the direction parallel to the brain surface. This difference in the direction of currents caused a monotone increase in the function F_2.

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