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Movement Related Cortical Potentials in Severe Chronic Stroke*

O. Yilmaz, W. Cho, C. Braun, N. Birbaumer, and A. Ramos-Murguialday, *Member, IEEE*

Abstract— **Movement related cortical potentials (MRCPs) have been studied for many years and controlled using brain computer interfaces (BCIs). Furthermore, MRCPs have been proposed as reliable and immediate indicators of cortical reorganizations in motor learning and after stroke. In this study MRCPs preceding and during hand movements in severe chronic stroke were investigated. Eight severely impaired (no residual finger extension) chronic stoke patients underwent EEG and EMG recordings during a cue triggered hand movement paradigm. Four patients presented subcortical lesions only while the other four presented mixed (cortical and subcortical) lesions. MRCPs were measured before (slow cortical potentials SCPs) and at movement onset (motor potentials MPs). SCPs were observed during paretic hand movements only. Latencies were longer and reached their negativity peak earlier during paretic hand movement. When dividing the patients in subcortical only and mixed lesion patients, we observed significantly bigger MP peak amplitudes over the lesioned hemisphere during paretic and healthy hand movements in subcortical stroke patients. Furthermore, we observed a significant difference in MP peak latency between subcortical and mixed stroke patients during paretic hand movements. We demonstrated for the first time significant differences between subcortical only and mixed (cortical and subcortical) stroke patients' MRCPs during motor preparation and execution. Furthermore, we demonstrated how stroke produces a longer MRCP and that lesion location affects MP peak amplitude and latency. Finally, we propose the use MRCP based BCIs to reduce their duration (towards normal) and induce motor function recovery.**

I. Introduction

Movement related cortical potentials (MRCPs) recorded using EEG can be divided into 2 main components: a) the slow cortical potentials (SCPs) occurring during intention or anticipation of an upcoming movement and b) the motor potential (MP) occurring during the execution itself [1]. An SCP is a bilateral low frequency (0-5Hz) negative shift occurring up to 1-2 sec before the movement onset. MP peak rises contralaterally around the onset of a voluntary movement as a continuation of the SCP negativity [2], which is also referred as late SCP or peak negative shift (NS) in some literature [3]. According to the threshold theory, during the preparation of a movement MRCPs serve as regulatory mechanisms of cortical excitability by facilitating the neuronal firing [4,5]. Therefore, MRCPs have been proposed as important indicators of cortical reorganization and motor learning. Several groups have demonstrated that MRCPs can be altered after a brain disease or injury, as well as the early and late phases of skilled performances [6,7,8].

Following stroke, a strong reorganization of the cortical neural networks occurs in the brain. Loubinoux and coworkers [9] showed that regaining the activity of ipsilesional supplementary motor area (SMA), which is a crucial generator of SCPs [10], is correlated with better motor recovery in recovered subcortical acute stroke patients. Kitamura and colleagues [11] reported in 2 subcortical stroke patients who had remaining synergistic movements of the paretic arm that SCP stayed bilaterally while MP was distributed symmetrically when performing voluntary elbow movements. Green et al. [12] supported these findings demonstrating that the intact hemisphere becomes more active after stroke in patients presenting mixed lesions. Similar ipsilateral (contralesional) activation was also observed by other groups [13,14,15].

Although most of the studies were performed with small number of acute stroke patients who mostly recovered afterwards, MRCP changes showed important evidence regarding cortical reorganizations. However, the underlying mechanisms need to be further investigated. In the here presented work, we studied MRCPs of 8 severely impaired chronic stroke patients who suffered from subcortical and mixed (cortical and subcortical) lesions. The aim of this work is to study MRCPs in severe stroke to compare the effects subcortical and cortical lesions and to investigate the involvement of the intact hemisphere in motor preparation and execution. MRCPs are reliable measures for the assessment of the course of motor learning as well as a useful motor intention feature for rehabilitative and assistive BCI technologies and can be also used as a predictor of recovery in stroke.

II. Methods

A. Patients

Eight hemiparetic patients with mean age of 54.5 ± 8.3 and time since stroke 6.1 ± 6.4 years participated in the study. Four patients (2 male, 2 female) presented subcortical lesions only and four (3 male, 1 female) presented mixed lesions (subcortical and cortical areas) (Table 1). The

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O. Yilmaz, W. Cho, C. Braun, A. Ramos-Murguialday, and N. Birbaumer are with the Institute of Medical Psychology and Behavioral Neurobiology and MEG Center, University of Tubingen, Germany (corresponding author O. Yilmaz: +49-7071-29-81195; e-mail: oezge.yilmaz@uni-tuebingen.de).

A. Ramos-Murguialday is also with TECNALIA, Health Technologies department, San Sebastian, Spain. N. Birbaumer is also with Ospedale San Camillo, Istituto di Ricovero e Cura a Carattere Scientifico, Lido, Italy.

TABLE I. SUMMARY OF THE PATIENTS

Patient	Age, Gender	Years since stroke	Paretic side	Lesion Location	FM Score
1	64, f	2	right	mixed	1
2	50, m	1	right	mixed	0
3	58, m	19	left	mixed	2
4	44, m	10	left	mixed	3
5	68, f	4	right	subcortical	0
6	51, f	2	right	subcortical	4
7	47, m	10	left	subcortical	4
8	54, f	1	left	subcortical	0

selection criterion included complete paralysis of hand extensors (no residual movement) and intact cognitive skills (no psychiatric or neurological condition was present). The degree of functional severity was measured using the impairment scale Fugl-Meyer (FM). The mean FM hand scores from the upper limb motor subsection were 1.75±1.75. The study was conducted at the University of Tubingen, Germany. Informed consent was obtained from all patients involved. The study was approved by the ethics committee of the Faculty of Medicine of the University of Tübingen.

B. Data acquisition

Patients underwent a 16 channel EEG recording (Acticap, BrainProducts GmbH, Germany). Surface electromyographic (EMG) activity was recorded from both arms using 8 bipolar Ag/AgCl electrodes from Myotronics-Noromed (Tukwila, WA, USA) on 4 different muscle groups (extensor carpi ulnaris, extensor digitorum, external head of the biceps and external head of the triceps) in order to detect the movement onset and involuntary muscle contractions on the contralateral arm. Electrooculography (EOG) recordings were also carried out for ocular corrections.

Patients performed an audiovisual task. The imperative cue was visually (an arrow pointing right or left or a cross indicating rest condition appearing on the screen for 5 sec) and auditory (a sound indicating right or left or rest when the visual cue appeared on screen) presented. Patients executed an opening and closing movement with the intact hand or tried to open and close the paretic hand at a comfortable personal pace during this 5 sec. The inter-trial-interval was randomized between 3 and 4 sec. Patients were asked to rest when the visual cue disappeared from the screen.

C. EEG Analysis

Data were analyzed using Brain Vision Analyzer 2.0 signal processing software (BrainProducts GmbH, Germany). During the EEG preprocessing a 50 Hz notch filter was applied to the data, which were cleaned from ocular artifacts using Gratton & Coles method [16]. We used the current source density (CSD) method to work on reference free data.

CSD is a spatial filtering technique reducing the redundancy and ambiguity of volume conduction measures in EEG [17]. Using these surface Laplacian methods like CSD we decreased the contribution of the muscle artifacts to the signal significantly [18], which is one of the main problems with these patients tending to evoke movement compensation.

EEG data were filtered between 0.1 Hz and 2.5 Hz [5] and segmented from -2500 ms to 2000 ms aligned to the EMG onset. -2500 ms to -2000 ms was used for baseline correction. The EEG data were analysed only in time domain, since both SCP and MP components were expected to be phase locked to the EMG onset.

Six frontal and central electrodes were used for statistical analysis (F3, Fz, F4, C3, Cz, C4) due to detected MRCPs distribution over the scalp. Statistical analysis was performed using peak latency, amplitude and SCP onset latency as dependent variables and lesion (subcortical and mixed) and hand movement (paretic and healthy) as independent variables. Nonparametric Mann-Whitney U test was used because, not Kolmogorov-Smirnov, but Levene's test was significant for some channels.

D. EMG Analysis

EMG was filtered 10 to 90 Hz and rectified. EMG data from 1500 ms to 1400 ms before each cue were used to calculate a resting baseline mean and standard deviation (SD). We determined an EMG activity onset to occur when a threshold at 4 SD from baseline mean is crossed. EMG data from 300 ms to 2000 ms after the cue were used to detect the EMG onset.

EMG onset of the healthy arm was detected clearly in all patients. But EMG onset was not detectable in the paretic arm for patients 4, 5, 7, 8. In order to set an EMG onset for these patients a constant (K) was calculated following equation 1.

$$K = \frac{1}{N} \sum_{i=1}^{N} \left(P_i / H_i \right) \quad (1)$$

Being P_i and H_i paretic and healthy EMG onset latency of patient i and N the number of patients where EMG was detected. After K was obtained, it was multiplied to the healthy hand EMG onset latency of the patients who did not have an EMG onset on the paretic hand. Equation 2 is showing how mean EMG onset was found for those patients.

$$P_k = K \times H_k \quad (2)$$

The EEG and EMG channel names were swapped for the left hand paretic patients during the averaging of the EEG and the EMG data in order to have same channel names presenting the paretic and healthy electrodes. Therefore left sided electrodes (C3, F3) were over the lesioned and right sided electrodes were over the intact hemisphere (C4, F4) after the re-positioning.

III. RESULTS

When analyzing all patients together, during healthy hand movements no SCP was detected in any of the electrodes, i.e. no early slow negative shift was observed. However, a

faster negative slope onset before MP was precisely time locked with EMG onset (Fig. 1A). On the other hand, for paretic hand movements SCP was detected during the preparation phase and the MP (peak of the negative shift) occurred concurrently to the EMG onset (Fig. 1B).

A. Healthy vs. paretic hand

A multivariate analysis on electrodes C3, C4, F3 and F4 revealed MP peak latency to be significantly shorter in paretic compared to healthy hand movements in all patients (p=.002). The onset of the SCP was also significantly earlier in paretic compared to healthy hand movements (p=.002) (Fig. 1).

However, a post hoc analysis demonstrated that this effect was observed in patients with subcortical lesions only. The MP peak latency was significantly shorter for paretic compared to healthy hand movements in subcortical stroke patients only (p=.005).

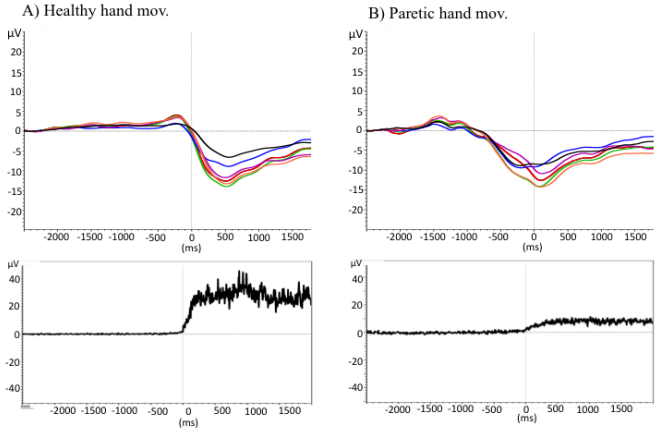

Figure 1. Grand average of all patients, 6 EEG channels (F4, Fz, F3, C4, Cz, C3) (up), EMG activity (down). A) Healthy hand movement, B) Paretic hand movement.

B. Subcortical vs. mixed lesions

For paretic hand movements, the mean peak latency and amplitude of MP in all six fronto-central channels were -293 ms and -12.9 μV in subcortical stroke patients and was 67 ms and -10.3 μV in mixed lesion stroke patients respectively (Fig. 2). The MP peak amplitude was significantly bigger over the lesion (contralateral) hemisphere in stroke patients with subcortical lesions only compared to mixed lesion patients (F3 p=.02, C3 p=.008). Additionally, the latency of MP peak was significantly earlier in the intact (ipsilateral) hemisphere (F4,C4) and fronto-medial region (Fz) in patients with subcortical lesions only compared to patients with mixed lesions during paretic hand movements (F4 p=.003, C4 p=.002, Fz p=.03).

In healthy hand movements, MP peak amplitude was significantly larger over the lesion (ipsilateral) hemisphere C3 (p=.004) and fronto-medial region Fz (p=.03) in subcortical lesions only compared to mixed lesions patients. There was no significant difference between the subcortical and mixed stroke patients MP peak latency for healthy hand movements (Table 2).

TABLE II. MRCP FEATURES

	Feat.	Healthy Mov.		Paretic Mov.	
		Lesion	*ContraL*	*Lesion*	*ContraL*
Sub	***SCP L***	-210	-269	-893	-861
	MP L	520	533	-296	-290
	MP A	-13.1	-15.4	-15.8	-10.1
Mix	***SCP L***	-296	-337	-688	-638
	MP L	480	330	-6	140
	MP A	-6.1	-10	-6.9	-13.8

a. Mean of slow cortical potential latency (SCP.L.), motor potential latency (MP.L.) and amplitude (MP.A.) for subcortical only and mixed lesion chronic stroke patients are presented. These MRCPs features are divided in lesion (C3, F3) or contralesional (C4, F4) hemisphere and during healthy and paretic hand movement and calculated as the mean of C3 and F3 or C4 and F4 channels for lesion and contralesional hemisphere respectively.

There was no significant difference in Cz neither in amplitudes nor in latencies when comparing subcortical only versus mixed lesion patients during healthy or paretic hand movements. Furthermore, no significant differences in SCP onset latencies between groups for both either paretic or healthy hand movements were observed.

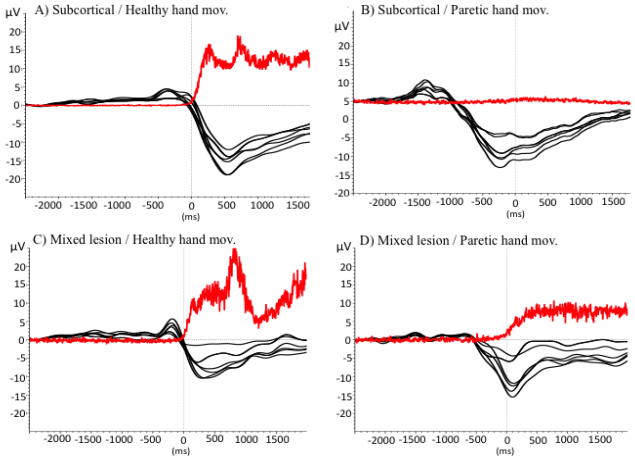

Figure 2. Grand average of all patients, 6 EEG channels (F4, Fz, F3, C4, Cz, C3) (black lines), EMG activity (red lines). Subcortical stroke patients performing A) healthy, B) paretic hand movement. Mixed lesion stroke patients performing C) healthy, D) paretic hand movement.

C. Laterality

A repeated measure ANOVA was performed to calculate the laterality differences between lesioned and contralesional hemisphere during healthy and paretic hand movements. Channels C3, F3 against C4, F4 were used as two levels of laterality factor. There were no significant differences neither in SCP onset, MP peak latencies nor MP peak amplitudes between hemispheres, i.e. no laterality effect. This means both hemispheres presented equal activity during the preparation and execution of the movement. This effect was observed when performing paretic and healthy hand movements.

IV. DISCUSSION

Negligible preparation time was detected before healthy hand movements. The onset of the negativity was time-

locked with the EMG onset and the time difference between the onset and the peak of the MP was significantly shorter (higher negative gradient) than during paretic hand movements. This result supports previous findings suggesting that the time between the onset of the MRCP and the EMG onset may indicate time needed to plan the required action [19]. In our study, the task was relatively easy (open/close the hand) which did not need a long time to prepare the movement. However, for the paretic hand movements this preparation time was significantly longer. We hypothesize this effect could be due to: a) chronic paresis b) a learned non-use effect [20] c) concentration and attention needed to contract the muscles with the paretic hand (longer planning phase).

The peak amplitude of the negativity was not significantly different when comparing paretic and healthy hand movements in evoked MRCPs. It has been previously suggested that the amplitude of the MP negativity may indicate the brain computational demand to perform the movement [21]. However, in our study, we did not find any difference in MP peak amplitude between paretic and healthy hand movements. Therefore, we hypothesize the SCP earlier onset and longer negativity effect to represent a higher neural computational effort to evoke the necessary brain excitation to induce a motor top-down command during paretic hand movements and the MP peak amplitude to be related to the ability to evoke motor intention, which remained intact in these patients (tested with imagery questionnaires).

The significant higher MRCP amplitudes over lesioned hemisphere during paretic and healthy hand movements in subcortical compared to mixed stroke patients, may be due to more intact cortical structures participating in generation of MRCPs.

Taking all these results together, we could hypothesize that we could use a BCI to train chronic patients to reduce SCP duration in order to induce motor recovery.

V. Conclusion

Further analysis with a larger group of patients would be needed to increase the statistical power and confirm our preliminary results. This work presented how lesion locations would effect motor preparation and execution. We would like to propose the use MRCP based BCIs to balance the MRCP features (towards normal) to induce motor function recovery in rehabilitation interventions.

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References

[1] G. Barrett, H. Shibasaki, R. Neshige, “Cortical potentials preceding voluntary movement: evidence for three periods of preparation in man.” Electroencephalogr Clin Neurophysiol., vol. 63, no. 4, pp. 327-339, Apr. 1986.

[2] L. Deecke, P. Scheid, H.H.Kornhuber, “Distribution of readiness potential, pre-motion positivity, and motor potential of the human cerebral cortex preceding voluntary finger movements.” Exp Brain Res., vol. 7, no. 2, pp.158-68, 1969.

[3] H. Shibasaki, M. Hallett, “What is the Bereitschaftspotential?” Clin Neurophysiol., vol. 117, no. 11, pp. 2341-2356, Nov. 2006.

[4] T. Elbert, B. Rockstroh, “Threshold regulation- a key to understanding of the combined dynamics of EEG and event-related potentials.” J of Psychophysiology, vol. 4, pp. 317-333, 1987.

[5] N. Birbaumer, T. Elbert, A.G. Canavan, B. Rockstroh, “Slow potentials of the cerebral cortex and behavior.” Physiol Rev., vol. 70, no. 1, pp. 1-41. Review, Jan. 1991.

[6] K. Sasaki, H. Gemba, “Compensatory motor function of the somatosensory cortex for the motor cortex temporarily impaired by cooling in the monkey.” Exp Brain Res., vol. 55, no. 1, pp. 60-68, 1984.

[7] P. Praamstra, A.S. Meyer, A.R. Cools, M.W. Horstink, D.F. Stegeman, “Movement preparation in Parkinson's disease. Time course and distribution of movement-related potentials in a movement precueing task.” Brain, vol. 119, no. 5, pp. 1689-1704, Oct. 1996.

[8] W. Lang, M. Lang, I. Podreka, M. Steiner, F. Uhl, E. Suess, C. Müller, L. Deecke, “DC-potential shifts and regional cerebral blood flow reveal frontal cortex involvement in human visuomotor learning.” Exp Brain Res., vol. 71, no. 2, pp. 353-364, 1988.

[9] I. Loubinoux, C. Carel, J. Pariente, S. Dechaumont, J.F. Albucher, P. Marque, C. Manelfe, F. Chollet, “Correlation between cerebral reorganization and motor recovery after subcortical infarcts.” Neuroimage, vol. 20, no. 4, pp. 2166-2180, Dec 2003.

[10] L. Deecke, “Bereitschaftspotential as an indicator of movement preparation in supplementary motor area and motor cortex.” Ciba Found Symp., vol. 132, pp. 231-250, Review, 1987.

[11] J. Kitamura, H. Shibasaki, T. Takeuchi, “Cortical potentials preceding voluntary elbow movement in recovered hemiparesis.” Electroencephalogr Clin Neurophysiol., vol. 98, no. 2, pp. 149-156, Feb. 1996.

[12] J. B. Green, Y. Bialy, E. Sora, and A. Ricamato, “High-resolution EEG in poststroke hemiparesis can identify ipsilateral generators during motor tasks.” Stroke, vol. 30, no. 12, pp. 2659-2665, Dec 1999.

[13] R. Verleger, S. Adam, M. Rose, C. Vollmer, B. Wauschkuhn, D. Kömpf, “Control of hand movements after striatocapsular stroke: high-resolution temporal analysis of the function of ipsilateral activation.” Clin Neurophysiol., vol. 114, no. 8, pp. 1468-1476, Aug. 2003.

[14] H. Wiese, C. Tönnes, A. de Greiff, K. Nebel, H.C. Diener, P. Stude, “Self-initiated movements in chronic prefrontal traumatic brain injury: an event-related functional MRI study.” Neuroimage, vol. 30, no. 4, pp. 1292-1301, May 2006.

[15] S.K. Jankelowitz, J. G. Colebatch, “Movement related potentials in acutely induced weakness and stroke.” Exp Brain Res, vol. 161, no. 1, pp. 104-113, Feb. 2005.

[16] G. Gratton, M.G. Coles, E. Donchin, “A new method for off-line removal of ocular artifact.” Electroencephalogr Clin Neurophysiol, vol. 55, no. 4, pp. 468-484, Apr. 1983.

[17] C.E. Tenke, J. Kayser, C.G. Manna, S. Fekri, C.J. Kroppmann, J.D. Schaller, D.M Alschuler, J.W. Stewart, P.J. McGrath, G.E. Bruder, “Current source density measures of electroencephalographic alpha predict antidepressant treatment response.” Biol Psychiatry, vol. 70, no. 4, pp. 388-394, Aug 2011.

[18] S.P. Fitzgibbon, T.W. Lewis, D.M. Powers, E.W. Whitham, J.O. Willoughby, K.J. Pope, “Surface Laplacian of Central Scalp Electrical Signals is Insensitive to Muscle Contamination.” IEEE Trans Biomed Eng, vol. 60, no. 1, pp. 4-9, Jan. 2013.

[19] I.M. Tarkka, M. Hallett, “Cortical topography of premotor and motor potentials preceding self-paced, voluntary movement of dominant and non-dominant hands.” Electroencephalogr Clin Neurophysiol, vol. 75, no. 2, pp. 36-43, Feb. 1190.

[20] E. Taub, G. Uswatte, R. Pidikiti, “Constraint-Induced Movement Therapy: a new family of techniques with broad application to physical rehabilitation--a clinical review.” J Rehabil Res Dev, vol. 36, no. 3, pp. 237-251, Jul. 1999.

[21] W. Lang, R. Beisteiner, G. Lindinger, L. Deecke, “Changes of cortical activity when executing learned motor sequences.” Exp Brain Res, vol. 89, no. 2, pp. 435-440, 1992.