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Asymmetries in vestibular evoked myogenic potentials in chronic stroke survivors with spastic hypertonia: Evidence for a vestibulospinal role

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HIGHLIGHTS

- Spastic stroke survivors display significant asymmetries in vestibulocollic drive to clinically affected and clinically spared motoneuron pools innervating cervical muscles.
- There is a strong correlation between the degree of asymmetry in vestibular mediated reflex amplitudes elicited on the clinically affected and clinically spared sides, and the severity of spasticity.
- Vestibular drive is a likely source of ionotropic excitation that places spastic-paretic motoneurons in a hyperexcitable state.

ABSTRACT

Objective: Indirect evidence suggests that lateralized changes in motoneuron behavior post-stroke are potentially due to a depolarizing supraspinal drive to the motoneuron pool, but the pathways responsible are unknown. In this study, we assessed vestibular evoked myogenic potentials (VEMPs) in the neck muscles of hemispheric stroke survivors with contralesional spasticity to quantify the relative levels of vestibular drive to the spastic-paretic and contralateral motoneuron pools.
Methods: VEMPs were recorded from each sternocleidomastoid muscle in chronic stroke survivors. Side-to-side differences in cVEMP amplitude were calculated and expressed as an asymmetry ratio, a proxy for the relative amount of vestibular drive to each side.
Results: Spastic-paretic VEMPs were larger than contralateral VEMPs in 13/16 subjects. There was a strong positive relationship between the degree of asymmetry and the severity of spasticity in this subset of subjects. Remaining subjects had larger contralateral responses.
Conclusion: Vestibular drive to cervical motoneurons is asymmetric in spastic stroke survivors, supporting our hypothesis that there is an imbalance in descending vestibular drive to motoneuron pools post-stroke. We speculate this imbalance is a consequence of the unilateral disruption of inhibitory corticobulbar projections to the vestibular nuclei.
Significance: This study sheds new light on the underlying mechanisms of post-stroke spasticity.

1. Introduction

Spastic hypertonia or "spasticity" is a frequent and often disabling sequel to hemispheric stroke (Watkins et al., 2002; Urban et al., 2010). It is a motor disorder, manifesting as a sharply lateralized muscular hypertonia on the contralesional side with

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exaggerated phasic and tonic stretch reflex activity (Lance, 1980). Clinically, spasticity presents as an increase in the resistance of a passive limb to externally applied joint motion and is commonly associated with deficits in both motor and functional performance (Bohannon et al., 1987; O'Dwyer et al., 1996; Watkins et al., 2002; Sommerfeld et al., 2004). Emerging evidence implicates changes in motoneuron excitability as central to the genesis of post-stroke spasticity, however the physiological basis underlying the lateralized hyperexcitability of spastic-paretic motoneurons is incompletely understood (Katz and Rymer, 1989), due in part to the lack of a widely accepted animal model of hemispheric stroke (Wright and Rang, 1990). However, one plausible explanation for the sharply lateralized nature of spasticity is that spastic-paretic motoneurons receive a tonic increase in excitatory synaptic drive generated by a sharply lateralized supraspinal pathway released from cortical suppression following a stroke mediated disruption of inhibitory corticobulbar projections (Katz and Rymer, 1989).

Previous studies provide indirect evidence suggesting that post-stroke changes in spastic-paretic motoneuron behavior are likely due to a depolarizing supraspinal drive to the resting spastic-paretic motoneuron pool (Burke and Ashby, 1972; Burke et al., 1972; Burne et al., 2005; Mottram et al., 2009). Mottram et al. (2009) showed that there was a greater incidence of co-modulation in the spontaneous discharge of spastic-paretic motor units that was not seen on the clinically spared side. In addition, they found a lack of initial acceleration in firing rate following motor unit recruitment in low threshold spastic-paretic motor units, a potential marker of a depolarized baseline membrane potential. While not definitive, both findings are highly suggestive of a common, low-level depolarizing drive to the spastic-paretic motoneuron pool. However, the specific supraspinal pathways that mediate these changes are unknown. The candidate supraspinal pathway or pathways mediating these changes should be sharply lateralized, project to the antigravity muscle groups, and be able to strongly modulate motoneuron excitability.

In humans, the major supraspinal pathways that influence motoneuron excitability arise from the brainstem, and are the reticulospinal, rubrospinal, and vestibulospinal pathways. The reticulospinal pathways are largely bilateral in both their anatomical spinal distribution (Nyberg-Hansen, 1965; Nathan et al., 1996) and synaptic action (Schepens and Drew, 2006; Davidson et al., 2007). Rubrospinal pathways are believed to be rudimentary in humans, with few fibers reaching the spinal cord (Nathan and Smith, 1982). Alternatively, the unilateral nature of the vestibular pathways, especially the lateral vestibulospinal tract is consistent with the sharply lateralized nature of spasticity (Nyberg-Hansen and Mascitti, 1964).

Vestibulospinal pathways have been long implicated as a prime driver of decerebrate rigidity, which occurs following transection of the brainstem between the red nucleus and vestibular nuclei. In quadrupeds, a hallmark of decerebrate rigidity is rigid extension of the limbs (decerebrate posturing) accompanied by hyperactive reflexes that appear to be driven by unopposed vestibulospinal drive to the antigravity motoneuron pools (Fulton et al., 1930; Bach and Magoun, 1947). While not a precise analog for decerebrate posturing, the antigravity limb posturing that follows an upper motoneuron lesion is modified though postural changes and abolished following VIIIth nerve transection (Denny-Brown, 1964, 1965), supporting a potential contributing role for vestibulospinal projections. Vestibulospinal drive is also an important facilitator of the tonic vibration reflex (Gillies et al., 1971a,b), a useful analog for the tonic stretch reflex (Kimura, 2013). Surgical transection of the vestibular nerve or interruption of central vestibular pathways results in a marked decrease in the tonic vibration reflex (Gillies et al., 1971a,b), motoneuron excitability (Molina-Negro et al., 1980) and antigravity muscle tone (Bach and Magoun, 1947), highlighting the potentially unique contributions of the vestibular nuclei.

While there are known deficits in vestibular functioning subsequent to stroke (Marsden et al., 2005), the role descending vestibular pathways play in generating lateralized spasticity in humans has yet to be comprehensively investigated. For these reasons, the aim of the current study was to quantify the relative levels of descending vestibular drive to spastic-paretic and clinically-spared or contralateral motoneuron pools in chronic stroke survivors with demonstrable spasticity. Specifically, we hypothesized that there would be asymmetries in the amplitudes of the cervical vestibular evoked myogenic potentials (cVEMPs) elicited in the spastic-paretic and contralateral sternocleidomastoid muscles, due to a disruption of inhibitory corticobulbar projections to the contralesional vestibular nuclei. The degree of asymmetry in cVEMP amplitude between the two sides was used as a proxy for the relative amount of vestibular drive impinging onto the spastic-paretic and contralateral motoneuron pools. We propose that the lateralized disruption of corticobulbar projections causes an imbalance in descending vestibular drive to the motoneuron pools that sets the baseline membrane potential of spastic-paretic motoneurons closer to neuron activation threshold.

2. Methodology

In order to differentiate between the two sides, the sternocleidomastoid muscle on the clinically affected side will be classified as spastic-paretic and the sternocleidomastoid muscle on the clinically spared side will be classified as contralateral. Additionally, the vestibular nuclear complex on the spastic-paretic side will be referred to as the contralesional vestibular nuclei while the vestibular nuclear complex on the contralateral side will be referred to as the ipsilesional vestibular nuclei.

2.1. Subject population

Informed, written consent was obtained prior to experimentation. The Northwestern University Institutional Review Board approved all experimental procedures. We enrolled 17 chronic stroke survivors (115.7 ± 105.9 months post stroke) ranging in age from 44 to 71 (56.5 ± 7.0 years) with a single brain lesion[1] that resulted in lateralized spasticity in at least one limb. Clinical assessments for each subject were performed by a dedicated research physical therapist. Spasticity was assessed in both the elbow flexors and plantar flexors using the modified Ashworth scale (MAS), a 6-point rating scale used to measure passive muscle resistance (Bohannon and Smith, 1987). For each subject, we calculated an antigravity spasticity index (AGSI) by dividing the sum of the MAS in the elbow flexors and plantar flexors by eight; the maximum possible attainable MAS score. Subject demographic and clinical information is detailed in Table 1.

At the time of the study, no subject was taking any vestibular suppressants or medications that would influence motoneuron excitability, such as SSRIs, benzodiazepines, or GABA analogues. To exclude significant hearing loss, hearing sensitivity was assessed at 500 Hz using pure-tone audiometry as the cVEMP amplitude is dependent upon ossicle integrity. Subjects were excluded if they had greater than a 10 dB difference between the left and right ears. Additionally, all subjects reported a negative history of vestibular disorders or prior neurological dysfunction.

[1] It should be noted that while subject 8 had a chronic focal lesion in the right periatrial white matter and a chronic microhemmorhage in the left medial temporal lobe, this subject presented with lateralized spasticity in both the upper and lower limbs on the left side. The left sided spasticity was presumably an outcome of the right-sided white matter lesion.