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ORIGINAL ARTICLE

Nonparetic Arm Force Does Not Overinhibit the Paretic Arm in Chronic Poststroke Hemiparesis

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Abstract

Objective: To determine whether nonparetic arm force overinhibits the paretic arm in patients with chronic unilateral poststroke hemiparesis.

Design: Case-control neurophysiological and behavioral study of patients with chronic stroke.

Setting: Research institution.

Participants: Eighty-six referred patients were screened to enroll 9 participants (N=9) with a >6 month history of 1 unilateral ischemic infarct that resulted in arm hemiparesis with residual ability to produce 1Nm of wrist flexion torque and without contraindication to transcranial magnetic stimulation. Eight age- and handedness-matched healthy volunteers without neurologic diagnosis were studied for comparison.

Interventions: Not applicable.

Main Outcome Measure: Change in interhemispheric inhibition targeting the ipsilesional primary motor cortex (M1) during nonparetic arm force. We hypothesized that interhemispheric inhibition would increase more in healthy controls than in patients with hemiparesis.

Results: Healthy age-matched controls had significantly greater increases in inhibition from their active to resting M1 than patients with stroke from their active contralesional to resting ipsilesional M1 in the same scenario (20%±7% vs −1%±4%, $F_{1,12}=6.61$, $P=.025$). Patients with greater increases in contralesional to ipsilesional inhibition were better performers on the 9-hole peg test of paretic arm function.

Conclusions: Our findings reveal that producing force with the nonparetic arm does not necessarily overinhibit the paretic arm. Though our study is limited in generalizability by the small sample size, we found that greater active contralesional to resting ipsilesional M1 inhibition was related with better recovery in this subset of patients with chronic poststroke.

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Motor performance of unimanual and bimanual tasks requires a balanced interaction between the 2 hemispheres of the brain.[1] After stroke, however, the diaschisis between brain areas (ie, abnormal function of brain areas either directly connected to or remote from the stroke-damaged area) is thought to negatively impact motor control. Although poststroke diaschisis has been well described and is shown to relate to function,[2-4] the direct effects on motor physiology and recovery are not well understood. The impairment in interhemispheric interactions may be critical to recovery from poststroke paralysis[5]; however, it is inadequately understood from the perspective of physiological mechanisms. Some forms of rehabilitation, including mirror and bimanual therapy, are based on a model of cooperative interactions between the 2 hemispheres.[6,7] On the other hand, another model argues that the nonparetic primary motor cortex (M1) may overinhibit the paretic M1 and hinder poststroke motor rehabilitation.[8-10] The latter model has been used to design interventions (eg, brain stimulation, nonparetic constraint) to inhibit

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the nonparetic corticospinal system to enhance rehabilitation. However, the benefits of inhibiting the nonparetic arm have been modest at best.[11]

One possible reason for the modest effect of these strategies may be that the current model of interhemispheric competition is incomplete and is limited to averaged interactions across time or studied primarily during paretic arm activity.[11] Therefore, a remaining question is how nonparetic arm activity affects interhemispheric inhibition (IHI) targeting the ipsilesional M1. The objective of this study was to determine whether nonparetic arm force overinhibits the paretic arm in patients with chronic unilateral poststroke hemiparesis. Based on previous findings in healthy participants, we hypothesized that IHI would increase more in healthy controls than in patients with hemiparesis.[12]

Methods

Ethical approval

All participants provided written informed consent under protocols approved by the National Institute of Neurological Disorders and Stroke Intramural Institutional Review Board in accordance with the Declaration of Helsinki.

Participants

Eighty-six patients with stroke were screened for this study. Nine patients (average age, 62y; range, 46−80y) with poststroke hemiparesis met the following inclusion criteria and were enrolled: (1) 1 episode of ischemic stroke occurring ≥6 months prior to enrollment; (2) anatomic magnetic resonance imaging (MRI) confirmation of stroke, excluding involvement of the brainstem or cerebellum; (3) lack of contraindication to transcranial magnetic stimulation (TMS) or MRI consistent with international guidelines[13]; (4) ability to produce wrist flexion ≥1Nm of torque with the paretic arm; (5) adequate cognitive function to participate in experimental sessions; and (6) lack of other medical or neurologic illness that would impair ability to participate.

Although we did not have a measure of spasticity in these patients, all of the patients had to be able to produce wrist flexion torque of at least 1Nm with their paretic arm and relax in between trials, which excluded participants with significant amounts of spasticity. Patient characteristics are listed in table 1. MRI scans of the brain were obtained for each patient for lesion localization (3-T scanner[a]; T1 scan: repetition time, 6.272s; echo time, 2.672s; field of view, 240×240; dimensions, .9375×.9375×1mm; T2 scan: repetition time, 8500s; echo time, 122.192s; field of view, 240.0256×240.0256; dimensions: .4688×.4688×1.5mm). Lesion masks were hand drawn for each patient (M.A.D.)[b]; then, cost function masked normalization of each patient's MRI and lesion mask was done to create a lesion overlap map[b,c] using previously described techniques (fig 1).[14,15] The 9-hole peg test (NHPT)[16] was used to obtain a measure of paretic arm function. The NHPT required participants to move 9 pegs from a shallow bowl to 1 of 9 holes as quickly as possible. Each participant completed this task 6 times while alternating between the paretic and nonparetic arm. The times were averaged, and the NHPT score was calculated (1−nonparetic/paretic). Seven of the 9 patients were able to complete the NHPT. A group of 8 healthy controls were also recruited for comparison. The healthy controls were matched to the stroke group for age (average age, 66y; range, 40−82y), premorbid handedness (1 left handed in each group), and sex (4 women in each group).

Table 1 Patient characteristics

Patient	Sex	Lesion Side	Age (y)	Years Since Ischemic Stroke	NHPT
1	F	R	67	4	67
2	F	L	80	5	31
3	M	R	58	8	83
4	M	R	47	32	75
5	F	R	63	6	*
6	M	L	53	5	*
7	F	L	64	8	6
8	M	L	61	1	87
9	M	R	72	3	8

NOTE. All patients were right handed prior to stroke except for patient 6 who was and remained left handed. Healthy controls were matched to premorbid handedness.
Abbreviations: F, female; L, left; M, male; R, right.
* Patient unable to hold pegs.

Experimental design

Subjects sat in an ergonomic dental chair watching a computer display. Surface electromyography was recorded via two 7-mm diameter silver-silver chloride electrodes placed over the belly of the flexor carpi radialis (FCR) muscles bilaterally with a 2-cm interelectrode distance[17] and a ground electrode placed on the dorsum of the resting hand. The signal was amplified, band-pass filtered (2−500Hz), digitally sampled at 2kHz, recorded, and displayed via a computer.[d] The resting arm was placed in the most comfortable position for the participant to reduce involuntary activity in the FCR muscle. The active arm was placed in a custom arm manipulandum with soft restraints; the palm of the hand was positioned against a joystick connected to a 6-degree-of-freedom load cell.[e] The device was designed to isolate wrist flexion from more proximal arm movements.[18] Maximum voluntary contraction (MVC) levels were determined by instructing subjects to produce isolated and isometric wrist flexion for approximately 3 seconds. The MVC levels for each arm were determined by averaging the torque from 3 trials.

List of abbreviations:

CCS10	**10-millisecond contralateral conditioning stimulus**
CCS10-MEP	**motor evoked potential produced by the contralateral conditioning stimulus given 10ms prior to the test stimulus**
FCR	**flexor carpi radialis**
IHI	**interhemispheric inhibition**
IHIc	**interehmispheric inhibition matched for the CCS10 amplitude between conditions**
MEP	**motor-evoked potential**
TS-MEP	**motor-evoked potential produced by the test stimulus**
MRI	**magnetic resonance imaging**
MVC	**maximum voluntary contraction**
M1	**primary motor cortex**
NHPT	**9-hole peg test**
SICI	**short-interval intracortical inhibition**
TMS	**transcranial magnetic stimulation**