Neuroscience Letters 617 (2016) 52–58

Contents lists available at ScienceDirect

Neuroscience Letters

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

Research paper

Role of contralesional hemisphere in paretic arm reaching in patients with severe arm paresis due to stroke: A preliminary report

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HIGHLIGHTS

- The functional relevance of contralesional hemisphere in paretic arm motor performance in individuals with severe arm paresis was examined.
- TMS pulses were delivered to the contralesional primary motor and dorsal pre-motor areas.
- Various temporal and spatial characteristics were measured in conditions with and without TMS.
- Movement time was significantly slower with TMS to contralesional hemisphere.
- The study suggests functionally relevant role of contralesional hemisphere motor areas during paretic arm reaching movements in stroke survivors.

ARTICLE INFO

Article history:
Received 26 October 2015
Received in revised form 1 February 2016
Accepted 2 February 2016
Available online 9 February 2016

Keywords:
Stroke
TMS
Reaching
Paresis

ABSTRACT

Stroke is highly prevalent and a leading cause of serious, long-term disability among American adults. Impaired movement (i.e. paresis) of the stroke-affected arm is a major contributor to post-stroke disability, yet the mechanisms of upper extremity motor recovery are poorly understood, particularly in severely impaired patients who lack hand function. To address this problem, we examined the functional relevance of the contralesional hemisphere in paretic arm motor performance in individuals with severe arm paresis. Twelve individuals with severe stroke-induced arm paresis (Upper Extremity Fugl-Meyer Assessment = 17.1 ± 8.5; maximum score = 66) participated in the study. Participants performed a reaching response time task with their paretic arm. At varying time intervals following a 'Go' cue, a pair of transcranial magnetic stimulation (TMS) pulses were delivered to contralesional hemisphere primary motor (M1) or dorsal pre-motor cortex (PMd) to momentarily disrupt the pattern of neural firing. Response time components and hand-path characteristics were compared across the 2 sites for trials with and without TMS disruption. There was no significant effect of TMS disruption on overall Response time or Reaction time, but Movement time was significantly longer (i.e. slower) with disruption of the contralesional hemisphere ($p = 0.015$), regardless of which area was stimulated. Peak hand-path velocity and hand-path smoothness were also significantly lower ($p = 0.005$ and $p < 0.0001$, respectively) with TMS disruption of the contralesional hemisphere. The data from this study provide evidence supporting a functionally relevant role of contralesional hemisphere motor areas in paretic arm reaching movements in individuals with severe post-stroke arm impairment.

1. Introduction

Stroke is a leading cause of serious, long-term disability among American adults. 6.8 million Americans have been estimated to have had a stroke. The annual stroke death rate decreased by 35.8%

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http://dx.doi.org/10.1016/j.neulet.2016.02.004
0304-3940/

over the last decade resulting in more patients living with stroke related disability. Among ischemic stroke survivors, at 6 months post stroke, 50% had some hemiparesis and 26% were dependent in activities of daily living (ADL; [9]). A major contributor to stroke-related disability is persistent impairment of the paretic arm, which significantly affects ADLs, many of which require the performance of functional reaching movements [6].

The brain regions contributing to motor recovery after stroke have been widely investigated [8,16,18,19]. Previous imaging studies have repeatedly demonstrated that patients with more impairment tend to have more prominent activation of the contralesional hemisphere, often including the contralesional dorsal pre-motor area (PMd), during paretic hand movements [1,5,13,15,18]. This common finding has sometimes been interpreted as an indication that contralesional hemisphere activation is maladaptive and may contribute to motor dysfunction. However, it is also possible that those with more severe lesioned-hemisphere damage recruit contralesional areas to support recovered arm movements. The finding that inhibitory brain stimulation applied to contralesional M1 improved paretic arm movement in mildly impaired patients, but worsened it in more severely impaired patients [2], lends support to the latter possibility.

Interestingly, within the contralesional hemisphere activation that is often observed during paretic hand movements, PMd is often shown to be particularly active, and this activation has been shown to be correlated with motor impairment severity [10,14]. While M1 is strongly lateralized to primarily distal muscles of the contralateral arm, PMd has substantial ipsilateral projections, particularly to proximal arm muscles [3], and is active during ipsilateral arm reaching movements in intact non-human primates [4,12]. Contralesional PMd may therefore be particularly well-suited to contribute to recovery of paretic arm reaching movements, a possibility that has not yet been prospectively studied.

In this preliminary report, we employed a transcranial magnetic stimulation (TMS) disruption paradigm to explore the role of contralesional hemisphere M1 vs. PMd in patients with severe post-stroke arm impairment. Patients performed a reaching response time task with their paretic arm while, on randomly occurring trials, TMS was applied just after the 'Go' cue and prior to movement onset. We compared temporal and spatial aspects of the subsequent reaching movements on trials with vs. without TMS, and with TMS applied to contralesional hemisphere M1 vs. PMd. We hypothesized that TMS applied to the contralesional hemisphere would slow paretic arm reaching, and that TMS applied to contralesional PMd would slow reaching movements more than TMS applied to M1.

2. Methods

2.1. Patients

Table 1 illustrates patient demographics. Twelve patients (6 females, mean age: 59.58 ± 8.77 years, mean duration post stroke: 78 ± 111.55 months, mean UEFM: 17.08 ± 8.5) with severe arm paresis due to chronic stroke participated in the study. We defined severe arm paresis as the inability to actively extend the wrist and fingers. Potential patients were excluded if they were less than 18 years of age, pregnant, had cerebellar or brainstem lesions, had a gross hemianopsia, or any TMS contraindications (e.g., metal objects inside eyes or skull, history of seizures). The study protocol was approved by the Institutional Review Board and written informed consent was obtained from all patients.

2.2. Procedure

Clinical measures included the Upper Extremity Fugl-Meyer (UEFM) test of post-stroke motor impairment, the Mini Mental Status Exam (MMSE) cognitive function questionnaire and the Modified Ashworth scale for spasticity. A brief neurological exam was conducted by the study physician and high resolution, anatomical, T1-weighted magnetic resonance imaging (MRI) brain scans were collected for subsequent stereotactic TMS coil localization.

2.3. Experimental set-up

Prior to the first experimental session, patients were familiarized with the behavioral task and with the sensation and sound of the TMS. The subjects were seated on a chair whose height and distance from table could be adjusted to ensure that the subject sits comfortably and as close to table as possible. We used a black tape to identify the starting or initial position on the table. This position was marked once the subject comfortable sits on the chair with the seat belt across the waist. After this position is achieved the chair was locked at that position to start the task. The distance of the frame of the chair and the seat height were also measured. The subjects kept their upper extremity on table rested at the starting position. This specific position was controlled for everyone. The trajectory was trying to reach from the starting position on table to the end point which was the sensor either right or left (~2 cm apart) on table at 80% of their maximum reach. For achieving this task the elbow went from a flexed position to extension with shoulder flexion. The task was controlled by visual feedback which was seen on a computer monitor placed in front of the patient (Fig. 1). In response to a visual 'Go' cue presented on the monitor, patients

Table 1
Patient demographics (NIHSS: NIH Stroke Scale, UEFM: Upper Extremity Fugl Meyer, MMSE: Mini Mental Status Exam).

Subject #	Gender	Age (yrs)	Stroke type	Affected Hemisphere	Hand dominance	NIHSS	Max paretic reach (cm)	UEFM	Modified Ashworth (paretic UE) (Biceps/Triceps)		MMSE	Time since stroke (months)
1	F	69	ischemic	right	R	6	13.8	10	3	3	29	12
2	M	57	hemorrhagic	left	L	3	30.2	24	1+	0	27	120
3	M	56	ischemic	right	L	6	14	8	3	0	30	16
4	M	63	ischemic	right	R	5	27.8	29	1	1	25	11
5	M	50	ischemic	left	R	8	26.4	30	1+	1+	27	51
6	F	68	ischemic	right	R	2	43.4	23	1	1	30	111
7	F	64	ischemic	right	R	4	14.5	11	2	1	29	128
8	F	44	ischemic	left	L	6	22	25	2	2	24	30
9	F	69	ischemic	right	R	4	27	14	2	2	30	9
10	M	51	hemorrhagic	right	R	4	19.2	10	3	1+	29	4
11	M	54	ischemic	left	L	11	4.1	7	3	3	26	43
12	F	70	ischemic	left	R	4	4	14	3	2	25	401
Mean		59.58				5.25	20.53	17.08			27.58	78.00
SD		8.77				2.42	11.35	8.50			2.19	111.55