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BRIEF COMMUNICATION

Neural coupling of cooperative hand movements after stroke: role of ipsilateral afference

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Abstract

We investigated the role of ipsilateral ascending pathways in the neural coupling underlying cooperative hand movements of stroke subjects. Ipsi- and contralateral somatosensory evoked potentials (SSEP) were recorded following ulnar nerve stimulation during cooperative and non-cooperative hand movements. The amplitude ratio, that is, ipsilateral divided by contralateral amplitude, was highest during the cooperative task when the affected arm was stimulated, reflecting an enhanced afferent volley to the unaffected hemisphere. The presence of ipsilateral SSEP from the paretic arm was closely related with the patients' hand function. This shows for the first time a laterality in ascending pathways after unilateral stroke and implies an involvement of the unaffected hemisphere in the control of paretic hand movements.

Introduction

Cooperative hand movements, defined as movements where the action of one hand is supported by counteraction of the other one (e.g., opening a bottle), are required in activities of daily living (ADL). These object-oriented movements are controlled by a task-specific neural coupling[1–3] which differs from that of neural networks underlying the control of non-cooperative bimanual tasks[4–11]. These bimanual separate hand movements, in contrast to cooperative hand movements studied here, do not use the neural coupling mechanism in movement control. The neural coupling is reflected in the appearance of electromyographic (EMG) reflex responses in activated forearm muscles of both sides following unilateral stimulation of ulnar nerve and activation of bilateral secondary somatosensory (S2) cortical areas in fMRI recordings[1]. These observations indicate that each hemisphere is task-specifically involved in the control of both hands during cooperative movements. The neural coupling underlying cooperative hand movements might be achieved by an involvement of ipsilateral pathways[2].

In stroke subjects, the neural coupling mechanism is preserved from the unaffected to the paretic side but defective from the affected side due to an impaired processing of afferent input[3]. For a better understanding of the compensatory role of the ipsilateral, unaffected hemisphere in movement control it is important to explore the function of ascending pathways in cooperative tasks. It is hypothesized that the strength of ipsilateral afference from the affected forearm to the unaffected hemisphere is reflected in ipsilateral somatosensory evoked potentials (SSEPs). This would indicate an involvement of the unaffected hemisphere in the control of the paretic arm/hand during cooperative movements and might determine outcome of hand function.

Materials and Methods

This study was approved by the local ethics committee (Ethics Committee of the Canton of Zurich). All subjects were previously informed about the study and gave written informed consent before enrolment.

Twelve chronic, that is, insult more than 6 months before study onset, post-stroke subjects (61.7 ± 8.4 years; three females) participated in this study. Characteristics of the patients are shown in table 1. Fugl-Meyer scores of the upper limb were related to the SSEPs. Eight age-matched (61.0 ± 8.0 years) healthy volunteers served as a control group.

SSEPs were evoked in a supine position with head fixation. Stimulation of the ulnar nerve was applied by KeyPoint XP (Medtronic A/S, Skovlunde, Denmark) through self-adhesive surface electrodes (5.96 mm^2, CareFusion, Middleton, WI) which were placed over both wrists with an interelectrode distance of 2 cm. Stimulation intensity of the ulnar nerve was set at 0.5 mA above motor threshold (MT), that is, lowest intensity resulting in visible twitching of the abductor digiti minimi. Stimulation frequency was set at 3.1 Hz and the pulse width was set at 0.2 msec.

Cortical potentials were bilaterally recorded by KeyPoint XP (Medtronic A/S,) through needle-electrodes (12 mm, Spes Medica S.r.l., Battipaglia, Italy) placed over Fz (as reference), C3 and C4. Signals were recorded with a frequency of 12 kHz and band-pass filtered between 500 Hz and 1 Hz.

Patients had to perform three different tasks during the recording: (1) resting (rest), (2) bimanual pro-/ supination movements with dumbbells (pro-sup) and, (3) cooperative hand movements (dyn-coop) using a device previously described[1,2]. Electrical ulnar nerve stimulation was consecutively applied at both wrists. The order of stimulated side and task performed during the measurement was randomly varied. Each side and condition was recorded in four traces of 100 stimuli each.

Table 1. Characteristics of patients and healthy volunteers.

ID	Age	Gender	Hemi-paresis	Time since stroke [y]	FM score	Ipsilateral potential
S01	64	F	Right	3.4	49	No
S02	65	M	Left	19.9	47	No
S03	49	M	Left	7.7	44	No
S04	59	M	Right	11.4	50	Yes
S05	51	M	Right	7.4	57	Yes
S06	66	F	Right	7.3	55	Yes
S07	50	M	Right	8.7	46	No
S08	72	M	Left	3.4	60	Yes
S09	62	M	Right	9.2	53	Yes
S10	56	F	Right	5.8	42	No
S11	75	M	Left	4.1	61	Yes
S12	71	M	Left	4.0	56	Yes

Left, Clinical characteristics of the post-stroke subjects included in the study including Fugl-Meyer (FM) score. Right, Presence of ipsilateral potential in the unaffected hemisphere following stimulation of the affected arm during the cooperative hand movement.

Analysis was done using Soleasy (Aleasol, Zurich, Switzerland) A Butterworth band-stop filter set between 45 Hz and 55 Hz was applied to exclude any 50 Hz noise from the signal. All four traces per side and condition were averaged for each subject before calculation of latencies and amplitudes. Latencies were automatically set at minima between 19 msec and 27 msec (N20) and maxima between 23 msec and 32 msec (P25). Amplitudes were calculated as differences between N20 and P25. Division of ipsilateral by contralateral amplitude resulted in amplitude ratio. Time normalization for illustrating purposes was achieved by setting the individual N20 peak of every trace to zero. Background EEG was quantified. Potentials were defined as EEG responses with amplitudes that exceed the mean of background EEG by at least one standard deviation. Statistics were calculated with IBM SPSS Statistics 19 (Armonk, New York, NY). Differences in thresholds, latencies, and FM scores were calculated using Wilcoxon signed-rank tests. Differences in amplitude ratios within groups were calculated with repeated measures ANOVA with post hoc t-tests with Bonferroni corrections and between groups with univariate one-way ANOVA.

Results

All participants were able to perform the cooperative as well as the bimanual pro-/ supination tasks without problems and tolerated the experiments well. In patients, both sensory thresholds (ST) and motor thresholds (MT) were slightly higher in the affected (ST: 5.4 ± 1.4 mA; MT: 9.7 ± 1.9 mA) than in the nonaffected arm (ST: 4.5 ± 0.8; MT: 9.1 ± 3.1). The differences were statistically not significant. The control group showed lower values (ST: 3.7 ± 0.6 mA; MT: 7.7 ± 1.7 mA). While differences in the ST were significant for both the affected and the unaffected arm of stroke patients, differences in MTs were not. Stimulation intensity of 0.5 mA above MT intensity was perceived as non-noxious by all subjects.

Figure 1 shows the grand averages of time-normalized EEG traces of post-stroke patients. Ipsilateral potentials (black traces) were usually smaller than contralateral potentials (gray traces). However, when stimulating the affected arm of stroke patients during dyn-coop the ipsilateral potential had a higher amplitude than the contralateral one (Fig. 1C). Therefore, the amplitude ratio was above 1 (1.23 ± 0.28) and differed significantly ($P < 0.05$) from the other conditions (Fig. 2A) as well as from the values obtained in healthy controls. Following stimulation of the affected arm of stroke subjects, the amplitude ratio was 0.62 ± 0.92 during pro-sup and 0.62 ± 0.33 during rest. Following stimulation of the

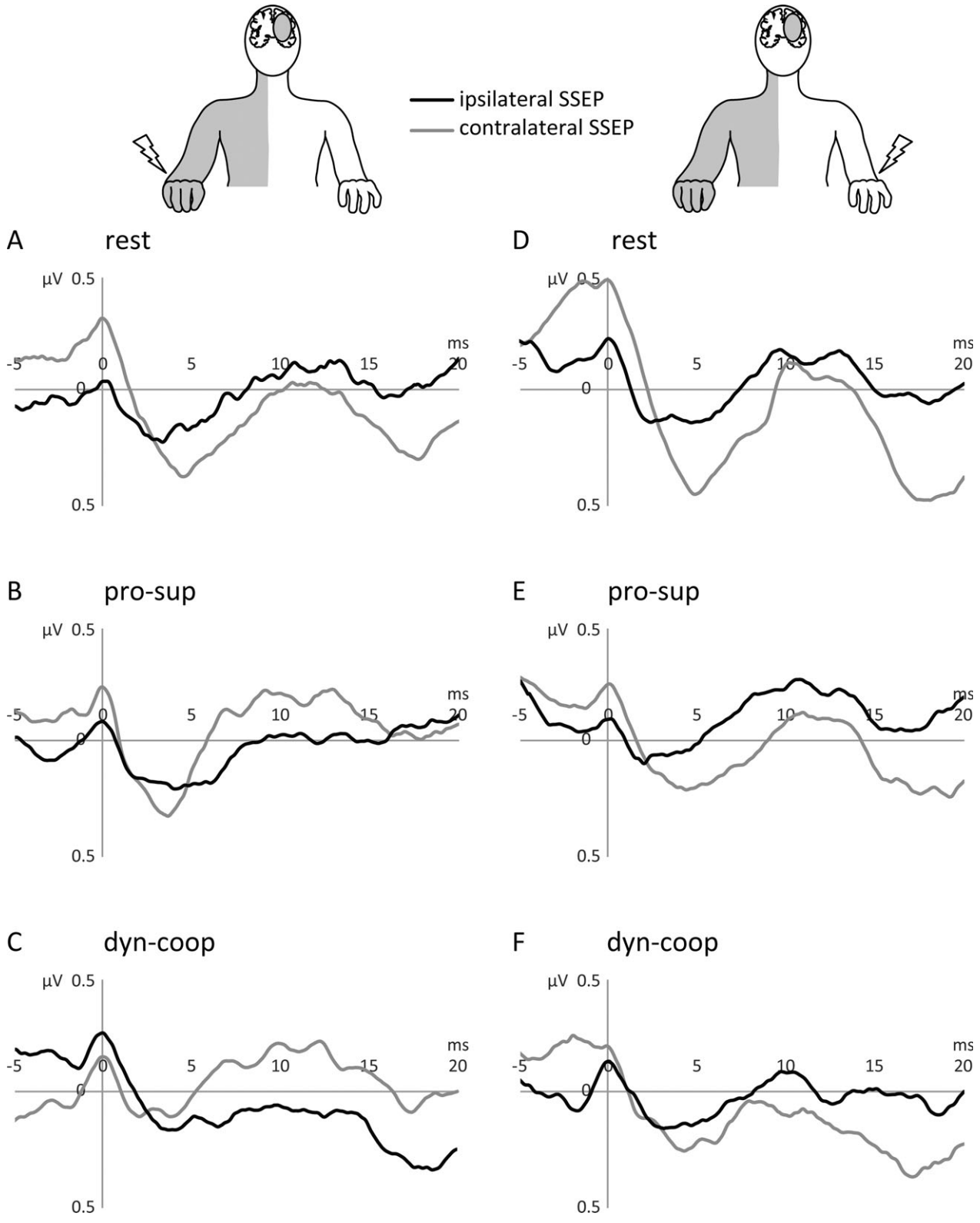

Figure 1. Time-normalized EEG traces of post-stroke patients. Grand averages ($N = 12$) of the somatosensory evoked potentials (SSEPs) are shown. They were evoked during three different conditions, that is, resting (rest, A and D), non-cooperative bimanual movements (pro-sup, B and E) and cooperative hand movements (dyn-coop; C and F). Electrical stimulation of the ulnar nerve was applied at the affected (A–C) and the unaffected (D–F) arm of the stroke patients. Gray traces: contralateral potential; black traces: ipsilateral potentials.

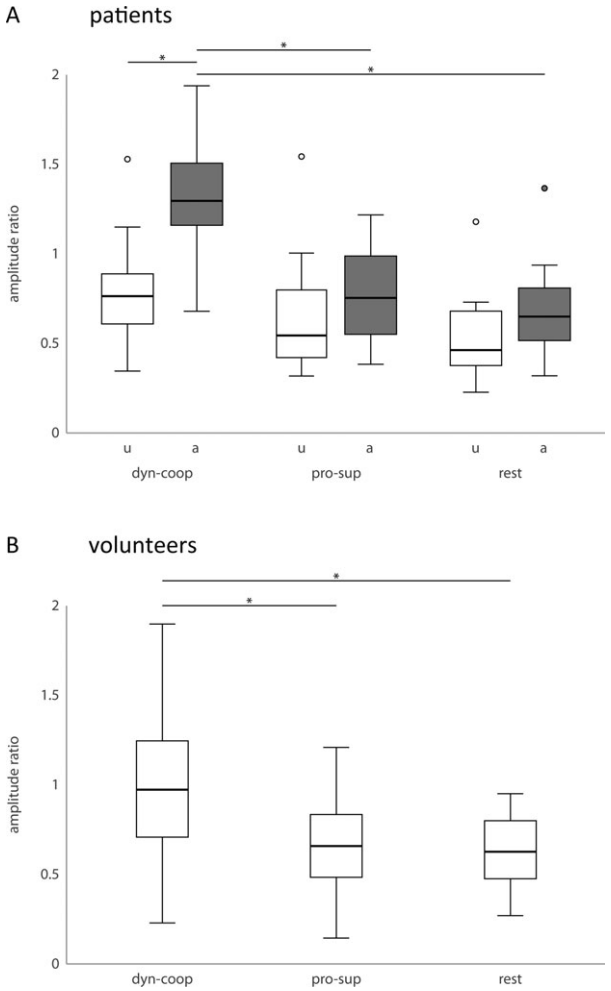

Figure 2. Amplitude ratios. (A) Amplitude ratio, that is, ipsilateral divided by contralateral SSEP amplitude, in post-stroke patients during the conditions dyn-coop, pro-sup and rest elicited by stimulation of the ulnar nerve of the affected (a; gray bars) and unaffected (μ; white bars) arm. (B) Amplitude ratio (ipsilateral amplitude divided by contralateral amplitude) in healthy volunteers during dyn-coop, pro-sup, and rest. *$P < 0.05$.

unaffected arm, the ratio was 0.61 ± 0.22 during dyn-coop, 0.53 ± 0.16 during pro-sup and 0.40 ± 0.18 during rest. Healthy volunteers showed amplitude ratios of 0.99 ± 0.44 during dyn-coop, 0.62 ± 0.21 during pro-sup, and 0.66 ± 0.27 during rest (Fig. 2B). The amplitude ratio during dyn-coop was significantly higher compared to the other conditions.

Amplitude of background EEG was similar in all subjects during all conditions (0.31 ± 0.05 μV). Minimal SSEP amplitude was set at 0.35 μV. During dyn-coop, all healthy volunteers showed an ipsilateral potential. In post-stroke patients, two groups could be separated when stimulating the affected arm: one without an ipsilateral potential associated with lower FM scores (G1) the other one with ipsilateral potentials over the unaffected hemisphere associated with high FM scores (G2). The upper limb FM scores of these two groups (G1: 45.6 ± 2.4; G2: 56.1 ± 3.4) differed significantly ($P < 0.05$).

SSEP latencies were similar for all conditions and sides in healthy and stroke subjects.

Discussion

The aim of this study was to explore the involvement of the ipsilateral ascending input in the neural coupling in stroke patients. Till now, only ipsilateral descending connections have been studied in CNS lesions[12–15]. Here, we show a dominance of ipsilateral ascending input from the paretic arm to the unaffected hemisphere during cooperative hand movements of moderately affected stroke patients reflected in the presence of ipsilateral potentials, suggesting an involvement of the unaffected hemisphere in movement control of the paretic hand. The presence of ipsilateral potentials is unlikely due to an imbalance of reciprocal inhibition of the hemispheres[16] or due to reduced potential of the affected hemisphere, as these were smaller in the control task.

The enhanced ipsilateral afference might converge in S2 cortical area as a task-specific activation of the S2 cortical areas in the fMRI was found during cooperative movements[1]. In these areas, a convergence and processing of shared afferent input from both hands occurs[17,18].

Only patients with a moderate FM score showed ipsilateral SSEP from the affected arm to the unaffected hemisphere. This indicates an involvement of ipsilateral cortical areas in the outcome of hand function. In severely affected patients, no ipsilateral SSEP responses could be elicited, that is, in these patients the unaffected hemisphere becomes not involved in the performance of cooperative movements. For these patients, the neural coupling mechanism might not be accessible due to the extent of brain damage.

Already in healthy subjects, ipsilateral SSEP amplitudes were larger during cooperative compared to non-cooperative bimanual movements[2], indicating a task-specific role of the ipsilateral ascending pathways in the control of cooperative movements. According to the present results, this afference is again enhanced from the paretic limb to the unaffected hemisphere indicating the importance of the unaffected hemisphere in movement control.

It is concluded that an enhanced ipsilateral afference from the paretic arm to the unaffected hemisphere might represent a compensatory involvement of the neural coupling in movement performance. The functioning of this mechanism is associated with a favorable outcome of paretic hand function. A next step will be to explore

which factors (e.g. extent of brain damage) determine the functioning of this part of neural coupling in longitudinal studies. With this knowledge, patients could be stratified at an early stage into patients who might profit from a training of cooperative movements, required during ADL.

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Author's contributions

Miriam Schrafl-Altermatt, PhD – Drafting and revising the manuscript for content, including medical writing for content; Study concept and design; Analysis and interpretation of data; Acquisition of data; Statistical analysis; Study supervision and coordination. Obtaining funding.

Volker Dietz, MD – Drafting and revising the manuscript for content, including medical writing for content; Study concept and design; Study supervision and coordination.

Conflict of Interest

None to declare.

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