eNeurologicalSci 8 (2017) 31–33

Contents lists available at ScienceDirect

eNeurologicalSci

journal homepage: www.elsevier.com/locate/ensci

Inhibition of the primary motor cortex and the upgoing thumb sign

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ARTICLE INFO

Keywords:
Corticospinal tract
Upper motor neuron lesions
Primary motor cortex
Transcranial magnetic stimulation

ABSTRACT

Background: The upgoing thumb sign has been frequently observed in patients with minor strokes and transient ischemic attacks as an indicator of brain involvement. We assessed the effect of primary motor cortex (M1) inhibition in the development of the upgoing thumb sign.

Methods: Used repetitive Transcranial Magnetic Stimulation (rTMS, 1 Hz frequency for 15 min, 1s ISI, 900 pulses) at 60% of resting motor threshold to inhibit the right or left primary motor cortex of 10 healthy individuals. Participants were examined before and after rTMS by a neurologist who was blind to the site of motor cortex inhibition.

Results: 10 neurological intact participants (5 women/5 men) were recruited for this study. 2 cases were excluded due to pre-existing possible thumb signs. After the inhibition of the primary motor cortex, in 6 subjects out of 8, we observed a thumb sign contralateral to the site of primary motor cortex inhibition. In one subject an ipsilateral thumbs sign was noted. In another case, we did not find an upgoing thumb sign.

Conclusion: The upgoing thumb sign is a subtle neurological finding that may be related to the primary motor cortex or corticospinal pathways involvements.

1. Introduction

The majority of physicians have examined lower limbs to find any signs of upper motor neuron (UMN) involvement. Nevertheless, subtle clinical findings in hands were also described. For example, *Souque* in 1907 noticed abduction of all fingers ipsilateral to hemiparesis (Souque's sign) [1]. Later, *Milton Alter* described an unilateral abduction of the little finger (the digiti quinti sign) [2]. In 1985, Vladimir Hachinski noticed the digiti quinti sign during the examination of a 27-year-old woman with a history of migraine. In addition to the previous standard description of the digiti quinti sign, he noticed an extension of the thumb on the same hand in the extended palms down position. He drew a picture and briefly described this finding [3]. After the examination of several subjects, he found that it was more accurate to perform this neurological exam while patients kept their palms facing each other, calling this finding an “upgoing thumb” [4]. Recently, a substantial level of agreement between independent physicians was found during the examination of 199 patients with stroke or transient ischemic attack (TIA) and stroke mimics [19]. We showed that the upgoing thumb sign was not only significantly more common in those with stroke or TIA, but also a substantial level of agreement with patient's neurological complaints.

These results were suggestive of a possible involvement of UMN in an upgoing thumb as correspondent to an upgoing toe (Babinski's) sign. However, a potential anatomic-physiological correlation of UMN involvement with an upgoing thumb has to-date not been proven. This study was designed to assess the possible role of the corticospinal tract in the appearance of the upgoing thumb sign. To do so, we applied repetitive Transcranial Magnetic Stimulation (rTMS) over the primary motor cortex (M1) of healthy participants in order to inhibit it and assessed them neurologically before and after stimulation.

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http://dx.doi.org/10.1016/j.ensci.2017.07.001
Received 27 April 2017; Accepted 18 July 2017
Available online 19 July 2017

2. Methods

2.1. Ethics

The study was approved by the Ethics Committee at the University of Western Ontario (No: HSREB 104919). Informed written consent was obtained from all participants before any neurologic examinations and rTMS evaluations.

2.2. Participants

Ten healthy right-handed participants (5 male, age range 19–46; 5 female, age range 23–46) were recruited from our research staff and students. Participants were from different ethnic backgrounds and were screened for any contraindications for rTMS according to the standard safety guidelines [5]. No past history of neurological disorders was reported.

2.3. The rTMS procedure

Participants were comfortably seated at a table with their arm resting on the surface. A Magstim Rapid 2 stimulator and a figure-of-eight, double 70 mm air-cooled coil were used (Magstim Company, Ltd., UK). Self-adhesive surface electrodes were placed in a belly-to-tendon fashion on the first dorsal interosseus (FDI) muscle contralateral to the TMS stimulation side.

The TMS coil was placed over M1 in correspondence of the hotspot for the first dorsal interosseus (FDI) muscle. rTMS was administered using an inhibitory stimulation protocol at 1 Hz frequency for 15 min (1s ISI, 900 pulses) at 60% of resting motor threshold (RMT) [6]. Resting motor threshold was defined as the minimum TMS intensity (in % of maximum stimulator output) required to elicit 5 out of 10 motor evoked potentials (MEPs) from FDI muscle with peak-to-peak amplitudes equal to or above 0.05 mV while the participant's right hand was relaxed.

Electromyography (EMG) signals were sampled 2 kHz, amplified 1000 times and bandpass filtered (25–250 Hz). Before and after rTMS, we assessed M1 excitability by recording MEPs from FDI on the contralateral hand while delivering 10 single TMS pulses (ISI = 3 s) over M1 at RMT intensity.

2.4. Clinical examinations

Past medical histories and clinical conditions were assessed by a stroke fellow. A senior neurologist, blind to the side of the stimulation, evaluated participants before and after stimulation. The upgoing thumb sign was also tested with a standard method in a sitting position. All examinations before and after rTMS were recorded with the permission of participants.

3. Results

After the inhibition of the primary motor cortex in 7 cases out of 8 (87.5%), an upgoing thumb was noted, including 6 contralateral and one ipsilateral to the site of inhibition. In one subject (case 6), we did not observe an obvious upgoing thumb after the rTMS. 2 cases were excluded as they had possible upgoing thumb sign before the rTMS. Some participants also had temporary neurologic symptoms and signs after the rTMS, such as tingling and changes in deep tendon reflexes (Table 1).

4. Discussion

The approval of any new clinical finding needs observational, clinical and experimental studies. In this study, we showed UMN involvement as a reason for the upgoing thumbs sign. After inhibition of primary motor cortex, all of our participants showed an upgoing thumb sign, in the majority of the cases, contralateral to the side of stimulation.

In the current study, we show the occurrence of an abnormal neurological finding, the upgoing thumb after inhibition of the primary motor cortex. This evidence strongly supports the involvement of the corticospinal tract in the generation of the upgoing thumb sign. Several studies showed a range of clinical findings in patients with localized brain lesions. According to *Edwin Smith Papyrus*, Egyptians were aware of hemiplegia after a head injury [7]. During the 19th and early half of the 20th century, clinicopathological studies proved the role of corticospinal involvement in animal experimental studies and human subjects after brain insults due to a range of diseases. Consequently, a circuit of inhibition/disinhibition was frequently proven to be causally responsible for abnormal findings, such as Babinski's sign or Hoffman's sign. Although structural neuroimaging studies have demonstrated a clear correlation between the lesion of brain/spinal cord structures and contralateral clinical signs, their findings have not significantly changed our previous clinicopathological knowledge. Lesions within the central nervous system may present with a wide range of symptoms, from permanent or progressive brain injury to paroxysmal and temporary manifestations. Indeed, in many patients, and in particular, those with a transient ischemic attack, a structural brain lesion might not be detectable, not even with current advanced imaging methods. As making decisions are difficult for physicians who suspect but cannot prove any lesion in the brain by imaging methods, the role of a thorough physical examination and the importance of even subtle clinical findings is highlighted in those without obvious neurologic deficits.

With the advent of functional imaging studies and electrophysiological studies, it gradually became possible to evaluate the localized brain function of healthy individuals and assess the clinical relevance of normal/abnormal neurological findings.

Early electrophysiological studies using electrical stimuli instead of mechanical stimuli, suggested the possible involvement of the central nervous system, from the cerebral cortex to the spinal cord, as the origin of UMN findings, such as Babinski's sign [8,9]. The somatotopic organization of the cerebral cortex, including the primary motor cortex and the supplementary motor area (SMA) has been assessed in surgical and imaging studies [10,11,12,13]. For example, an event-related functional magnetic resonance imaging study demonstrated that the spinal flexor reflex is under the modulation of the supplementary motor area. It was postulated that inhibition of this area may lead to the appearance of Babinski's sign [14].

Despite the sample size being small, the high number of positive signs suggests a role of the primary motor cortex or its connections in the origin of the thumb sign. An upgoing thumb sign was seen ipsilateral to the side of stimulation in one of our cases. Inhibition of contralateral cortex or stimulation of contralateral corticospinal tract is a possibility. In addition, a growing body of evidence suggests that neurological impairments can be also seen ipsilateral to corticospinal tracts lesions [15] [16] [17,18].

In summary, our study demonstrates that the upgoing thumb sign may be related to the involvement of the upper motor neuron system via the inhibition of the primary motor cortex or its connections.

Author disclosures

The authors have nothing to disclose.

Acknowledgments

We are grateful to the 10 study volunteers, without whose participation in this study, would not have been possible.

Table 1
Participants' demographics and the result of thumb sign after repetitive Transcranial Magnetic Stimulation (rTMS).

Subjects	Age	Sex	Site of rTMS	An upgoing Thumb after rTMS	Other clinical findings after rTMS
1	31	Female	Left	Right thumb sign	Hyperreflexia on the right side
2	46	Female	Left	Right thumb sign	Numbness in the right arms that lasted 6–7 h
3	23	Female	Left	Right thumb sign	Temporary tingling in her nose
4	46	Male	Left	Right thumb sign	Right
5	40	Male	Left	Right thumb sign	Temporary tingling in his cheek
6	40	Female	Right	No thumb sign, query right thumb sign	Temporary left-sided hyperreflexia
7	38	Female	Left	Right thumb sign	Right Babinski' sign
8	39	Male	Left	Left thumb sign	Temporary tingling in his left cheek

Conflict of interest

Authors do not have any conflict of interest to declare.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

Antonia Nucera: Study design, data acquisition.

Mahmoud Reza Azarpazhooh: Writing the paper, critical revision of the manuscript.

Lucilla Cardinali: Data acquisition, analysis and interpretation, critical revision of the manuscript.

Rasha Alsubaie: Study design, writing the paper.

Tzu-ching Chiang: Data acquisition, data interpretation.

Nina Weishaupt: Study design, writing the paper.

Vladimir Hachinski: Study design, writing the paper, study supervision.

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