previous ECoG study, in which two classes of actual and imagined movements (hand and tongue) were predicted with an average of 94% and 77% correct, respectively (Shenoy et al., 2008).

In Fig. 5b, the performance of all patients is compared among the electrode groups. A kappa coefficient between the performed and the decoded movement classes was introduced as a measure for relative performance that compensates for the difference between the 2-class and the 3-class tasks (see Subjects and methods). Comparison of the electrode groups revealed that even though 'sulcal M1' had only four electrodes, it achieved a relatively high decoding accuracy, similar to the accuracy obtained using all electrodes (20 to 28) or all gyral electrodes (12 to 20). When compared with 'sulcal S1', 'gyral (4) – mean of all combinations', and 'gyral (4) – highest F', each of which had equally-sized electrodes, 'sulcal M1' showed significantly better

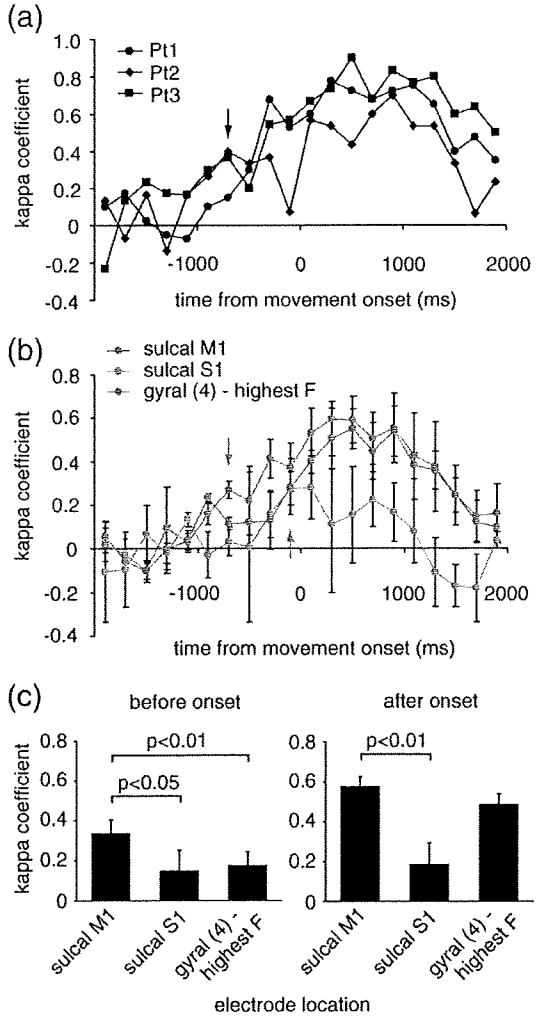

Fig. 6. Time dependence of classification. For patients 1–3, classification was performed with the ECoG of a short time duration (200-ms without overlap). a: For the three patients, the kappa coefficients obtained using 'all' electrodes were plotted against each time duration. An arrow indicates the earliest time point reaching an above-chance decoding performance for two of the three patients (binomial test, $p<0.01$). b: The time course of the performance was compared between three electrode groups ('sulcal M1', orange; 'sulcal S1', blue; 'gyral (4) – highest F', green). The mean of the kappa coefficients for all patients were plotted against the time from movement onset (error bar, standard error). The classification performance of more than two patients exceeds the chance level at an arrow of the same color (binomial test, $p<0.01$). c: The kappa coefficients for the time windows before or after the movement onset were compared between the three electrode groups by a paired t-test (before onset, −500 to 0 ms; after onset, 0 to 500 ms). The mean of the kappa coefficients were plotted among the groups (error bar, standard error).

decoding performance (paired t-test vs. 'sulcal S1', $p<0.01$; vs. 'gyral (4) – mean of all combinations', $p<0.01$; vs. 'gyral (4) – highest F', $p<0.05$). Even the best combination of four electrodes ('gyral (4) – best combination') did not outperform 'sulcal M1' (no significant difference). These results indicate that the intrasulcal ECoG on M1 provided useful signals for the decoding of upper limb movements.

Time course of decoding accuracy

The time course of decoding accuracy was examined for patients 1–3, who performed the execution task. The ECoG signals of −2000 ms to +2000 ms from movement onset were divided into 200-ms time windows without overlap (a total of 20 time windows). In each time window, the decoding performance was calculated for the four electrode groups ('all', 'sulcal M1', 'sulcal S1', and 'gyral (4) – highest F').

Fig. 6a shows the results obtained using 'all' electrodes for the three patients. The kappa coefficients of all patients gradually increased before movement onset and peaked after onset. Interestingly, even at 700 ms before movement onset (arrow in Fig. 6a), the classification performances of the two patients (patients 2 and 3) exceeded the chance level (binomial test, $p<0.01$). Thus, the movement class was predicted even before the actual movement using ECoG signals from the sensorimotor areas.

The time course of decoding performance was compared between the equally-sized subgroups of electrodes: 'sulcal M1', 'sulcal S1' and 'gyral (4) – highest F'. As shown in Fig. 6b, the kappa coefficients for 'sulcal M1' and 'gyral (4) – highest F' gradually increased before movement onset and peaked around 500 ms, while those for 'sulcal S1' remained relatively small throughout the time course. The time window in which at least two of the three subjects began to show significant decoding performance was found at −700 ms and −100 ms for 'sulcal M1' and 'gyral (4) – highest F', respectively (binomial test, $p<0.01$; orange and green arrows). In contrast, 'sulcal S1' rarely exceeded the chance level in individual patients. When the kappa coefficients for all the time windows before movement onset (within the range of −500 to 0 ms) were compared between the three electrode groups, those of 'sulcal M1' were significantly higher than those of 'sulcal S1' and 'gyral (4) – highest F' (paired t-test, $p<0.05$ and $p<0.01$, respectively) (Fig. 6c, left). However, the difference between 'sulcal M1' and 'gyral (4) – highest F' became less prominent after movement onset (Fig. 6c, right). These results suggest that intrasulcal electrodes on M1 can provide reliable signals to infer upper limb movements earlier than other electrodes, even before an actual movement is performed.

Discussion

In the present study, we investigated the properties of the signals from intrasulcal electrodes placed on M1, in comparison with other electrodes, in terms of inferring upper limb movements. To our knowledge, no previous human studies have presented data from intrasulcal ECoG obtained during execution and imagination of upper limb movements. First, we showed, by univariate analysis, that the signals of 'sulcal M1' varied significantly across movement classes. Then, we compared the performance of movement classification between gyral and intrasulcal ECoGs, and found that intrasulcal electrodes on M1 provided more reliable signals than equally sized electrodes from other areas. Finally, superior performance of intrasulcal electrodes on M1 was found even before movement onset. These results strongly suggest the usefulness of intrasulcal electrodes on M1 for BCI.

Importance of M1 for movement classification

Several previous studies proved the importance of the motor cortex to infer movement with spike activities and ECoG. Georgopoulos et al.

and other groups have shown that the firing of small ensembles of neurons within the M1 arm area carries information about arm position and velocity for both monkey models (Georgopoulos et al., 1986; Serruya et al., 2002; Wessberg et al., 2000) and humans (Hochberg et al., 2006; Truccolo et al., 2008). The information about arm position and velocity can be inferred by local field potential recorded from the monkey motor cortex (Andersen et al., 2004; Mehring et al., 2004; Rickert et al., 2005) and ECoG data recorded from the human hand/arm motor cortex (Pistohl et al., 2008; Schalk et al., 2008). The present study compared the performance in classifying three classes of executed or imagined simple upper limb movements among ECoGs on the sensorimotor cortex. Although the movement types performed in this work were fairly simple ones compared to those used in previous reports (Taylor et al., 2002), the comparison of performance across electrode groups revealed which part of the ECoG on the sensorimotor cortex contains relatively reliable information for neural decoding. Our results demonstrated that intrasulcal M1 electrodes are particularly informative. However, the performance of decoding could vary with which movements were performed. Further investigation on intrasulcal ECoG is necessary to reveal the optimal ECoG location for different kinds of movement.

Imaginary movement and implication for practical BCI

In this study, decoding performance was evaluated with the ECoG signals during both executed and imagined upper limb movements. Although the differences in task types could affect the results, the results of both types of movement were similar enough to examine together in this study. According to the results of the univariate analysis, the *F*-value distributions were similar among all patients (Fig. 4). For both executed and imagined tasks, *F*-values were high at the sulcal M1 and adjacent gyral ECoG electrodes; the statistical property of the signals was revealed to be similar between actual and imagined movements. Moreover, in a previous study of functional MRI of spinal cord-injured patients, an attempt to move a paralyzed limb resulted in similar macroscopic activation pattern in the motor cortex as did real movements of the same limb in healthy subjects (Hotz-Boendermaker et al., 2008; Shoham et al., 2001). This result is comparable with our findings, because our patients performed the imagined movements with limbs paralyzed due to brachial plexus avulsion, thought to be similar to the spinal cord-injury in the way they attempt to move a paralyzed limb. With this evidence, we examined the ECoG data from both tasks together. Performance of imagined movements could vary among subjects, though stable performance of decoding is required to realize practical BCI for paralyzed patients. Further investigation of imagined movement in paralyzed patients is necessary to understand the sulcal M1 ECoG in practical BCI.

Decoding features

As a feature of decoding, we used sMCP, a sliding average of ECoG signals. The physiological origin of this feature is a matter of speculation, but the values seem to have a slow component of motor-related cortical potential (MRCP). The MRCP is a trial average of cortical potential by time-locked movements; it is observed over the M1 during motor preparation and execution, peaking close to movement onset and lasting for several seconds (Satow et al., 2003). These same properties were observed in the feature values used in our study (Fig. 2). Notably, gradual elevation of feature values during motor preparation could be used for classification before onset of movement.

The low frequency component of the signal has already been reported to be suitable for inferring human upper limb movements on a trial-by-trial basis by ECoG (Pistohl et al., 2008; Schalk et al., 2007) and by MEG (Waldert et al., 2008). In general, the high frequency components of the signals have lower signal-to-noise ratio than the slower components, and thus may not be suitable for trial-by-trial analysis. Nevertheless, the high frequency component of the signal has the potential to improve the decoding performance. Many previous studies have shown that the movement-related changes involve multiple frequency bands (Crone et al., 1998a,b; Leuthardt et al., 2004; Schalk et al., 2007). The amplitudes of higher frequency bands were suggested to provide additional information about movements (Leuthardt et al., 2004; Pistohl et al., 2008; Schalk et al., 2007). Therefore, the optimal choice of frequency bands for the decoding of the movement still deserves further investigation.

Implications for non-invasive techniques

The superior performance of intrasulcal ECoG in comparison with gyral ECoG has an implication for the interpretation of the results obtained using noninvasive techniques, e.g. MEG and EEG. MEG is thought to be more sensitive to sulcal activity (current sources parallel to the scalp surface) than to gyral activity (current sources perpendicular to the scalp surface) (Hämäläinen et al., 1993), while EEG is thought to be more sensitive to gyral activity, or rather directionally unspecific. Thus, MEG may have a relative advantage for decoding movement-related signals represented in the sulcal M1. Consistent with this, it has been reported that the direction of the hand movement can be better decoded by MEG than by EEG (Waldert et al., 2008).

Conclusions

Overall, the present findings demonstrate the high performance of intrasulcal ECoG on the M1 in classifying executed and imagined upper limb movements in humans. We propose that the use of intrasulcal ECoG on the M1 along with gyral ECoG will improve the neural decoding ability of upper limb movements and realize a more practical BCI system. The current data justify further research on intrasulcal ECoG for an understanding of the human sensorimotor cortex and proficient operation of the human BCI system.

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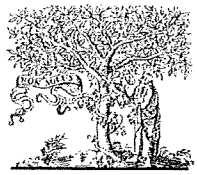

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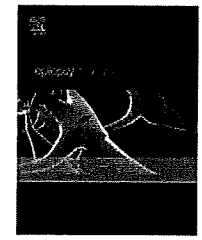

Movement induces suppression of interictal spikes in sensorimotor neocortical epilepsy

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Summary Epileptic activities are known to be modulated by cortical excitability, which is altered with normal brain functioning such as movement. However, the relationship between the epileptic activity and movement has not been well studied. Here, we investigated movement-induced modulation of interictal spikes to reveal the relationship between epileptic activity and the movement-induced modulation of cortical activity. Two patients (three cases) with focal cortical dysplasia (FCD) of the pre- and/or post-central gyrus performed voluntary movements of their hands or mouths. During the movement, the interictal spikes of the sensorimotor cortex, which were measured by electrocorticograms (ECoG), were significantly reduced. This reduction strongly correlated with the event-related desynchronization (ERD) of the cortical oscillatory activity at the lower frequency bands (<25 Hz) during movement. The epileptic activity was suggested to be modulated by the movement, which correlates with the ERD of the cortical oscillatory activity.

Introduction

Voluntary movement is associated with an increased excitability of the primary motor cortex (M1) (Chen et al., 1998), which is linked to the power spectral changes of electrocorticograms (ECoG) (Pfurtscheller, 1992). Notably, event-related desynchronization (ERD) of alpha and beta rhythms correlates with cortical excitability (Leocani et al., 2001; Neuper and Pfurtscheller, 2001; Rau et al., 2003). The cortical excitability is also associated with pathological states of the brain such as epileptogenesis. Some investigations in animals and humans have shown that modulation of the cortical excitability have a modulatory effect on epileptic activity (Chen et al., 1997; Matsumoto et al., 2005).

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Though, the relationship between the epileptic activity and the modulation of cortical excitability during movement has not been well studied.

In this study, we investigated the modulation of epileptic activity associated with the movement-induced alteration of cortical activity. In three cases of intractable epilepsy with focal cortical dysplasia (FCD) of the pre- and/or post-central gyrus, the modulation of the epileptic activity during movement was evaluated by counting interictal spikes recorded by ECoG. The power spectral changes of ECoG were analyzed to evaluate cortical activity. A relationship between the modulation of interictal spikes and the power spectral changes of ECoG was analyzed.

Methods

Subjects and electrode implantation

The two patients (representing three cases) in this study were suffering from medically intractable epilepsy with FCD of the pre- and/or post-central gyrus (Fig. 1). The clinical profiles of the patients are summarized in Table 1. Patient 1 was a 31-year-old male suffering frequent medically refractory seizures immediately after his birth. His seizure consisted of a rapid bending of his head and raising both of his arms that progressed to a secondarily generalized tonic-clonic seizure. He underwent surgeries to remove epileptic foci twice due to the frequent recurrence of seizures (1A, first operation; 1B, second operation). Patient 2 was a 24-year-old woman suffering from frequent medically refractory seizures from 3 years old. Her seizure consisted of the convulsion of her right oral angle and right limbs that progressed to a secondarily generalized tonic-clonic seizure. Both patients were orally administered the therapeutic dose of anti-epileptic drugs throughout the study period (Table 1). Although the two patients had FCD of M1, no motor deficit was observed even after the removal of the epileptic foci with FCD. The brain tissue resected from the epileptic lesion was histologically diagnosed as cortical dysplasia in both patients. Before removing the epileptic lesion, subdural electrodes were temporarily implanted to determine the epileptogenic areas by simultaneous monitoring of video and ECoG. High-frequency stimulation was performed for cortical functional mapping. We explained the purpose and possible consequences of this study to both patients, and obtained written informed consent (approved by the Ethics Committee of Osaka University Hospital).

Each patient had a total of 40–56 planar-surface platinum electrodes (configured in grids, 4×5, 3×5 or 3×7 arrays; Unique Medical Co., Tokyo, Japan) placed over the sensorimotor and temporal cortices for presurgical evaluation (Fig. 1). Each electrode had

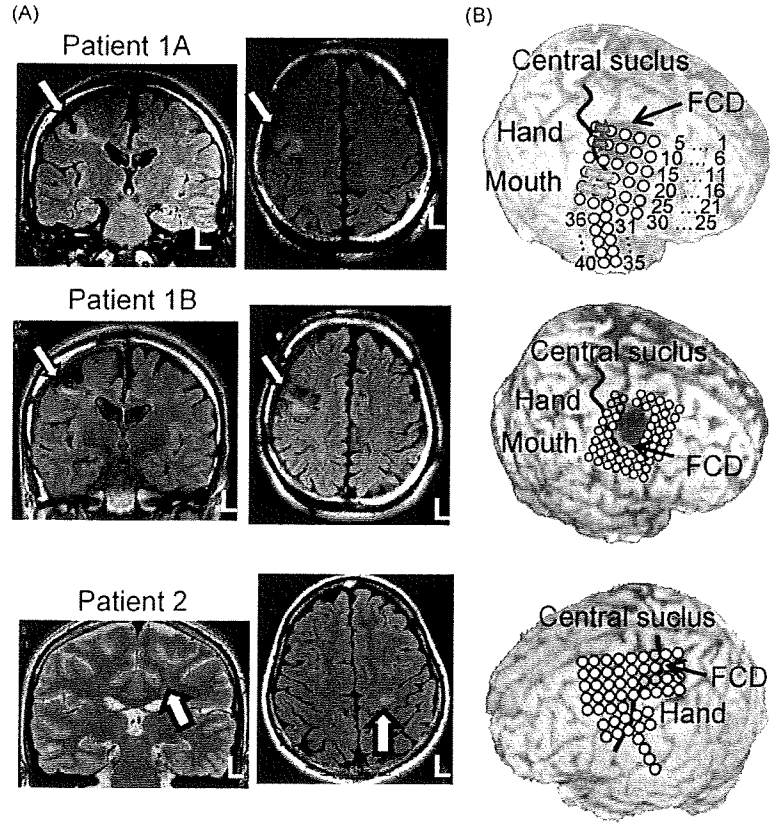

Figure 1 Location of focal cortical dysplasia and implanted subdural electrodes. (A) Magnetic resonance (MR) images of the three cases (FLAIR, coronal, sagittal, except for the left panel of Patient 2 which is a T2-weighted image). A well-demarcated high-intensity lesion in the precentral gyrus (white arrow) was diagnosed as focal cortical dysplasia (FCD). (B) Reconstructed individual MR images with superimposed white circles indicating the position of the 40- to 56-channel grid electrodes. A red colored brain surface indicates the suspected cortical lesion with FCD. Bipolar (arrow) or monopolar (circle) electrical stimulation of the cortex induced muscle contraction of the hand (blue) or the mouth (orange). The black line indicates the location of the central sulcus.

Table 1 Clinical profiles and performed movement types.

Patient	Age/sex	Epilepsy	Medication	Number of electrodes	Performed movement
1A	31/M	Right FLE	VPA, PHT, GBP	40	Opening mouth
1B	33/M	Right FLE	VPA, PHT, GBP	56	Lip pursing left hand grasping
2	24/F	Left FLE	PRM, PB	54	Right hand grasping

Abbreviations: M, male; F, female; FLE, frontal lobe epilepsy; VPA, valproic acid (1600 mg); PHT, phenytoin (300 mg); GBP, gabapentin (1200 mg); PRM, primidone (500 mg); PB, phenobarbital (60 mg).

a diameter of 3.0 mm and an inter-electrode center-to-center distance of 1.0 cm (Patient 1A, 2) or 0.7 cm (Patient 1B). Electrode placements were based solely on the patients' clinical requirements, without any consideration for utility in this study.

Movement tasks

Experiments were performed approximately one week after electrode placement. Patients were seated upright in hospital beds and were instructed to perform movements of their mouth or the hand contralateral to the implanted electrodes. The patients pursed their lips or opened their mouths (mouth movement) or grasped with their unilateral hand (hand movement) successively 38–96 times at a self-paced rate of approximately once per 4–6 s. Electromyogram (EMG) recordings of the contralateral orbicular muscle of the mouth, abductor pollicis brevis muscle, the flexor digitorum superficialis muscle, and the biceps brachii muscle were collected simultaneously. The movement onset was determined by the initial rising edge of the EMG waveforms.

Data collection and analysis

ECoGs and EMGs were measured using a 64-channel digital EEG system (EEG 2000; Nihon Koden Corporation, Tokyo, Japan) and digitized at a sampling rate of 1000 Hz. All subdural electrodes were referenced to a scalp electrode placed on the nasion. In the case of Patient 1A, one electrode was eliminated from the analysis due to severe noise contamination. The bandpass filter for data analysis was set to 0.16–120 Hz. A spike was defined as a clearly outstanding transient sharp activity with a duration of 20–200 ms and with an amplitude of $\geq$200 μV, followed by a slow wave. The number of spikes during each second was counted by a neurosurgeon, who was blinded to the timing of the movement.

Spiking rate (1/s) was defined as the mean number of spikes for 1 s time-locked to the movement onset. The decrease rate of spiking rate was defined as ((spiking rate before movement onset) − (spiking rate after movement onset))/(spiking rate before movement onset); spiking rate before movement onset: −2.0 to −1.0 s, spiking rate after movement onset: 0–1.0 s from the movement onset. A Student's *t*-test was applied between the spiking rates before and after the movement onset to show the statistical significance of the spiking reduction.

A time-frequency power spectrum analysis of ECoG was performed with EEGLAB v5.03 (Delorme and Makeig, 2004) implemented on Matlab, 2006b (Mathworks; Natick, MA). ECoGs of 1024 ms, sliding by 25 ms, were transformed to a time-frequency power spectrum from 0 to 80 Hz. Mean power modulation time-locked to the movement onset was normalized by the power spectrum from 5 (or three) to 2 s before the movement onset (normalized power); this normalization permits comparison across frequencies. Among the electrodes with spikes, a correlation coefficient between the mean normalized power of 1 s from the movement onset and the decrease rate of spiking rate for each electrode was calculated.

Results

In Patient 1A, frequent spikes were observed with ECoG from the sensorimotor cortex with the FCD lesion (Fig. 2). The spikes were observed broadly on the sensorimotor cortex (Fig. 3A). The mean spiking rate of all electrodes was 0.14 ± 0.02 (mean ± standard error), that did not exceed the spiking rate in resting state before tasks (0.2 ± 0.03) (Student's *t*-test, $p > 0.05$). When the patient moved his mouth, spiking rate was simultaneously decreased (Fig. 2). An example of the time course of the spiking rate (electrode #23) showed a significant decrease of the spiking rate after the movement onset compared to that before the movement

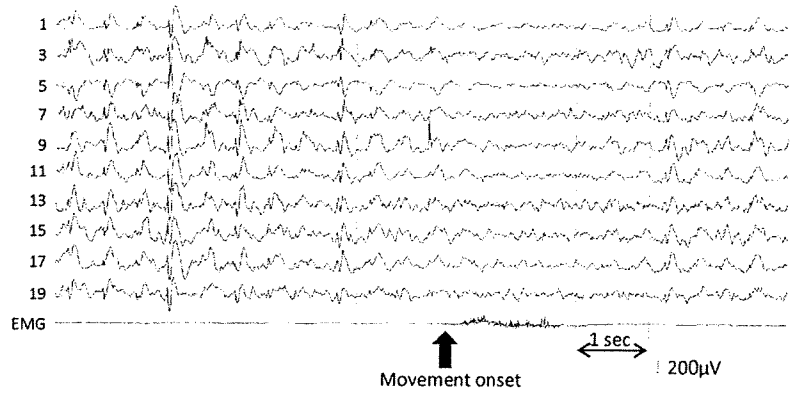

Figure 2 An example of ECoG waveforms from Patient 1A during mouth movement. An example of ECoG waveforms from Patient 1A with the EMG recorded on the left side of the orbicular muscle of his mouth (bottom trace). The number of the electrode was indicated on the left. A movement onset is indicated by an arrow head.

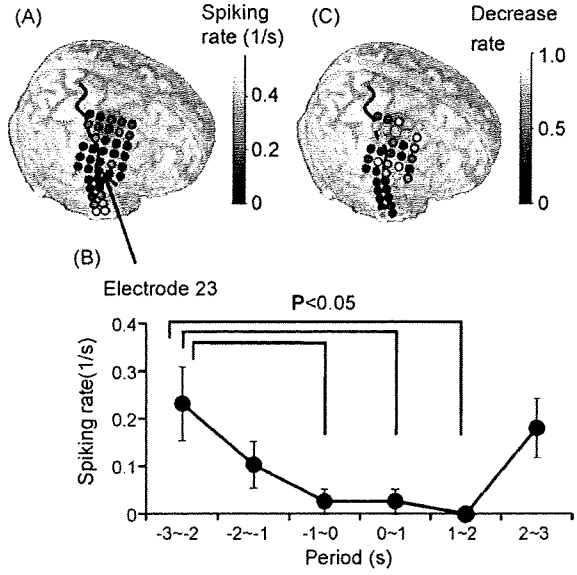

Figure 3 Decrease of the spiking rate associated with the mouth movement. (A) For each electrode, the spiking rate before the movement onset (−2.0 to −1.0 s from the movement onset) is shown as a color-code on the electrode superimposed on his reconstructed MR image. (B) The spiking rate of electrode #23 was plotted with the time from the movement onset (mean ± standard error), where time zero corresponds to the movement onset. The spiking rate was compared among six time periods by ANOVA. (C) The color-coded decrease rate of spikes was superimposed on each electrode. The electrodes with a significant decrease of the spiking rate after the movement are shown as blue circles (Student's t-test, $p < 0.05$).

onset (ANOVA, $p < 0.05$) (Fig. 3B). The significant decrease of spiking rate was observed broadly among the electrodes on the sensorimotor cortex (Fig. 3C). Therefore in Patient 1A, the spiking rate of the sensorimotor cortex was shown to be decreased corresponding to the movement of his mouth.

Among the electrodes with spikes, the relationship between the decrease rate of the spiking rate and the power spectral changes of the ECoG during the movement was examined. A representative time-frequency plot of mean power modulation of ECoG (electrode #23) time-locked to the movement onset showed power reduction (ERD) in the lower frequency bands (θ: 4–8 Hz, α: 8–13 Hz and β: 13–25 Hz) and power enhancement (event-related synchronization, ERS) in the higher frequency bands (high γ: 50–100 Hz) around the movement onset (Fig. 4A). A correlation coefficient between the decrease rate of the spiking rate and the normalized power of 1 s after the movement onset was significantly large around the θ band (Fig. 4B). The larger the decrease of the power (ERD) of the θ band was, the larger the decrease rate of the spiking rate ($R = 0.66$, $p < 0.01$) (Fig. 4C). The spiking rate of Patient 1A was suppressed with the ERD related to the movement of his mouth.

The movement-induced suppression of spiking, which was significantly correlated with the ERD at the lower frequency bands, especially at the θ (4–8 Hz) band, was also observed in the other cases (lip pursing or hand-grasping by Patient 1B and Patient 2) (Fig. 5). For these two patients with FCD of the pre- and/or post-central gyrus, the spiking rate was suppressed with mouth or hand movements and correlated with the degree of ERD in the lower frequency bands.

Discussion

The present study demonstrated the movement-related suppression of interictal spikes from the sensorimotor cortex with FCD of the pre- and/or post-central gyrus. The suppressive effect was linked to the movement-related desynchronization at the lower frequency band of the affected cortical areas, which has been reported to correlate with cortical excitability (Leocani et al., 2001; Neuper and Pfurtscheller, 2001; Pfurtscheller, 1992; Rau et al., 2003). The present study suggests that the modulation of cortical excitability during movement suppresses epileptic activities of the sensorimotor cortex.

The suppression of interictal spikes has been produced by a variety of cortical activations including electric cortical stimulation (Kinoshita et al., 2005) and alteration of some behavioral states, such as attention and arousal (Autret et al., 1999; Jasper, 1954; Pinel and Chorover, 1972), that involve the desynchronization of the cortical oscillatory activities (Wagner et al., 1975). Moreover, recent reports showed that the 'desynchronization' itself affects the epileptic activities (Chavez et al., 2003; Jouny et al., 2003; Kiss et al., 2008). Our results showed that the suppressive effects are also observed during some simple movements with movement-related desynchronization. Although it is not clear whether these spike suppression effects were generally observed through various cortical activities, a unique mechanism involving 'desynchronization' may suppress the interictal spikes regardless of the activities.

Moreover, the spike suppression effects associated with the movements do not seem to be restricted to the motor cortex. In Patient 1A, significant suppression was observed not only near the FCD lesion but also at areas distant from the lesion, even in the temporal lobe. Although the cause of this 'remote' effect is not clear, it might be due to the suppression of the epileptogenesis at the FCD lesion or the long-range inhibitory effect of the diffusely distributed ERD. This 'remote' effect suggests that the ERD suppressed the spikes in a broad cortical area. An examination of the anatomical relationship between the epileptogenic lesion and the activated cortical area correlated with the ERD will reveal the general properties of these spike suppression effects and the possibility to modulate the spikes in the broad cortical area.

The physiological origins of the spike suppression effect and its relation to the ERD are a matter of speculation. In this study, the movement-related desynchronization was observed in the lower frequency band (4–25 Hz), especially in the θ band (4–8 Hz), over a broad cortical area around the sensorimotor cortex. The spike suppression by attention and arousal has been shown to be linked to activity of the thalamus (Sterman and Egner, 2006; Wagner et al., 1975), which is known to be correlated the alpha rhythm (Neuper and Pfurtscheller, 2001). Our results suggest that the theta rhythm also affects the spike suppression. Although the characteristic frequency band might become slower as a

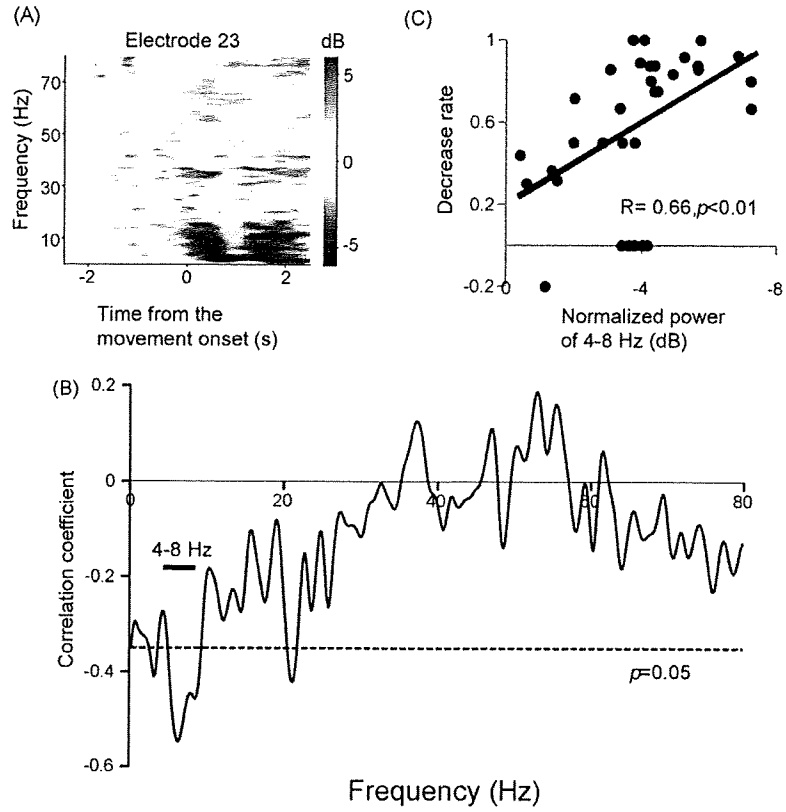

Figure 4 Correlation between decrease rate and spectral power of each electrode of Patient 1A. (A) A time-frequency plot of the mean normalized power modulation time-locked to movement onset (electrode #23). (B) The correlation coefficient between the decrease rate and the normalized power of each frequency of 1 s after movement onset was evaluated among all the electrodes with spikes. The dotted line indicates the statistical significance level at $p = 0.05$. (C) The decrease rate of each electrode with spikes was plotted with the normalized power of the θ band (4–8 Hz) for 1 s after the movement onset. The black line is a regression line ($R = 0.66$, $p < 0.01$).

result of the pathophysiological effects of the FCD lesion, the origins of the spike suppression effects linked to the desynchronization could be different among the frequency bands.

On the other hand, the spatial distribution of the spike suppression suggests an existence of a broad network modulating the cortical activities. This network may suppress the generation and/or propagation of the interictal spikes by the same mechanisms that generate the ERD during the movement (Netoff et al., 2004). Although the suppression of the interictal spikes does not necessarily mean a suppression of epileptogenesis (de Curtis and Avanzini, 2001), it may modulate the activity of the irritative zone, which strongly correlates with the seizure onset zone (Tyvaert et al., 2008). Investigation of the physiological mechanisms of the oscillatory modulations related to normal brain functions will reveal the mechanisms that modulate epileptogenesis.

The suppressive effect on interictal spikes demonstrated in the present study has the potential to be applied to the treatment of intractable epilepsy especially with neocortical foci. As the ERD on the sensorimotor cortex is observed during the imagination of movements (Leuthardt et al., 2004), there is a possibility that the voluntary imagination of the movements suppressed the spikes. The seizures might be controlled by the imagination or by the voluntary control of

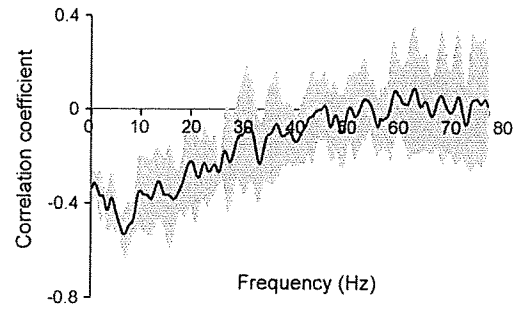

Figure 5 Mean correlation coefficient between the movement-induced reduction of spiking and the normalized power after movement onset The correlation coefficient between the decrease rate of spiking and the normalized power after movement onset was averaged over all four cases (opening mouth by Patient 1A, Lip pursing or hand-grasping by Patient 1B, grasping hand by Patient 2). The mean of the correlation coefficients at each frequency was plotted with the standard deviation (gray shadow).

the power at the lower frequency bands (Sterman and Egner, 2006). Investigation of the voluntary control of cortical oscillatory activities would contribute to the improvement of treatment strategies for neocortical epilepsy.

Acknowledgements

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脳卒中後疼痛に対する脊髄電気刺激療法

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要　旨

脊髄電気刺激療法（SCS）は末梢性神経障害性疼痛の治療に有効であるが，中枢性疼痛である脳卒中後疼痛に対しての有効性は確立されていない．われわれの施設での30症例の難治性脳卒中後疼痛に対するSCSの経験を述べる．すべての症例にSCS試験刺激を施行し，一旦は抜去して，患者が希望すればSCSを埋め込んだ．疼痛の程度は，疼痛尺度（VAS）とpatient global impression of change（PGIC）で行った．SCS試験刺激では9症例（30%）でgood（50%≦VAS低下），6症例（20%）でfair（30～49%），15症例（50%）でpoor（30%>）と判定された．10症例が埋め込みを希望し，うち9症例が長期（mean 28カ月，6～62カ月）フォローされ，うち7症例で有意な疼痛軽減が得られた（5症例がgood，2症例がfair）．PGICでは，この7症例中6症例がrank 2（much improved），1症例がrank 3（minimally improved）と判定され，残りの2症例はrank 4（no change），rank 5（minimally worse）と判定された．9症例のVAS中間値は86 mmから45 mmに有意に低下した（p=0.007）．明らかな合併症はなかった．SCSは，難治性脳卒中後疼痛の一部において，良好な疼痛コントロールを提供することが示され，治療法としての可能性が示唆された．

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キーワード：脳卒中後疼痛，脊髄電気刺激療法

はじめに

脳卒中後疼痛は，難治性求心路遮断痛の中でも，特に難治であり，脳卒中の1～8%に発症する[1,2]．脳卒中で障害された脳部位に一致した知覚障害と疼痛が体表面に現れる[3]．一旦，疼痛が生じると長期にわたって日常生活レベルを低下させる[4]．投薬治療としてアミトリプチリン，ガバペンチンが，通常，第一選択だが有効性が高いとはいえない[5]．脳深部刺激療法の有効性はばらつきがあり[6]，大脳一次運動野電気刺激療法（MCS）が約50%に有効であるが，高額医療であり，開頭術を必要とする[7,8]．

一方，SCSはfailed back surgery syndrome（FBSS），CRPS，末梢性虚血性疾患，帯状疱疹後疼痛，脊髄損傷後疼痛に対し，その有効性が報告されているが[9]，脳卒中後疼痛に関してはまとまった報告はない[4]．われわれの施設では，脳卒中後疼痛に対して積極的に脊髄電気刺激の試験刺激を行って，有効な症例には刺激装置の埋め込みまで勧めている．そこで，その有効性について報告したい．

1．症例（Table 1）と方法

大阪大学脳神経外科で，2002年5月から2009年7月までに，87症例の脳卒中後疼痛患

〈Special Article〉 Electrical spinal cord stimulation for chronic pain
Efficacy of spinal cord stimulation on post-stroke pain
Youichi Saitoh
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者に対して何らかのニューロモデュレーション治療を施行した（大脳一次運動野電気刺激術：13症例，反復経頭蓋磁気刺激療法：59症例，SCS：30症例，一部の症例はオーバーラップ）．SCS 30症例は男性21症例，女性9症例，平均年齢は64.8±7.4（歳±SD），平均疼痛罹病期間は44.8±35カ月である．脳卒中後疼痛の診断は，i）脳卒中後に疼痛を発症，ii）脳血管障害に伴う知覚障害，iii）知覚障害部位に疼痛がある，iv）侵害性または末梢性神経障害性疼痛などの原因が排除できる，の4項目がそろっていることを条件とした[10]．また，心因性疼痛や認知症のある症例，脳卒中後の肩手症候群は除外した．全症例が6カ月以上にわたる疼痛期間がある．視床出血が9症例，被殻出血12症例，他である（Table 1，Figure 1）．すべての患者が半身の痛みを訴え，一肢から半身，全体まで様々である．Allodyniaが18症例（60%），知覚過敏が11症例（37%）にみられた．軽度の運動障害がある症例が20症例，中等度が3症例であった．

腹臥位で透視を使用して，脊髄硬膜外腔を穿刺して，4極電極（Medtronic社，PISCES-Quad®）を挿入して，通電しながら疼痛部位に電気刺激感がくるように留置し[11]，約2日間試験刺激を行い，パラメータを変えて除痛効果を判定した後，効果の有無に関わらず一旦抜去している．上肢痛の場合は$C_{4\text{-}7}$に留置し，下肢痛の場合は$T_{9\text{-}12}$に留置した．抜去した後，患者の希望があれば，再度，電極を脊髄硬膜外腔に挿入して，コネクターを接続，皮下に埋没して，試験刺激を施行して有効性が認められれば，刺激装置（Medtronic社，ITREL III®またはSYNERGY®）を前胸部か腹部に埋め込んでいる．

疼痛の評価はVAS（visual analogue scale）で行い，除痛効果はexcellent（VASでの痛みの低下率80%以上），good（VASでの痛みの低下率50～79%），fair（VASでの痛みの低下率30～49%），poor（VASでの痛みの低下率30%未満）に分類し，6カ月ごとに評価した．Patient global impression of change（PGIC）を最終フォローアップ時に評価した．Rank 1：very much improved，2：much improved，3：minimally improved，4：no change，5：minimally worse，6：much worse，7：very much worse．Rank 1，2は臨床的に有意な改善と判断した[12]．

試験刺激の時の疼痛低下の程度を2群に分けて解析した．“good”と“fair”を1群にまとめ，“poor”をもう1群とした．臨床因子である年齢，性別，疼痛部位（上肢，下肢），疼痛期間，脳卒中の原因，知覚過敏またはallodyniaの有無，運動障害の程度と試験刺激の時の有効性の2群を検定した．

2．結　果（Table 1）

1）試験刺激

試験刺激では，すべての症例で1個のリードを埋め込んだ（24症例は下肢痛の治療のための胸椎レベル，6例は上肢痛のため頸椎レベル）．テスト刺激で，goodと評価した症例は9症例（30%），fairと評価した症例は6症例（20%），poorと評価した症例が15症例（50%）存在した．VAS中間値は80mmから60mmに有意に低下した（$p<0.001$）．

試験刺激を受けた30症例のうち，20症例は埋め込みを希望せず，10症例が永久埋め込みを希望した．2症例は2個の電極（1個頸椎，1個胸椎）を埋め込みした（No. 24，30）．永久埋め込みした10症例の臨床的な特徴をTable 2にまとめた．

永久埋め込みした10症例のうち，試験刺激で，7症例はgood，2症例はfair，1症例はpoorと判定した．試験刺激でpoorと評価された1症例は永久埋め込みを希望した（No. 2 Table 2）．その患者はVASで25%の除痛効果

Table 1. Patient characteristics and results of trial stimulation

Patient No.	Age (y/sex)	Pain duration (months)	Underlying disease	Painful region treated	Motor weakness	Sensory disturbance		Baseline VAS	VAS after trial	% VAS change	Trial stimulation result	IPG implantation
						Allod	Hyperp					
1	59, M	48	Lt sc inf	Rt LL	Mild	+	−	7	7	0	Poor	−
2	54, F	12	Lt thal hem	Rt UL	Mild	+	+	10	7.5	25	Poor	+
3	59, F	97	Rt put hem	Lt LL	Mild	−	+	8	4	50	Good	+
4	65, M	30	Rt thal hem	Lt LL	−	−	−	9	4	56	Good	+
5	71, M	19	Lt thal hem	Rt UL	Moderate	+	−	10	10	0	Poor	−
6	64, F	68	Lt put hem	Rt LL	Mild	+	−	10	7	30	Fair	+
7	74, F	156	Lt put hem	Rt LL	Mild	−	−	8	8	0	Poor	−
8	75, F	24	Lt thal hem	Rt LL	Mild	−	−	7	3	57	Good	+
9	75, M	24	Rt put hem	Lt LL	−	−	−	10	7	30	Fair	−
10	58, M	60	Lt pontine inf	Rt LL	Mild	+	−	6	3	50	Good	−
11	66, F	32	Rt put hem	Lt LL	Mild	+	−	7	3	57	Good	+
12	67, M	52	Lt thal inf	Rt UL	Mild	+	+	8.5	8.5	0	Poor	−
13	57, M	80	Rt put hem	Lt LL	−	+	+	6	6	0	Poor	−
14	72, M	83	Lt thal hem	Rt LL	Moderate	−	−	8.5	7.5	12	Poor	−
15	65, M	33	Lt thal inf	Rt UL	Mild	−	−	9	6	33	Fair	+
16	48, M	11	Rt put hem	Lt LL	Mild	+	−	8.6	3	65	Good	+
17	69, M	6	Lt thal hem	Rt LL	Mild	+	+	8	8	0	Poor	−
18	66, M	81	Rt put hem	Lt LL	−	−	+	8.5	7	18	Poor	−
19	67, M	14	Brain stem inf	Rt LL	−	+	−	5	5	0	Poor	−
20	61, M	29	Lt pontine inf	Rt UL	Mild	+	−	9	6	33	Fair	−
21	72, M	16	Lt put hem	Rt LL	Mild	+	+	9	9	0	Poor	−
22	76, M	41	Lt thal hem	Rt UL	Moderate	−	−	8.5	2.5	71	Good	−
23	62, F	6	Rt sc hem	Lt LL	Mild	+	+	8	5.6	30	Fair	−
24	51, F	46	Rt put hem	Lt LL & UL	Mild	+	−	7	3	57	Good	+
25	65, F	20	Rt medullary inf	Lt LL	−	+	+	9.5	8.5	10	Poor	−
26	64, M	56	Rt put hem	Lt LL	Mild	+	+	8	8	0	Poor	−
27	56, M	6	Rt thal hem	Lt LL	−	−	−	7.8	5	25	Poor	−
28	74, M	93	Lt thal inf	Rt LL	Mild	−	−	8	5	38	Fair	−
29	62, M	19	Lt put hem	Rt LL	Mild	−	−	7	7	0	Poor	−
30	71, M	82	Rt thal hem	Lt LL	Mild	+	+	6.5	1.5	77	Good	+

Allod : allodynia, Hyperp : hyperpathia, VAS : visual analogue scale, M : male, F : female, Rt : right, Lt : left, put : putaminal, thal : thalamic, hem : hemorrhage, inf : infarction, sc : subcortical, LL : lower limb, UL : upper limb, + : presence, − : absence. median VAS in target regions significantly decreased from 8.0 to 6.0 after trial ($p < 0.001$).

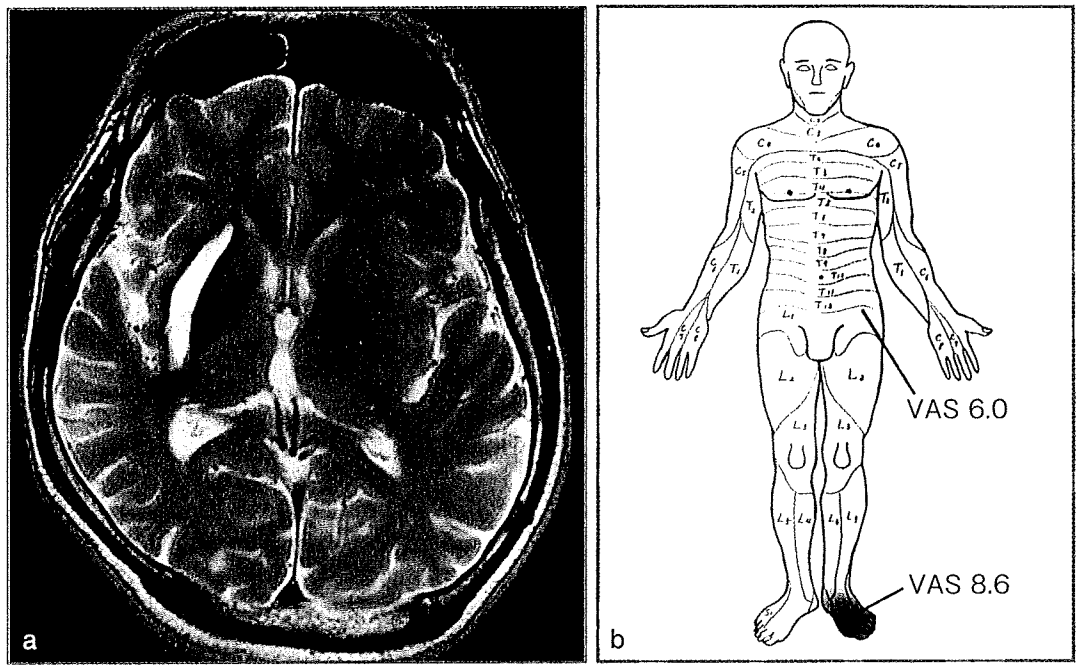

Figure 1. Illustrated case (No. 16)
MRI T2 強調画像では右被殻に陳旧性の脳出血を認める (a). 左半身の疼痛の中では左足の痛みが最も強かったので，足の領域に paresthesia がくるように胸椎レベルに電極を留置した (b)

Table 2. Patients characteristics and long-term follow-up for ten patients with permanent implantation

Patient No.	Age (y/sex)	Pain duration (months)	Underlying disease	Painful region treated	Motor weakness	Sensory disturbance		%VAS reduction during trial	Latest Follow-up		Follow-up (months)
						Allod	Hyperp		% VAS reduction	PGIC	
2	54, F	12	Lt thal hem	Rt UL	Mild	+	+	25	20	5	16
3	59, F	97	Rt put hem	Lt LL	Mild	−	+	50	50	2	62
4	65, M	30	Rt thal hem	Lt LL	−	−	−	56	50	2	60
6	64, F	68	Lt put hem	Rt LL	Mild	+	−	30	30	3	6
8	75, F	24	Lt thal hem	Rt LL	Mild	−	−	57	57	2	41
11	66, F	32	Rt put hem	Lt LL	Mild	+	−	57	57	2	24
15	65, M	33	Lt thal inf	Rt UL	Mild	−	−	33	33	2	25
16	48, M	11	Rt put hem	Lt LL	Mild	+	−	65	19	4	12
24	51, F	46	Rt put hem	Lt LL & UL[a]	Mild	+	−	57	57	2	12
30	71, M	82	Rt thal hem	Lt LL	Mild	+	+	77	ND[b]	ND[b]	ND[b]

[a]This patient had less than 6 N months follow-up at the time of latest follow-up and was therefore excluded from long-term-follow-up analysis.
[b]This patient had two electrodes implanted, but only results for the thoracic electrode are included in statistical analysis.
For PGIC : 2 = much improved ; 4 = no change ; 5 = minimally worse.
VAS : visual analogue scale, PGIC : patient global impression of change, M : male, F : female, Rt : right, Lt : left, put ; putaminal, thal : thalamic, hem : hemorrhage, inf : infarction, LL : lower limb, UL : upper limb, ND : not determined

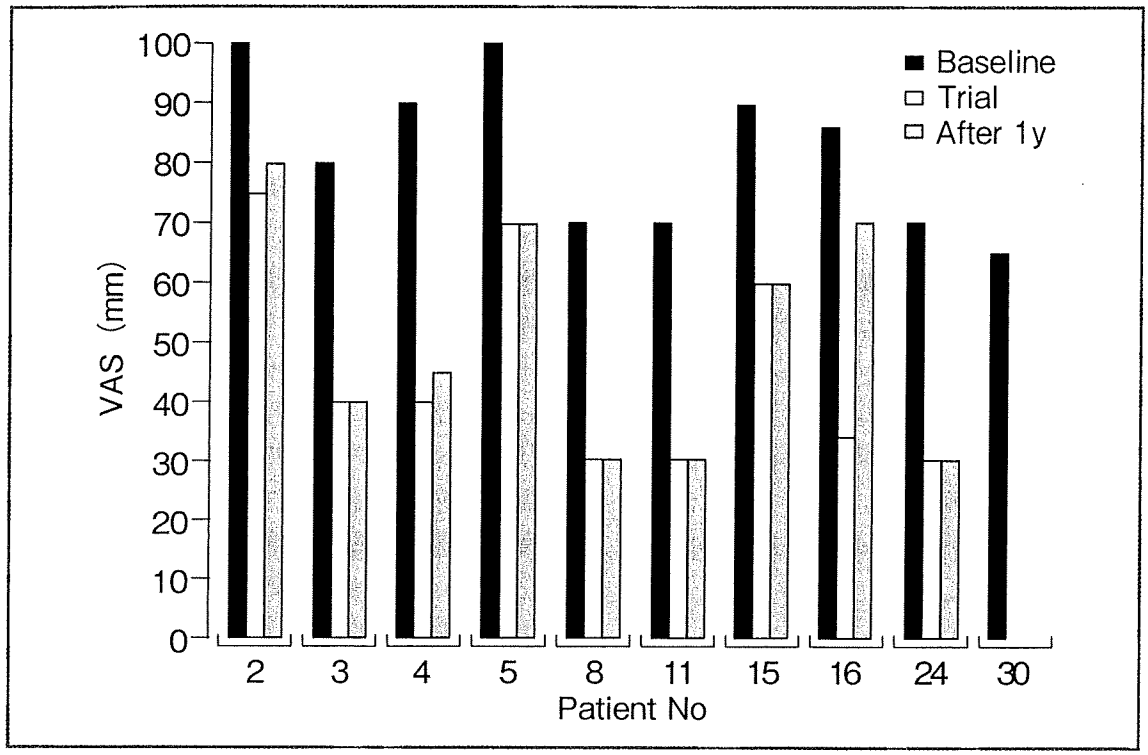

Figure 2. VAS pain scores for ten permanently implanted patients
No. 30 の患者はフォローアップが 6 カ月に満たないので，長期フォロー成績の解析から除外した．最新のフォローアップにおける VAS の中間値は 8.6 から 4.5 に有意に低下した（p = 0.007）．
Baseline：刺激前の VAS，Trial：試験刺激時の VAS，After 1 y：SCS 埋め込み 1 年後のフォローアップ時の VAS

が得られ，長期効果は定かでないが永久埋め込みを希望した．

2）最新のフォローアップ結果（Figure 2）

最新のフォローアップでは，1 症例（No 30）は 6 カ月にフォローアップが満たないので長期フォロー評価からは除外した．残りの 9 症例は平均 28 カ月（12～62 カ月）のフォローアップ期間であった．最終フォローアップ時には 7 症例が VAS で有意な除痛効果（5 症例 good，2 症例 fair）が得られた．PGIC scale では 6 症例が rank 2（much improved），1 症例が rank 3（minimally improved）であった．7 症例全症例が 1 日 2～10 回の刺激を使用していた．Poor と評価された 2 症例のうち，1 症例は rank 4（no change），もう 1 症例は rank 5（minimally worse）であった．9 症例の VAS の中間値は 86mm（70～100mm）から 45mm（30～80mm）（p＝0.007）に低下した．9 症例の平均 VAS 低下率は 41.5%（19～57%）であった．7 症例の長期フォローで良好な除痛が得られている群では，平均 VAS 低下率は 46.5%（30～57%）であった．

Poor と評価した 2 症例のうち，1 症例は試験刺激および初期には，少し除痛効果がみられた（No. 2）．長期フォロー中は，刺激に伴う paresthesia を不快と感じて，除痛効果が得られなかった．もう 1 人の患者（No. 16）は試験刺激および初期には good と評価されたが，徐々に SCS の効果が消失した．

使用した刺激のパラメーターは 1.5～6.0 V，パルス幅は 210 μsec，周波数は 31 Hz（10～50 Hz）のバイポーラー刺激である．

3）合併症

2症例で電極の位置がわずかに（半椎体以内）ずれたが，治療には支障がなかった．フォローアップ中に1症例（No. 4）がSCSとは無関係な原因で死亡した．

4）試験刺激の除痛効果と臨床的特徴の関係

特に試験刺激の除痛効果と臨床的特徴の間に有意な相関性は見い出せなかった．疼痛部位が知覚過敏であることがpoor群において，goodまたはfair群よりも多い印象があるが，有意差はなかった（$p=0.074$）．

3．考　察

SCSは，これまで脳卒中後疼痛に対しては報告数が少なく，効果がないと考えられてきた[6]．本研究は，薬物抵抗性の脳卒中後疼痛の患者において，SCSが除痛効果を示すことを報告した最初の研究である．試験刺激においては，約半数の患者が有意な除痛効果を示した（Table 1）．さらに9症例中7症例の患者で平均28カ月（6～62カ月）のフォローアップ期間中に有意な除痛効果が得られた（Table 2）．この7症例中，6症例はrank 2 (much improved)，1症例はrank 3 (minimally improved) とPGIC scaleで評価され，平均のVAS低下は46.5%であった．

過去の報告では，FBSS患者の80%が，試験刺激で50%以上の疼痛減弱が得られるとされている[9]．今回の脳卒中後疼痛に対するSCSでは，50%の患者が30%以上の除痛効果を示し，30%が50%以上の除痛効果を示し，過去のFBSS患者に対する治療効果の報告よりは劣る結果となった．しかし，脳卒中後疼痛は他に治療法が少なく，治療抵抗性で，疼痛が著しいことを考えると，この程度の治療効果でも重要であると考えられる．

われわれの知る限り，過去の2つの報告が脳卒中後疼痛に対するSCS効果を報告している[6]．最初の報告はわれわれの知見に近く，10症例中3症例で，長期有効性が示されているが[13]，2報目の報告は，45症例中3症例のみで60%以上の除痛効果が長期に得られた[14]．われわれの研究では，30%以上の除痛効果を成功閾値としており，30症例中6症例で（平均VAS低下率が51.5%）満足のいく除痛効果と判定された．その6症例はPGIC scaleでmuch improvedを選択した．われわれの知見とKatayamaらの知見[14]は，goodと判定する閾値の違いによるものである．慢性疼痛治療の良好と判定する定義に関するコンセンサスは存在しないが，多くの研究において30%の除痛が有意な臨床的改善として判定されている[12]，50%の除痛効果の定義はやや厳しいとも考えられる．それゆえ，過去の報告では不適切な成功の閾値設定のため，SCSの脳卒中後疼痛に対する有効性を過小評価していたのでないかと考えられる．

薬物抵抗性の脳卒中後疼痛の治療オプションは限られている．MCSは約50%に有効であると報告されている[7]．しかし，MCSは開頭が必要で特殊な施設に限られる．一方，SCS手技は比較的簡単で，低侵襲で，脳神経外科医，整形外科医の脊椎専門医だけでなく，麻酔科医，ペインクリニック医でも施行できる[15]．他の神経刺激手技に比べて，経皮的SCS試験刺激は患者が受け入れやすく，試験刺激が有効と判断されなくても電極は簡単に抜去することができる．われわれの施設では，問題となる合併症を認めていない．

脳卒中後疼痛の疼痛部位の分布は様々であるが，最も多いのは半身全体が痛む様式で，特に手や足の末梢側に強く痛むことが特徴である[16]．疼痛部位全体を刺激のparesthesiaでカバーすることが，SCS治療成功の必要条件であるので，SCSのターゲットとして限局された疼痛部位であることが望ましい[17]．今回の検

討では，被殻出血による足の疼痛が最も多く，内包後脚の一部を含む被殻出血が足に限局するひどい疼痛を起こす傾向がみられた[18]．また，足に強い脳卒中後疼痛がSCSに適していると考えられた．その理由として，頸椎よりも胸椎の方が電極留置後も電極のずれが少ないことが挙げられる[19]．加えて，足の疼痛はMCSの適応としては適しておらず，一次運動野の足の領域が半球間裂に主に存在するため，平板電極で刺激することが困難であるためである[20]．

試験刺激に対する反応性を予測する臨床因子の解析では，疼痛部位が知覚過敏になっている場合，知覚低下例に比べてSCS反応性がよくないという結果が得られた．この知見は過去の報告で，SCSは自発痛よりも誘発痛に効果が少ないという知見を裏付けている[21]．試験刺激の有効性は，永久埋め込み後の大多数で同様に継続した．SCS試験刺激は，永久埋め込み前の有効性判断の試験として，低侵襲で意味のあるものと考えられる．

今回の検討では，症例数が多いとはいえないこととと，後方視的研究であることが問題と考えられる．脳卒中後疼痛の発生頻度は低く，見過ごされていることも多いと考えられ[3]，１つの施設で多数症例を解析することは困難である．もう１つの問題点として，対照群がないことが挙げられる．SCSは刺激感があるので，２重盲験試験でシャム刺激対照を置くことも困難である[22]．未手術群を対照として設定するのも適切とはいえない．対照群がないことより，SCSの有効性の中に疼痛が自然寛快したものが含まれていると考える人もいるかもしれないが，一般に脳卒中後疼痛は長期間持続し，寛快するのは稀である[4]．これらの臨床研究の限界より，難治性脳卒中後疼痛の一部の患者ではSCSが良好な疼痛コントロールを提供するとわれわれは考えている．より強力なエビデンスを得るには，多数症例での前方視的研究が必要であると考えられる．

4．結　論

この研究はSCSが薬物抵抗性の脳卒中後疼痛の一部の患者に除痛コントロールをもたらすことを報告した最初の報告である．脳卒中後疼痛に対するSCSの効果は，成功率も除痛の程度も高いものではなかった．しかし，脳卒中後疼痛は耐えがたく，治療抵抗性であり，他の治療法がないことから，この程度の除痛効果でも重要であると考えられる．今後，前方視的研究を多数症例で行うことで，SCS治療に反応する患者群を選定することが望ましい．

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知って得する最新情報

難治性疼痛に対する運動野刺激治療

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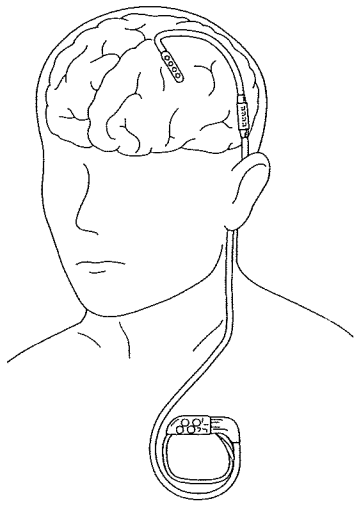

図 1　大脳運動野刺激術のシェーマ

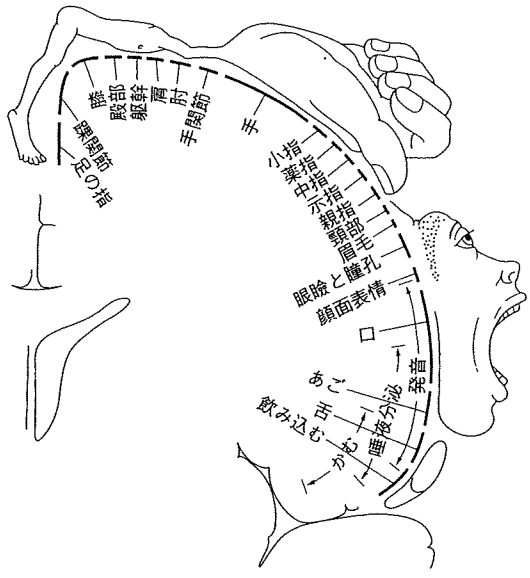

図 2　ヒトでの大脳一次運動野局在分布
Penfield's homunculus とも呼ばれる．(Crosby EE, et al. Correlative anatomy of the nervous system. New York：The Macmillan；1962. より)

はじめに

求心路遮断痛には視床痛に代表される脳卒中後疼痛，脊髄損傷後疼痛などの中枢性のものと，腕神経叢損傷後疼痛，幻肢痛，複合性局所疼痛症候群(complex regional pain syndrome；CRPS)などの末梢性のものがあり，有効な薬剤はあまりなく，慢性難治性疼痛に移行することがある．この治療として，大脳一次運動野(M 1)の電気刺激(motor cortex electric stimulation；MCES)[1]，反復的経頭蓋磁気刺激 (repetitive transcranial magnetic stimulation；rTMS)[2]が有効なことが報告されている．これらは疼痛をあくまで緩和させる治療である．

MCES の治療(図 1)

電極を硬膜外，硬膜下脳表，中心溝内，大脳半球間裂に留置する手技が報告されている[3]．Penfield's homunculus (図 2)に基づいて，疼痛部位に対応した M 1 を刺激するのが一般的である．

われわれは完全麻痺の患者には，中心溝内に電極を留置している．なぜなら，ヒト M 1 の細胞構築は中心溝内に主

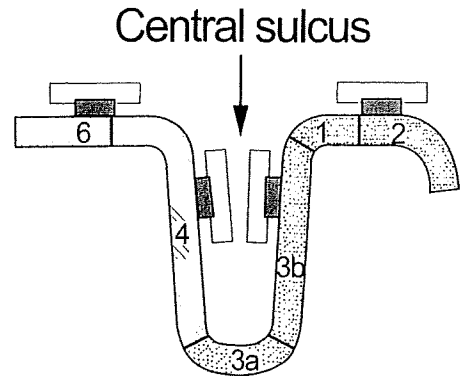

図 3　ヒトにおいては中心溝内に一次運動野の主要な部分が存在する

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要部分が存在するためである(図3). 足の運動を司るM1は中心溝が浅く，大脳半球間裂に面しているので，大脳半球間裂脳表に電極を置いている．中心溝を剝離することで，一時的な除痛が得られ，中に著効するケースがある[4].

MCESの有効性については，脳卒中後疼痛の運動麻痺の軽い症例では73%の有効率で，感覚障害の程度，状態には依存しないと報告されている[5]. 主な報告をまとめると，概ね有効率は約50%と考えられている[3]. 経時的に除痛効果が低下するケースがあるが，理由は不明である.

ナビゲーションガイドrTMS(図4)

われわれの臨床研究ではM1，一次感覚野(S1)，前運動野，補足運動野を刺激した結果，M1刺激のみが除痛に有効であった．これらの大脳皮質は近接しており，M1刺激のみが除痛に働く事実は非常に興味深い[2]. 刺激頻度として1Hzは有効性がなく，5，10Hzの高頻度刺激によってのみ除痛が得られる[6]. rTMSの有効性とMCESの有効性の間には有意な相関が得られた[4]. rTMSの有効率も約半数であるが[2]，脳卒中後疼痛よりも脊髄損傷後疼痛または末梢性疼痛の方が有効率が高く[6]，また高齢者よりも55歳未満の比較的若年齢で有効性が高い結果を得ている.

運動野刺激療法による除痛効果のメカニズム

除痛効果のメカニズムとして，坪川らは脊髄後索-内側毛帯系が脊髄視床路系をさまざまなレベルで抑制性の調節を行っていると推測し，求心路遮断された脊髄視床路よりも上位で，脊髄後索-内側毛帯系を活性化させることで，除痛が得られるのであろうと考えた[7]. これはあくまで仮説である.

われわれは$H_2{}^{15}O$によるPET activation studyによってMCESによる除痛メカニズムの解析を行った[8]. 他施設も含めてMCESにより，視床，前帯状回，前頭葉底部，脳幹に除痛後，局所脳血流の増加，つまり神経活動の高揚が観察されている．S1の血流増加の報告はない．よって，MCESによる除痛効果は，視床，脳幹，前頭葉および前帯状回の神経活動の高揚による複合的なメカニズムが推測されている．rTMSも同様の除痛メカニズムが想定される.

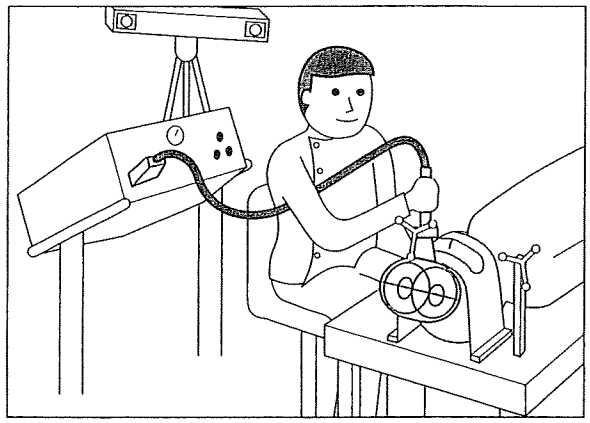

図4 ナビゲーションガイド経頭蓋磁気刺激療法のシェーマ

むすび

MCESによる難治性疼痛治療は偶然に見出された治療法であるが，そのメカニズムを解明していくことで，より治療成績を向上させることが可能となろう．また脳内での痛みの認知機構をより明らかにすることも可能となろう.

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慢性疼痛に対する脳刺激療法

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要　旨

難治性疼痛の治療において一次運動野電気刺激療法の有効性が世界的に認められている．また，以前より脳深部電気刺激療法も幻肢痛などで有効性の報告がある．一方，被験者に苦痛を与えることなく局所の大脳皮質ニューロンを刺激できる反復的経頭蓋磁気刺激療法によって，電気刺激と同様の疼痛軽減効果が得られるとの報告がされている．一次運動野を刺激すると，帯状回，視床，前頭葉底眼窩面，脳幹などが賦活されて包括的に除痛されると考えられている．非侵襲的刺激法である経頭蓋磁気刺激による継続的治療の可能性が検討されている．

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キーワード：経頭蓋磁気刺激，一次運動野，難治性疼痛

はじめに

米国では，人口の45%が一生の間には一時，慢性疼痛に悩むという報告もある．慢性痛は精力的に研究されている割には，治療手段は限られており，疼痛期間が長引くと痛みはより治療困難になる傾向がある．投薬治療が一般的に試みられるが，効果が限られており，自殺企図者は10%に上るとの報告もある．そこで投薬以外の新しい治療が求められるわけである．

慢性疼痛の中でも，特に神経障害性疼痛または求心路遮断痛が最も難治であると考えられている．神経障害性疼痛とは神経系の機能障害が原因と考えられる疼痛であり，視床痛に代表される脳卒中後疼痛，帯状疱疹後神経痛，複合性局所疼痛症候群（CRPS），幻肢痛，脊髄損傷後疼痛などがあるが，治療は難航することが多い．薬物療法，神経ブロック療法，心理療法，電気痙攣療法などが選択されるが，難治性疼痛に移行し，生活の質（quality of life）に重大な影響を与えている症例も多い．

ところで，痛みは脳で情報処理されているわけで，たとえ末梢に慢性難治性疼痛の原因が存在したとしても，脳に治療を施すことで痛みの軽減を図ることができる．一つの方法として，手術により電極を設置する一次運動野電気刺激療法（motor cortex stimulation：MCS）[1]，脳深部電気刺激療法（deep brain stimulation：DBS）[2]などが行われており，有効例が報告されている．しかしこれらの治療法は費用が高価であり，侵襲的であるため，治療をためらう患者もいる．また，それらの理由に加えて，全員に十分な除痛効果が認められるわけでもない．一方，1985年，Barkerらによって磁気刺激装置が開発されて以来，コイルに電流を瞬間的に流すことにより電磁誘導を発生させて，大脳皮質に誘起電流を起こし，非侵襲的に局所的に大

〈Special Article〉 Pain and brain function
Repetitive transcranial magnetic stimulation (rTMS)
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