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Acute and cumulative effects of rTMS on behavioural and EMG parameters in Focal Hand Dystonia

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ABSTRACT

Previous studies suggest that low-frequency repetitive Transcranial Magnetic Stimulation (rTMS) over contralateral premotor cortex (PMC) might ameliorate Focal Hand Dystonia (FHD) symptoms. In the present study behavioral and muscle activity outcomes were explored in a patient with FHD following a single and multiple sessions of rTMS. The patient's behavior was assessed on handwriting tasks, while surface EMG signals were recorded. In Experiment 1 evaluations were performed before and after one session of active and sham 1Hz rTMS over contralateral PMC. In Experiment 2, evaluations were performed before and after six sessions of the same treatment. In Experiment 1 active rTMS improved the patient's performance, although the EMG amplitude did not change. In Experiment 2, the patient showed an improvement of performance along with a decrease of 20% in the EMG amplitude. These results demonstrated that a single session of rTMS ameliorated the patient's performance, while multiple sessions were necessary to reduce muscles activity.

1. Introduction

Focal hand dystonia (FHD) is a task-specific form of dystonia [1], resulting from abnormal neuroplasticity. An electromyographic (EMG) study [2] has demonstrated higher muscles activity during writing tasks in patients with FHD with respect to healthy subjects while other investigations suggested that low-frequency repetitive Transcranial Magnetic Stimulation (rTMS) over contralateral premotor cortex (PMC) might ameliorate FHD [3,4]. Although a previous study combining the use rTMS with the assessment of FHD trough a multi-channel EMG technique found that co-contraction and overflow showed by dystonic patients during handwriting decreased after one rTMS session over the PMC [4], the effects of multiple rTMS sessions on muscle activity have never been investigated.

Here, we explored behavioural and muscle activity outcomes, following single (Experiment 1: Acute Effects-AE) and multiple sessions (Experiment 2: Cumulative Effects-CE) of rTMS in a 41-year-old man who developed FHD, mainly affecting the right index and middle fingers, six years before our evaluations. At the onset of the disorder, his symptoms appeared during mouse manipulation, but over time they appeared during the execution of actions requiring fine movement control. Despite the severity of his condition, he was free of medications.

2. Material and methods

In Experiment 1, we administered one rTMS session (1-Hz, 900 stimuli, 90% of resting Motor Threshold-rMT) over the left PMC, defined as 2 cm anterior and 1 cm medial to the previously defined M1 hotspot [5], and a sham session after a week. In Experiment 2, we administered six sessions of the same treatment, every other day, for two weeks. The evaluations were performed before (Pre-Acute: Pre-A) and after (Post-A) the single and the sham rTMS sessions (Pre-Sham: Pre-S/Post-S) in Experiment 1, and before rTMS (Pre-Cumulative: Pre-C), one day after the end of the rTMS sessions (Post-C). Furthermore, an additional evaluation was performed two weeks after the intervention (Follow-up: FU) in Experiment 2. For each evaluation, the signature and the word copying were performed two times (one pre and one post the rTMS application), except for the FU, where the evaluation was performed only once.

In addition, the patient's dystonia was evaluated by the neurologist pre and post the single and the six rTMS sessions. A healthy man (32-

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year-old) was evaluated using the same tasks and EMG recording. Handwriting was assessed on two tasks (producing the own signature and copying two words), while surface EMG signals were registered from the eight upper limb muscles reported in the figure caption. A verbal command to start the task was given to the patient and the time spent for the execution of each task (Execution Time-ET) was calculated with the help of the videotape recordings. The estimation of the muscle activity was computed as the EMG signal amplitude averaged among the whole task(s). The patient, as well as the healthy volunteer, were screened for inclusion/exclusion criteria for TMS, and they signed a written informed consent to participate to the study, which was approved by the Local Ethical Committee.

3. Results

In Experiment 1 active rTMS considerably improved the patient's performance, reducing the ET by 73% in signature (*rTMS*: Pre-A = 26.16 s, Post-A = 7.16 s; *Sham*: Pre-S = 24.00 s, Post-S = 21.00 s) and by 37% in words coping (*rTMS*: Pre-A = 19.00 s, Post-A = 12.00 s; *Sham*: Pre-S = 24.00 s, Post-S = 21.00 s) although the overall EMG amplitude did not change after both sessions (See Supplementary Video 1, 2 and 3). In Experiment 2, reduction in ET by 22% was found in signature (Pre-C = 19.84 s, Post-C = 15.48 s) and by 23% in words coping (Pre-C = 22.00 s, Post-C = 17.00 s) in the Post-C ET. Ameliorations were maintained at the FU evaluation with a reduction of 17% in ET for the signature and of 36% in words coping with respect to the Pre-C rTMS evaluation (See Supplementary Video 1, 4 and 5).

Importantly, in the Post-C assessment the overall EMG amplitude decreased by 20% (the reduction of muscles contraction was more pronounced for the signature, Fig. 1 and Table 1 for more details), although the reduction was not maintained at the FU. The healthy control showed shorter ET and lower muscles activity than patient for both handwriting tasks (≈6 s for each task). However, the dystonic symptoms evaluation did not reveal significant improvement associated with these ameliorations. In relation to the rMT, in Experiment 1, it did not change in the pre- and post evaluation for both active and sham sessions (i.e. 37% of the machine output). In Experiment 2 the rMT decreased of 3% (i.e. 34% of the machine output), although the decrease of rMT was not maintained at the FU evaluation (i.e. 37% of the machine output).

4. Discussion

The feature unique to this study is the assessment of both acute and cumulative rTMS effects on FHD symptoms with the analysis of behavioural performances and EMG signals recorded from as many as eight upper limb muscles. Previous studies [3,5] have investigated the effects of low-frequency rTMS in FHD. Overall, our results are in line with previous evidences, suggesting that inhibitory low-frequency rTMS over contralateral PMC may ameliorate handwriting performance. However, with respect previous evidences [3–5], here we investigate the changes in muscles co-contraction and overflow showed by dystonic patient during handwriting from as many as eight upper limb muscles following single and multiple sessions of rTMS. Results have shown a global reduction of more than 20% in the observed muscles after six rTMS sessions, demonstrating that multiple rTMS interventions could reduce the abnormal muscle activity in FHD. Since the co-contraction of muscles is one of the characteristics of FHD, which lead to abnormal posturing and reduced fine motor control [1], future rTMS studies should take into account their potential changes after application of rTMS treatment.

5. Conclusions

These results suggest that rTMS represents a useful tool for the treatment of FHD symptoms, since it decreased muscle over-excitation and improved the patient's performance. They also show that a single session of rTMS may ameliorate patient's performance, but multiple sessions are necessary to reduce the muscle activity of the upper affected limb, although after two weeks the initial changes were not maintained. These findings indicate also that surface EMG represents a non-invasive and useful method to evaluate neuromuscular modulations after rTMS treatment. Finally, due to the differences we found in the behavioural outcomes between the Post-A and the Post-C evaluation, we strongly support the utility to assess both acute and cumulative effects of a single rTMS session in case of multiple sessions for the treatment of the FHD.

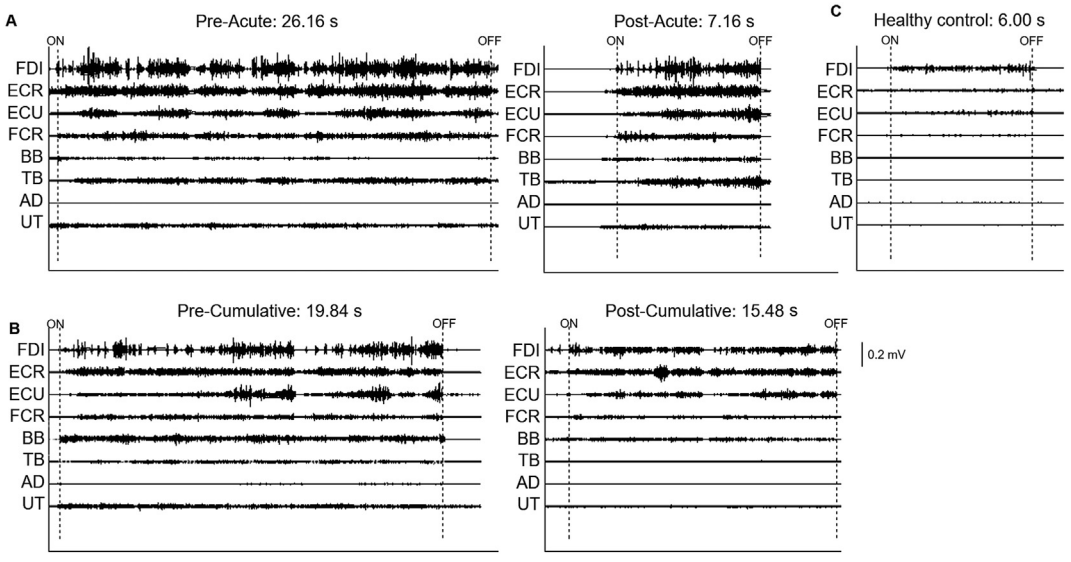

Fig. 1. Representative examples of the EMG signals during signature for the patient and for the healthy participant. The figure shows representative examples of the EMG signals during signature for the patient (A/B) and for the healthy participant (C). The patient and the healthy participant had approximately the same full name length (patient's name and surname: 14 characters; healthy participant's name and surname: 13 characters). For each trial the beginning and the end of the actual task execution are pointed out by the dashed lines and the actual duration of each trial is reported (in seconds). EMG signals are reported from: first dorsal interosseous (FDI), extensor carpi radialis (ECR), extensor carpi ulnaris (ECU), flexor carpi radialis (FCR), long head of biceps brachii (BB), long head of triceps brachii (TB), anterior deltoid (AD), upper trapezius (UT). The EMG signals were registered using bipolar Ag/AgCl surface electrodes (Spes Medica, Battipaglia, Italy) and they were amplified (gain = 2000, amplifier EMG-USB, OT Bioelettronica, Torino) and sampled at 2048Hz and bandpass filtered (20–450 Hz).

Table 1
Values of the EMG amplitude, i.e. the average rectified value (ARV) of the EMG signals expressed in microVolt.

Muscles	Pre-ACUTE	Post-ACUTE	% of Change	Pre-CUMULATIVE	Post-CUMULATIVE	% of Change
FDI	48.4	41.3	-14.7	49.8	33.5	-32.7
ECR	44.9	46.8	4.2	88.9	69.3	-22.0
ECU	29.2	33	13.0	39.7	29.2	-26.4
FCR	20.4	21	2.9	30.3	14.1	-53.5
BB	7.3	9.2	26.0	46.2	35.7	-22.7
TB	24	20	-16.7	24.5	5.2	-78.8
AD	4.5	4.4	-2.2	3.6	2.9	-19.4
UT	27.3	17.9	-34.4	37	22	-40.5

The values of the EMG ARV for the eight muscles observed, in both the Experiments (Acute and Cumulative). In the column "**% of Change**" is reported the change, expressed in percentage between the pre and the post evaluation for both the Experiments.

However, given that the present data were collected on a single FHD patient, no clear conclusions can be drawn from this finding. Therefore, the ability to draw generalizable conclusion is severely hindered by this limitation. Future studies on large number of patients, also targeting different brain areas [6], are necessary to further investigate the physiologic and behavioral effects of multiple sessions of rTMS in FHD.

Declarations

Author contribution statement

Adriana Salatino: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Gennaro Boccia: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Davide Dardanello, Donato Formicola, Giulia Spadea: Performed the experiments; Analyzed and interpreted the data.

Marcello Nobili: Conceived and designed the experiments; Analyzed and interpreted the data.

Annamaria Berti: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

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