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SPINAL EVOKED POTENTIALS FOLLOWING TRANSCRANIAL
MAGNETIC STIMULATION

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Abstract : Motor evoked potentials by magnetic stimulation is less invasive and causes no pain as opposed to high current electric stimulation. However, the distribution of the magnetic field generated by the round coil has not been fully studied. In this report, we mapped the extent of the magnetic induction flux density, and then the evoked potentials from the spinal cord were investigated by transcranial magnetic stimulation. We also examined the origin of the evoked potentials obtained by the magnetic stimulation. The following results were obtained. The magnetic induction flux density was at its maximum at the edge of the coil. The potentials consisted of a first negative wave and subsequent multiphasic waves. The first negative wave was similar to a response of the subcorticospinal tract in the lower brain stem, while the subsequent multiphasic waves were similar to those of the pyramidal tract. Although magnetic stimulation has certain advantages over electric stimulation, several problems remain to be solved for the monitoring of motor functions in the clinical settings.

Key words : magnetic stimulation, spinal evoked potential, motor function

INTRODUCTION

Several evoked potentials, such as the somatosensory evoked potentials, the auditory brain stem response and the visual evoked potentials, have been widely utilized for the evaluation of cerebral functions. All such potentials are utilized for the evaluation of sensory pathways, however, in 1980, Merton *et al.*¹⁾ measured motor evoked potentials for the evaluation of motor functions using high intensity

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transcranial electric stimulation over the motor cortex. This method, however, has not been widely accepted because of severe pain due to the high intensity electric current. In 1985, Barker *et al.* first reported a magnetic stimulation method²⁾ which caused no pain when stimulating over the scalp³⁻¹⁰⁾.

Magnetic stimulation is based on the following principle: when a discharge current passes through a round coil, the magnetic field around the coil changes rapidly, an eddy current is induced, and thus stimulates neurons. In order to obtain an accurate measurement of the intensity, focus, and extent of the stimulation, the intensity and direction of the magnetic induction flux density generated by the coil were measured using a gauss meter. Evoked potentials from the spinal cord by transcranial magnetic stimulation were also measured. The potentials were compared with those obtained by direct cortical electric stimulation to assess the origin of the potentials. The possibility of evaluating motor functions by magnetic stimulation was discussed.

MATERIALS AND METHODS

Measurement of magnetic induction flux density

We used an apparatus (NEC Sanei Instruments) for magnetic stimulation with the following characteristics: maximum voltage, 1,200 V; maximum coil current, 12.0 KA; maximum magnetic force, 1.5 T; rising time, 200 μ s. The coils, 6 cm in diameter and 9.0 μ H in inductance or 12 cm and 3.0 μ H, were composed of an 8 turns-copper plate. A 10 A constant current was passed through a round coil of either 6 or 12 cm in diameter and the magnetic induction flux density generated by the coil in the direction of the X- and Y-axis was measured using a gauss meter (F.W. Bell, 6400). The Y-axis corresponded to the central axis of the coil, and the X-axis to a line perpendicular to the Y-axis. Measurements were made at the center of the coil, the midpoint between the center and the inner edge of the coil, the inner and outer edges of the coil, and then at points 2 and 4 cm away from each of the measured points, respectively. In the central axis of the coil, this density was measured every 1 cm away from the coil.

Evoked potentials in cats

We measured the evoked potentials from the spinal epidural space following transcranial magnetic stimulation. As a circular coil used for magnetic stimulation stimulated various sites of the brain simultaneously, it was unlikely that the evoked potentials originated from a single neural pathway. Accordingly, 3 sites were arbitrarily selected, and we stimulated those sites by direct electric stimulation. The potentials evoked by magnetic stimulation were compared with those by electric stimulation to determine the origin of the potentials.

Thirty cats, 3 to 4 kg in weight, were used. They were anesthetized with 25 mg/kg of intraperitoneal sodium pentobarbital, intubated and connected to a respi-

rator and breathing was inactivated with pancuronium bromide. A catheter was inserted in the groin artery to monitor arterial blood pressure and blood gases. Respiration was controlled to maintain PaO_2 and PaCO_2 at levels of 90 to 100 mm Hg and 35 to 45 mm Hg, respectively. The rectal temperature was maintained at 37 to 38°C. Conditions for magnetic and electric stimulation were as follows:

1. Magnetic stimulation

Twenty cats were used for the experiments. The center of the round coil, 6 cm in diameter, was placed over the scalp in the midline 1 cm rostral from a line between the right and left external auditory canals. The stimulation intensity was 800 V. Ten signals were averaged. The stimulating coil was reversed after each averaging to eliminate the polarity artifacts of the stimulation.

2. Electric stimulation

Fifteen cats were used. After craniotomy, the dura mater was incised to expose the cortex. The cerebral motor cortex was located under the anterior edge of the coil, and the cerebellar vermis and medulla oblongata was located under the posterior edge of the coil. Accordingly, electric stimulation was applied to the 3 sites, the cerebral motor cortex, cerebellar vermis and medulla oblongata (Figure 1). Two silver ball electrodes (NEC Sanei Instruments, 45182) were placed 5 mm apart on each site. Bipolar stimulation (duration, 100 μs ; interval, 10 Hz; summation, 100 times) was applied. Stimulation intensities were 10 to 15 mA for the motor cortex, 1 to 4 mA for the cerebellar vermis and 1 to 2 mA for the medulla oblongata.

In six cats, we recorded the evoked potentials at 4 points by moving the electrode rostrally at intervals of 1 cm, in order to calculate the conduction velocity.

Method

Fig. 1. Stimulation site. a: motor cortex, b: cerebellum, c: medulla oblongata.

Fig. 2. Cross section of the spinal cord at C2 level. The pyramidal tract exists in the dorsal half of the spinal cord.

In five cats, the dorsal half of the spinal cord, including the pyramidal tract which is involved in motor functions (Figure 2), was transected at the C2 level. Then transection of the ventral half was added in order to examine the changes after total transection of the spinal cord. The recording apparatus was a bipolar catheter electrode (Unique Medical), placed on the spinal epidural space at Th7 on the midline. The caudal part of the electrode was used as a cathode (distance between the anode and cathode, 15 mm). Evoked potentials were amplified through a 3 to 3,000 Hz filter, and recorded with a signal processor (NEC Sanei Instruments, 7T17).

RESULTS

Measurement of magnetic induction flux density

When a 10 A current, which corresponds to the intensity used for this study, passed through the coil, the magnetic induction flux density generated at angles between the generated directions and X-axis at the center of the coil, the midpoint between the center and inner edge of the coil, and the inner and outer edges of the coil, was 0.86 T/89.3°, 0.93 T/88.7°, 1.07 T/65.5° and 1.09 T/−9.8° with the small coil, and was 0.87 T/88.7°, 0.95 T/80.0°, 1.07 T/54.4° and 1.10 T/−9.5° with the large coil, respectively. The density was approximately 1.3 times larger at the edge than at the center of the coil. Furthermore, the density decreased with increasing distance from the coil. The density in the Y-axis direction at the central axis decreased with every 1 cm step away from the coil, such as 0.92 T, 0.55 T, 0.32 T, 0.21 T and 0.13 T with the small coil and 0.89 T, 0.72 T, 0.56 T, 0.42 T, 0.31 T, 0.24 T and 0.10 T with the large coil. The density decreased more rapidly with the small coil than with the large coil (Figure 3).

Magnetic field generated by the coil

Fig. 3. a : The magnetic induction flux density was maximum at the edge of the coil.
b : The density decreased with increasing distance from the coil.

Evoked potential

Fig. 4. The potentials following magnetic stimulation consisted of the first negative wave (black arrow-head) and subsequent multiphasic waves (white arrow-heads). The subsequent multiphasic waves following magnetic stimulation were with those following electric stimulation of motor cortex. The former was a latency of 2 to 6 msec, the latter was 3 to 8 msec. The peak latency of the first negative wave was almost equal to that of cerebellar or medulla oblongata stimulation.

Fig. 5. After transection of the dorsal half of the spinal cord, the multiphasic waves (arrow-heads) by magnetic stimulation and potentials by electric stimulation of motor cortex disappeared, whereas the first negative wave by magnetic stimulation and those by electric stimulation of the cerebellum and medulla oblongata did not change. After total transection of the spinal cord, the first negative waves disappeared.

Evoked potentials in cats

1. Magnetic stimulation

In 17 of 20 cats, a negative wave of approximately $90\ \mu\text{V}$ in amplitude was recorded with a peak latency of 1.71 ± 0.37 msec (mean $\pm$ SD, $n=17$), and the conduction velocity was 112.1 ± 7.2 m/sec. Furthermore, multiphasic negative waves of approximately $20\ \mu\text{V}$ in amplitude with a latency of 2 to 6 msec were recorded in 10 cats (Figure 4). In 5 cats with transection of the dorsal half of the spinal cord, the amplitude of the first negative wave decreased by $14.3 \pm 6.3\%$, and the multiphasic waves disappeared. The first negative wave disappeared after total transection of the spinal cord (Figure 5).

2. Electric stimulation

1) Cerebral motor cortex

Tetraphasic to octophasic waves were observed with a latency of 3 to 8 msec when the motor cortex was electrically stimulated. The peak latency of the initial negative wave was 3.56 ± 0.46 msec, and the conduction velocity was 50.1 ± 4.3 m/sec (Figure 4). All waves disappeared after total transection of the spinal cord (Figure 5).

Fig. 6. Cerebellar stimulation. When stimulation intensity was increased to 3 mA or higher, the negative wave was observed with a latency of 1.83 msec.

Fig. 7. The conduction velocities of both potentials were almost the same. They were equal to the conduction velocity of the subcorticospinal tracts.

2) Cerebellar vermis

Biphasic to quadriphasic waves were observed with a latency of 2 to 4 msec when weak electric stimulation was applied (Figure 6). When the vermis was stimulated at a 3 mA or higher current, a negative wave of approximately $80 \mu\text{V}$ in amplitude was obtained with a peak latency of 1.83 ± 0.30 msec and the conduction

velocity was 110.7 ± 9.9 m/sec (Figure 4 and 6). The amplitude of the negative wave, when recorded using 3 mA or higher current stimulation, decreased by $17.4 \pm 6.5\%$ by transection of the dorsal half of the spinal cord, and all waves disappeared after total transection of the cord (Figure 5).

3) Medulla oblongata

A negative wave of approximately $90 \mu\text{V}$ in amplitude was obtained with a peak latency of 1.73 ± 0.33 msec and the conduction velocity was 114.4 ± 8.8 m/sec (Figures 4 and 7). The amplitude of the negative wave decreased by $19.1 \pm 7.9\%$ after transection of the dorsal half of the spinal cord and all waves disappeared after total transection of the cord (Figure 5).

DISCUSSION

In magnetic stimulation, neurons are stimulated by an eddy current which is generated by rapid changes in the magnetic field around the coil.¹¹⁾ In order to use this technique for clinical cases, it is essential that the intensity and site of stimulation is well understood. Therefore, we attempted to measure the magnetic induction flux density, which is proportional to the intensity of an eddy current. The results showed that the density was maximal not at the center but at the edge of the coil. This means that the edge of the coil should be used to provide effective stimulation. The magnetic induction flux density decreased rapidly with increasing distance from the coil. As the decrease in the density was smaller with the large coil, the large one is more appropriate for stimulation of the deeper areas of the brain.

When stimulating the cerebral motor cortex through the scalp, the skull, dura mater and spinal fluid which lie between the scalp and cortex are magnetized, but the intensity of the magnetic force is less than $10^{-9} \text{ T}^5)$. This level is extremely low compared with 1 to 2 T generated by magnetic stimulation, and is therefore negligible. Accordingly, the degree of change in magnetic induction flux density by transcranial magnetic stimulation is almost equal to that measured in the air by a gauss meter. The distance between the coil and motor cortex is approximately 2 cm in human, and the magnetic induction flux density in the motor cortex decreases to approximately 60% using a round coil of 12 cm in diameter. When electric stimulation is applied through the scalp, the current generated on the motor cortex decreases to about 1/30th of its initial value¹²⁾, because of the skull, which has high electrical resistance. Magnetic stimulation, therefore, is more effective than electric stimulation when stimulating transcranially.

Evoked potentials were recorded from the spinal cord following transcranial magnetic stimulation. Magnetic stimulation was not highly localized and it was likely that broader areas of the brain were stimulated. Accordingly, we stimulated electrically 3 arbitrarily chosen sites to which the magnetic force definitely reached, and the evoked potentials thus obtained were compared with those by electric

stimulation.

If evoked potentials can be recorded from the peripheral muscles by transcranial magnetic stimulation during animal experiments or surgical operations, the recorded potentials are motor evoked potentials and thus allow for the monitoring of motor functions. However, anesthesia, especially inhalation anesthesia, has a strong inhibitory effect on synaptic conduction¹³, and it is difficult to record the evoked muscle action potentials during operations. Recording electrodes were therefore placed on the spinal cord, where the anesthetic effect has a minimal influence.

Potentials following magnetic stimulation consisted of a negative wave (latency, 1.71 ± 0.37 msec; conduction velocity, 112.1 ± 7.2 m/sec) and subsequent multiphasic waves. The amplitude of the initial negative wave was distinctly high enough for recording, but the multiphasic waves were of low amplitude, so the polarity of the stimulating coil was altered in order to confirm the waveforms.

When electric stimulation was applied to the cerebral motor cortex, multiphasic waves were observed with a latency of 3 to 8 msec. These waves, consisting of a negative wave with latency of 3.56 ± 0.46 msec and conduction velocity of 50.1 ± 4.3 m/sec (D-response) and subsequent waves (I-response), were so-called motor evoked potentials¹⁴. Potentials obtained by electric cerebellar stimulation at 1 to 2 mA were thought to be cerebellar evoked potentials originating from the cerebellum, because of their characteristic multiphasic potentials with a latency of 2 to 4 msec and low amplitude^{15,16}. When the stimulation intensity was increased to 3 mA or higher, a negative potential was observed with a latency of 1.83 ± 0.30 msec and a conduction velocity of 110 ± 9.9 m/sec. This negative potential was obtained by a weak electric stimulation of the medulla oblongata, at 1 mA. For this potential, the latency was 1.73 ± 0.33 msec and the conduction velocity was 114.4 ± 8.8 m/sec. The latency and conduction velocity of the two negative waves were almost the same. The negative waves observed when the cerebellum was stimulated at 3 mA or higher were thought to originate from the medulla oblongata. A conduction velocity of 100 to 120 m/sec was twice as fast as that of the pyramidal tract, and was similar to the velocity of the subcorticospinal tracts, 90 to 150 m/sec¹⁷.

Based on the above results, the first negative wave and the subsequent multiple waves obtained by magnetic stimulation were compared with evoked potentials obtained by electric stimulation.

The peak latency of the negative wave after magnetic stimulation was 1.71 msec, and the multiphasic motor evoked potentials were observed with a latency of 3 to 8 msec after electric stimulation. Therefore, these two waves had different peak latencies and conduction velocities. The first negative wave after magnetic stimulation was not considered to reflect the pyramidal tract volley. On the other hand, the negative wave after either magnetic or electric stimulation of the medulla oblongata had almost the same latency and conduction velocity, suggesting that these waves might originate from the same tracts. After transection of the spinal cord, negative waves following magnetic stimulation or electric stimulation of the

medulla oblongata or cerebellum showed similar changes. When the dorsal half of the spinal cord was transected, only a slight decrease in amplitude was observed, and then all waves disappeared following ablation of the ventral half of the cord. These results suggest that the majority of the negative waves reflect the neural conduction in the ventral half of the spinal cord. The subcorticospinal tracts pass mainly through the ventral half of the spinal cord at the C2 level, at which transection experiment was performed in this study. The conduction velocity of these waves was almost equal to that of the subcorticospinal tract. Thus the first negative wave following magnetic stimulation was thought to originate from the subcorticospinal tracts in the medulla oblongata.

Subsequent multiphasic waves after magnetic stimulation were compared with the evoked potentials after electric stimulation of the motor cortex. The former was observed with a latency of 2 to 6 msec, the latter was 3 to 8 msec, suggesting that multiphasic waves of magnetic stimulation are motor evoked potentials. The transection of the dorsal half of the spinal cord, where the pyramidal tract exists, showed that the multiphasic waves as well as motor evoked potentials disappeared. Besides the pyramidal tract, however, other pathways, such as the posterior funiculus and the spinocerebellar tract, lie in the dorsal half of the spinal cord. These potentials following magnetic stimulation are thus complex potentials thought to originate from these various pathways in orthodromic and antidromic manners. This complexity indicates that the pyramidal tract cannot be monitored by the evoked potentials following magnetic stimulation.

In magnetic stimulation, an eddy current is the actual stimulus, while in electric stimulation, a current running between an anode and a cathode electrode is the stimulus. Because the characteristics of the stimulus are different between magnetic and electric stimulation, it is impossible to compare precisely the evoked potentials obtained by the two different methods. Nevertheless, the present study showed that the first negative wave after magnetic stimulation might originate from the subcorticospinal tract in the lower brain stem and the subsequent multiphasic waves might be the evoked potentials reflecting the activity in the dorsal half of the spinal cord which may well involve the pyramidal tract. The subsequent multiphasic waves were, however, of low amplitude and unstable, so that it is difficult to monitor the pyramidal tract during surgical operation using this technique.

If potentials are obtained from a peripheral nerve or muscle, the obtained evoked potentials reflect motor functions when the stimulus is applied to a large area including the motor cortex. However, if potentials are obtained from the spinal cord, it must be clarified that the generator is localized to the pyramidal tract. If the magnetic stimulation can be localized to the motor cortex, motor evoked potentials can be recorded from the spinal cord, but it is impossible, at present, to confirm this idea in practice. Attempts have been made using a figure-eight shaped coil, in order to apply magnetic stimulation to a restricted area⁷⁾, but such work remains experimental. Clearly, a large number of problems are yet to be solved

before magnetic stimulation can be put to use in clinical applications. However, the present study would indicate that at least the descending volleys can be consistently recorded by the spinal epidural electrode, when transcranial magnetic stimulation is applied and the recorded potentials certainly reflect the integrity of the neural structures above the recording site.

CONCLUSION

We measured the distribution of magnetic induction flux density generated by a coil, and the spinal evoked potentials generated by transcranial magnetic stimulation were correlated to the direct current motor cortex stimulation in cats. The following results were obtained. 1. The magnetic induction flux density was maximum at the edge of the coil, and the density decreased rapidly with increasing distance from the coil. 2. In cats, the first negative wave recorded from the spinal cord following transcranial magnetic stimulation originated from the subcorticospinal tract in the medulla oblongata, and the subsequent multiphasic waves are thought to reflect activities in the dorsal half of the spinal cord, where the pyramidal tract, posterior funiculus, and other descending and ascending tracts exist. These waves were not stable, and did not reflect the pure pyramidal tract conduction. Therefore, magnetic stimulation cannot be considered useful for the evaluation of corticospinal motor functions. Yet, this method may serve an index of the global functions of the descending motor tracts.

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