ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2015;96:2112-9

ORIGINAL RESEARCH

Increased Lower Limb Spasticity but Not Strength or Function Following a Single-Dose Serotonin Reuptake Inhibitor in Chronic Stroke

Krishnaj Gourab, MD,[a] Brian D. Schmit, PhD,[a,b] T. George Hornby, PT, PhD[b,c]

From the [a]Department of Biomedical Engineering, Marquette University, Milwaukee, WI; [b]Sensory Motor Performance Program, Rehabilitation Institute of Chicago, Chicago, IL; and [c]Department of Physical Therapy, University of Illinois at Chicago, Chicago, IL.

Abstract

Objective: To investigate the effects of single doses of a selective serotonin reuptake inhibitor (SSRI) on lower limb voluntary and reflex function in individuals with chronic stroke.

Design: Double-blind, randomized, placebo-controlled crossover trial.

Setting: Outpatient research setting.

Participants: Individuals (N=10; 7 men; mean age ± SD, 57±10y) with poststroke hemiplegia of >1 year duration who completed all assessments.

Interventions: Patients were assessed before and 5 hours after single-dose, overencapsulated 10-mg doses of escitalopram (SSRI) or placebo, with 1 week between conditions.

Main Outcome Measures: Primary assessments included maximal ankle and knee isometric strength, and velocity-dependent (30°/s−120°/s) plantarflexor stretch reflexes under passive conditions, and separately during and after 3 superimposed maximal volitional drive to simulate conditions of increased serotonin release. Secondary measures included clinical measures of lower limb coordination and locomotion.

Results: SSRI administration significantly increased stretch reflex torques at higher stretch velocities (eg, 90°/s; $P=.03$), with reflexes at lower velocities enhanced by superimposed voluntary drive ($P=.02$). No significant improvements were seen in volitional peak torques or in clinical measures of lower limb function (lowest $P=.10$).

Conclusions: Increases in spasticity but not strength or lower limb function were observed with single-dose SSRI administration in individuals with chronic stroke. Further studies should evaluate whether repeated dosing of SSRIs, or as combined with specific interventions, is required to elicit significant benefit of these agents on lower limb function poststroke.

Archives of Physical Medicine and Rehabilitation 2015;96:2112-9

© 2015 by the American Congress of Rehabilitation Medicine

Unilateral stroke produces the characteristic upper motor neuron (UMN) syndrome, which includes "positive" signs of spasticity[1,2] and "negative" signs of hemiparesis[3,4] and disrupted coordination.[5,6] While increased spasticity is considered a major barrier for recovery of function,[1,7-9] evidence suggests that weakness is the primary determinant of motor function of both lower and upper extremities.[4,10-13] Most strategies to enhance strength poststroke focus on physical training and electrical stimulation paradigms, whereas pharmacologic interventions are directed primarily to decrease spasticity[14-16] rather than to increase strength.

Previous data suggest that selective serotonin reuptake inhibitors (SSRIs) may mitigate weakness[17] and improve function poststroke.[18-20] In general, SSRIs facilitate 5-hydroxytryptamine (serotonin) (5-HT) transmission by decreasing presynaptic sequestration in axon terminals originating primarily from brainstem (raphe) projections.[21] Such pathways are active during wakefulness with increased activity during rhythmic, repetitive movements such as locomotion.[22,23] While the central effects of 5-HT are complex, the net result on motor systems is excitatory.[24,25] In humans poststroke, most studies using SSRIs or other 5-HT reuptake inhibitors (eg, fluoxetine, paroxetine, venlafaxine) focus

Supported by the National Institute on Disability and Rehabilitation Research (grant no. H133G060124).

Clinical Trial Registration No.: NCT01751854.

Disclosures: none.

0003-9993/15/$36 - see front matter © 2015 by the American Congress of Rehabilitation Medicine
http://dx.doi.org/10.1016/j.apmr.2015.08.431

on the upper extremity and indicate enhanced cortical excitability and motor performance in subacute and chronic stroke (grip strength, rate of finger tap, and 9-hole peg test[17,20,26]). Interestingly, with repeated SSRI administration, data from intact individuals demonstrate potential decreased motor cortical excitability,[27,28] while studies[19,29] with patients early poststroke undergoing rehabilitation indicate improved motor recovery. Although changes in lower extremity function have not been well studied poststroke, single-dose SSRI (escitalopram) administration may improve leg strength in chronic, incomplete spinal cord injury (SCI).[30,31]

Despite the focus on increased supraspinal excitability with SSRIs, these agents may also increase spinal excitability.[32,33] For example, longstanding and recent data in human SCI[30,31,34] suggest increased spastic motor activity after single or repeated doses of SSRIs, although similar findings have not been reported in patients with stroke. In 1 study,[35] greater antagonist muscle activity was observed during volitional upper extremity motor tasks after use of an SSRI poststroke, with no changes in strength or task performance. However, spasticity was not assessed. Whether the findings of increased spasticity with SSRIs are selective to patients with SCI or attributable to differences in the extremities tested is not clear. Increased spasticity with SSRI administration poststroke may be of interest to rehabilitation professionals because spastic hypertonia with UMN syndrome is still considered by many to be a major barrier to functional recovery.[8,9]

The objective of this study was to determine the effects of single SSRI doses on lower extremity motor function in patients with chronic stroke. Using a double-blind, randomized, placebo-controlled crossover design, we hypothesized that SSRIs would increase volitional strength in patients with chronic hemiparesis poststroke, consistent with data from upper extremity studies and patients with incomplete SCI. We focused on the single-dose effects here to minimize potential habituation with repeated SSRI use,[27,28] and because of the potential increase in spasticity that may interfere immediately with lower limb function or patient comfort. Considering the potential effects on spinal excitability,[36,37] we also evaluated the effects of SSRIs on stretch reflexes during passive (resting) conditions, and during and after rhythmic, repeated volitional tasks designed to simulate conditions of increased 5-HT release.[22,23] The immediate effects of SSRIs on lower limb motor function are of clinical interest given their common use for treatment of depressive symptoms in this patient population,[38] and the potential consequences of altering motor function during functional tasks.

Methods

Participants

Individuals with chronic (>1y) hemiparesis after unilateral supratentorial stroke, and lower extremity Fugl-Meyer scores <34[39] were recruited. Additional criteria included passive ankle range of motion from 0° to 30° plantarflexion, Modified Ashworth Scale score ≥1 of the paretic plantarflexors,[40] and the ability to ambulate without physical assistance but with assistive devices and below-knee orthoses if necessary. Exclusion criteria included use of oral antispastic medications <14 days previously or receiving a botulinum toxin injection <6 months ago, the presence of uncontrolled cardiorespiratory or metabolic diseases, or having a score <23/30 on the Mini-Mental State Examination.[41] Written consent was obtained from all subjects, with procedures approved by the local ethics committee. A sample size of 10 individuals was targeted from previous findings in patients with stroke with fewer subjects (n=4–8[17,20]) and data of altered volitional strength after single-dose SSRI assessments in human SCI.[30] Power analyses from the latter data indicate that 10 subjects would provide 91% power (effect size, 1.34).

List of abbreviations:

5-HT	**5-hydroxytryptamine (serotonin)**
MG	**medial gastrocnemius**
MVC	**maximum volitional contraction**
SCI	**spinal cord injury**
6MWD	**6-minute walking distance**
SSRI	**selective serotonin reuptake inhibitor**
TA	**tibialis anterior**
UMN	**upper motor neuron**

Study protocol

Subjects were randomly assigned to receive 10mg of escitalopram on day 1 and placebo (microcrystalline cellulose) on day 2, or with the order reversed. The half-life of escitalopram is 27 hours,[42] and 7 days between testing ensured drug elimination before reassessment. Agents were overencapsulated and block randomized (4 subjects per block) by the pharmacist who maintained blinding. Subjects were tested before and 4 to 5 hours after drug administration (time for peak plasma concentration[42]). Testing was completed in 1.5 to 2 hours, and the time of day was similar for all procedures across drug conditions (ie, morning for pretesting, afternoon for posttraining). The randomization code was broken after all completed analysis. Figure 1 provides a schematic of the study design.

Experimental session

Biomechanical measures of lower extremity strength and reflexes, and clinical assessments were performed in the same order during each session. Clinical assessments were obtained in the beginning of each session and consisted of lower extremity Fugl-Meyer scores, 6-minute walking distance (6MWD) at subject's normal comfortable speed, and the fastest gait speeds over 10m. Biomechanical measures were obtained using an isokinetic dynamometer (Biodex[a]) with an attached 6-degree-of-freedom load cell.[b] For ankle measures, subjects were seated with the foot secured in a footplate coupled to the load cell/Biodex, and the ankle and Biodex motor axes were aligned,[43] with the knee and hip at 0° and 75° flexion, respectively. For knee measures, the Biodex and knee axes were aligned with the shank secured to an attachment. Position and velocity signals were recorded from Biodex transducers. All signals were sampled at 1000Hz using data acquisition cards and custom software.[c] Surface electromyographic activity was recorded by active electrodes[d] on the paretic tibialis anterior (TA), medial gastrocnemius (MG), and soleus. Signals were amplified (1000×) and filtered (20–450Hz) before sampling. Torque and electromyographic signals were measured during the following tasks: maximal volitional contractions (MVCs) of knee flexion/extension and ankle plantarflexion/dorsiflexion; passive paretic plantarflexor stretches; and passive and active-assist stretch responses. To normalize electromyographic measures, the maximum M wave was elicited through 1-millisecond stimuli applied to the tibial or peroneal nerve to elicit a maximum response of paretic TA and MG recordings.

Download English Version:

https://daneshyari.com/en/article/3448193

Download Persian Version:

https://daneshyari.com/article/3448193

Daneshyari.com