Assessment of Proprioceptive Acuity in Patients with Stroke with Left Hemiplegia Compared to Healthy Controls

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Abstract

Proprioceptive information from mechanoreceptors within muscles, tendons, and skin, gives rise to kinesthesia and the sense of joint position. This information is not only crucial for bodily awareness, but it also impacts voluntary motor control, the maintenance of muscle tone and posture. Cortical stroke is known to cause impairment of proprioception, thus diminishing motor learning, postural control, and the ability to carry out activities of daily life. In this research we obtained objective measures of wrist position sense to elucidate the extent of the proprioceptive deficits in patients with chronic stroke compared to healthy age-matched controls. In addition, we examined the relationship of wrist proprioceptive impairment with the degree of upper extremity motor dysfunction as measured by the Motor Evaluation Scale for Upper Extremity in Stroke Patients (MESUPES) (Van de Winckel et al., 2006). Eight patients with chronic stroke with left hemiplegia and eight healthy age- and gender-matched controls participated. Wrist position sense was assessed under two conditions: 1) an ipsilateral wrist joint position matching task requiring active movement to reproduce a reference position, and 2) a psychophysical discrimination threshold test, in which the wrist joint was passively rotated using a 3 degrees-of-freedom wrist robot. The results showed that, in comparison to healthy controls, patients with stroke demonstrated increased joint position error bias and variability during active matching (p's $< .05$) and highly elevated mean position sense threshold for passive displacement ($p < .05$). This study documents that cortical stroke is associated with proprioceptive deficit of the wrist/hand complex, which likely contributes to the observed fine motor deficits in this population.

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1. INTRODUCTION AND REVIEW OF LITERATURE

Proprioceptive information is integral to the maintenance of balance and posture, as well as to motor learning, movement coordination, and online error correction during movement execution (Hughes et. al, 2015). Proprioception is comprised of joint position sense and the sensation of limb movement, or kinesthesia (Gandevia et al., 2002). Joint position sense information is encoded by muscle spindle afferents and defines an individual's ability to sense the static position of a certain body part (Proske and Gandevia, 2009). Kinesthesia entails the perception of active and passive motion. Active and passive motion, however, are encoded by different receptors (Hughes et al., 2015). The perception of passive motion is predominantly encoded by slower adapting mechanoreceptors, such as secondary muscle spindle endings and tendon organs in the muscle, as well as Ruffini endings and tendon organs in other deep tissues (Hogervorst and Brand, 1998). Conversely, the perception of active motion is encoded by more rapidly adapting mechanoreceptors, such as muscle spindle primary endings and lamellated corpuscles in other deep tissues (Hogervorst and Brand, 1998). Proprioceptive deficits are frequently observed following stroke and are associated with poor health-related outcomes (Hughes et al., 2015). Furthermore, proprioceptive deficits detrimentally affect balance and coordination and therefore impede one's ability to carry out activities of daily living.

The aim of the present research was to elucidate the extent of the proprioceptive deficit in patients with stroke compared to healthy age-matched controls on two measures of proprioceptive acuity. The first of which, a robot-guided discrimination task, entailed the passive movement of the wrist joint to two different positions, at which point the participant was asked to report which position they felt was further from the start position. The second measure entailed an ipsilateral remembered active matching task using a wrist joint bimanual manipulandum. The use of these two devices provided a comprehensive assessment of wrist joint position sense in participants with chronic stroke (≥6 months) and healthy controls.

The following literature review initially examined some of the existing literature pertaining to the nature of proprioceptive deficits in individuals post-stroke. Proceeding is the discussion of the relationship between proprioceptive dysfunction and motor recovery and the comparison of healthy individuals and individuals post-stroke on certain measures of proprioception to elucidate the differences between these populations in the existing literature. Finally, this review discussed some of the existing therapies and their effects on proprioceptive and motor recovery and provided the rationale for the present study.

Proprioceptive deficits in patients with stroke

Proprioceptive deficits are frequently observed following stroke and are associated with poor health-related outcome measures such as length of hospitalization, decreased likelihood of discharge, and increased mortality rates (Hughes et. al, 2015). About 41% to 63% of patients with stroke are experiencing a deficit in one of the somatosensory modalities within the first week post-stroke and 3% to 50% at 6 months post-stroke (Meyer et al., 2016b). Furthermore, these deficits have detrimental effects on balance, coordination and performance of activities of daily living (Carey et al, 1993).

Depending on the size and location of the cortical infarct, impairments can manifest in a variety of disruptions to various somatosensory modalities. Somatosensory loss post-stroke can range from a disruption of one type of sensation modality, such as primary tactile senses, sharp/dull touch discrimination, temperature discrimination and proprioception, to a disruption of multiple or all modalities (Carey, 1995).

Data from neuroimaging studies have highlighted some of the brain regions that are implicated in proprioceptive dysfunction after stroke. Lesions to the thalamus, internal capsule, primary somatosensory cortex and the posterior parietal cortex have been reported to be associated with proprioceptive impairments (Kim, 1992). In the healthy brain, these regions are involved in the processing of somatosensory information (Riehle and Vaadia, 2004). It is understood that the ventral posterolateral nucleus of the thalamus relays somatosensory information from the upper and lower extremities to the primary somatosensory cortex (S1), and the superior parietal lobule of the posterior parietal cortex receives input from the primary somatosensory cortex and projects to numerous areas of the premotor cortex (Hughes et al., 2015). Recent studies have investigated voxel-wise associations between lesion location and somatosensory deficit in stroke, and found that lesions to the secondary somatosensory cortex, the anterior and posterior insular cortex, the putamen, and white matter connections reaching ventrally toward prefrontal brain areas were associated with impaired light touch perception (Meyer et al., 2016a). Additionally, damage to the arcuate fasciculus, inferior frontal gyrus, superior temporal gyrus, transverse temporal gyrus, insula and Rolandic operculum were associated with poor position sense (Findlater et al., 2016).

Unfortunately, there is still relatively little information about the specific relationship between brain lesion location and proprioceptive dysfunction.

Dukelow et al. (2012) compared upper extremity joint position sense in patients with stroke in a stroke rehabilitation unit compared to non-disabled age-matched controls. Results from this study indicated that a large proportion of individuals with right- or left-sided lesions to the middle cerebral artery displayed proprioceptive deficits. The magnitude of these deficits, however, were not statistically different when compared to other lesion locations such as the left pontine artery, left basilar artery and left anterior cerebral artery (Dukelow et al., 2012).

Previous studies have reported increased frequency of tactile deficits compared to deficits in other sensory modalities such as proprioception (Hughes et al, 2015). However, this frequency is not consistent throughout the literature. A study conducted by Tyson et al. (2007) measured tactile and proprioceptive sensation in 93 patients with acute stroke (2-4 weeks post-stroke). Using the Rivermead Assessment of Somatosensory Performance (RASP), Tyson et al. (2007) discovered that tactile impairment was significantly more common than proprioceptive impairment. Contrarily, Carey and Matyas (2011) reported no difference between tactile and proprioceptive deficits in an acute stroke population (47% and 49%, respectively) using the Tactile Discrimination Test (TDT) and the Wrist Position Sense Test (WPST) to measure each somatosensory modality, respectively. Furthermore, a study conducted by Connell et al. (2008), which employed the Nottingham Sensory Assessment (NSA), found proprioceptive impairment to be more frequent than tactile impairment in several upper extremities in their sample of

70 patients with stroke. Differences between the results of these studies are perhaps attributable to the nature of the assessments themselves. The RASP measures joint movement and movement discrimination, but not joint position sense, and as such is less likely to accurately detect proprioceptive impairment compared to the NSA (Hughes et al., 2015).

Following a unilateral hemispheric stroke, the ipsilesional upper limb can be affected following stroke (Kitsos et al., 2013). There are several pathophysiological mechanisms posited to underlie this phenomenon. Damage to the uncrossed descending corticospinal tracts may disrupt one's ability to perceive and interpret somatosensory information from ipsilateral inputs (Ziemann et al., 1999). Additionally, these ipsilateral deficits may occur because of a disruption of interhemispheric transfer via the corpus callosum (Shimizu et al., 2002). This suggests that activation of the ipsilateral hemisphere during unilateral upper-limb movements is related to excitatory or inhibitory effects in the contralateral hemisphere (Shimizu et al., 2002). Furthermore, patients with stroke with severe somatosensory impairments showed significantly lower intrinsic functional connectivity of the somatosensory network, reflected in both inter- and ipsilateral intrahemispheric connectivity (De Bruyn et al., 2018).

Proprioceptive decline in elderly adults

Deterioration of somatosensation in elderly populations due to the process of biological aging poses significant health risks, the most problematic of which is falling (Ribeiro and Oliveira, 2007). Results from numerous studies demonstrate that older adults have reduced proprioception compared to younger adults (Van de Winckel et al., 2017; Hurley et al., 1998; Kaplan et al., 1985; Kokmen et al., 1978). The mechanisms that underlie this deterioration are attributable to the biological aging process (Ribeiro and Oliveira, 2007). Specifically, structural modification of mechanoreceptors, such as the muscle spindle, occurs with biological aging and diminished function of these receptors results in deficits in peripheral proprioception (Ribeiro and Oliveira, 2007). Altogether, proprioceptive decline with biological age is an amalgam of both peripheral and central neurodegenerative mechanisms, which may underlie and exacerbate the proprioceptive deficits associated with stroke (Hughes et al., 2015).

Proprioceptive and motor recovery in patients with stroke

Significant recovery of proprioceptive ability is seen during the first 6 months post-stroke (Connell et al., 2008; Winward et al, 2002). Winward et al. (2002) reported that five out of nine adults with stroke achieved full proprioceptive recovery by the end of the first month (Winward et al., 2002).

On the other hand, there are variable results in the literature regarding the association between the recovery of proprioception and the recovery and motor recovery post-stroke.

Conversely, a comprehensive study conducted by Rand et al. (1999), concluded that proprioceptive deficits did not influence motor recovery during the first six weeks of rehabilitation. As such, the authors suggest that the upper extremity of all patients, irrespective of proprioceptive deficit, should be treated due to the high likelihood of improvement in all cases (Rand et al., 1999). Furthermore, the authors found that despite some improvement, most patients with combined sensory and motor deficits still exhibited moderately to severely impaired proprioception (Rand et al., 1999). More recently, Meyer et al. (2016b) observed low associations between somatosensory and motor impairments (r = 0.03-0.20) after 1 week post-stroke, whereas at 6 months, low to moderate associations (r = 0.32-0.69) were found for perceptual threshold of touch, thumb finding test, and stereognosis with motor impairment and activity limitations (Meyer et al., 2016b).

These variations could be attributable to numerous factors, such as differences in the proprioception measures, metrics, population differences, and differences in the number and type of somatosensory modalities assessed.

Proprioception-based therapeutic modalities

Based on the potential for improvement and the importance of proprioceptive integrity for activities of daily living, proprioception-based therapeutic interventions are integral to the recovery process for patients with stroke. These interventions can entail both passive and active training to improve somatosensation (Aman et al., 2015). For the purposes of the present literature review, I will focus on the discussion of active training protocols.

It has been suggested that learned non-use, which can occur with sensory loss, leads to further deterioration of motor abilities (Carey et al., 1993). Studies with experimentally lesioned primates demonstrate the recovery of most fine discriminatory abilities with extensive proprioceptive training (Schwartzman, 1972). This recovery is concurrent with reorganization of the somatosensory cortex, which may occur in a compensatory fashion for impaired sensory function (Carey et al., 1993). The observed neuroplasticity of the somatosensory cortex has also been highlighted in studies with non-lesioned animals (Jenkins et al., 1990). The study conducted by Carey et al. (1993) demonstrated that a therapeutic intervention based on specific graded discrimination tasks, which were comprised of tactile discrimination and proprioceptive discrimination with quantitative feedback, can produce marked improvements in specific sensory impairments in patients with stroke.

More recently, Carey et al. (2011) determined the efficacy of a somatosensory discrimination program for sensory recovery in people with chronic stroke, compared to non-specific exposure to sensory stimuli. The experimental protocol entailed passive movements of the upper limb and an object grasping task in 50 patients with chronic stroke (Carey et al., 2011). The sensory discrimination group received proprioceptive training comprised of generalized texture discrimination, limb position sense discrimination, tactile object recognition, and temperature discrimination. The non-specific training program entailed non-systematic repeated exposure to stimuli, which varied in texture, size, temperature, and weight, in addition to passive movements of the upper limb. Results indicated that almost all (n=22/25) participants in the sensory discrimination group demonstrated augmented discrimination capacity (a composite score of the measured modalities). Conversely, participants in the non-specific training group exhibited virtually no improvement in functional discrimination capacity (Carey et al., 2011). Similarly, Chanubol et al. (2012) demonstrated significant recovery of arm function following the administration of Cognitive Sensory Motor Training in a group of patients with acute stroke. While improvement was comparable to traditional occupational therapy for the total group, improvement with Cognitive Sensory Motor Training was better than traditional occupational therapy in patients with stroke with the most severe motor impairment (Chanubol et al., 2012).

A systematic review conducted by Aman et al. (2015) determined that proprioceptive training can yield meaningful improvements in both somatosensory and sensorimotor function (Aman et al., 2015). Furthermore, the training protocols which employed an active and passive task both with and without visual feedback were most beneficial (Aman et al., 2015).

There is evidence that active and passive movements are processed differently in the brain (Findlater & Dukelow, 2017). There are relatively few studies that employ a standardized active somatosensory training rehabilitation protocol, which is problematic due to the potential improvement in quality of life as a result of improved proprioception under such protocols. As such, future research is warranted with a larger sample size to truly observe the effects of these protocols.

Due to the frequency, intensity, and type of feedback possible with robotic rehabilitation devices, robotic rehabilitation is becoming an increasingly accessible and more highly utilized therapeutic modality (Hughes et al., 2015). Robotic rehabilitation devices are capable of administering both active and passive sensorimotor training protocols with unmatched frequency and intensity compared to conventional therapy with the addition of real-time quantitative feedback (Maciejasz et al., 2014). A study conducted by Cuppone et al., (2016) employed a robot-aided proprioceptive training protocol with added vibro-tactile feedback to measure the effect of such a protocol on somatosensory and motor performance. The participants, with vision occluded, had to perform goal-directed wrist movements to reach several haptically specified targets (Cuppone et al., 2016). Results from this study indicated that the participants who received combined proprioceptive/haptic and vibro-tactile feedback (irrespective of the site of application of the vibration) achieved greater improvements in wrist-position sense acuity. Although the participants in this study were not patients with stroke, the results elucidate the potential of robot aided proprioceptive exercises for general improvement in proprioceptive function.

The present review discussed some of the existing literature on proprioceptive function, recovery, and improvement in stroke populations and in populations of healthy older adults. The present review sought to reveal some of the gaps in the literature, especially pertaining to the differences in proprioceptive acuity between patients with stroke and healthy age-matched controls. Future research in this direction, especially with the use of robotics, will provide normative data on proprioceptive function in healthy adults from which we can draw comparisons during the administration of a therapeutic regimen designed to improve proprioceptive function in patients with stroke. The present review also discussed some of the existing therapeutic modalities by which proprioception is improved in both stroke and healthy populations. The use of robot-assisted training and assessment protocols is particularly noteworthy and can provide unparalleled quantitative data from which we can generate a normative database for proprioception in these populations. Furthermore, these protocols would enable augmented frequency and intensity of therapeutic administration, thereby increasing the probability of proprioceptive improvement.

Rationale for study

The aim of the present research was to elucidate the extent of the proprioceptive deficit in patients with stroke with right hemiplegia compared to healthy, age-matched controls on two measures of proprioceptive acuity. The first of which, a robot-guided discrimination task, entailed the passive movement of the wrist joint to two different positions, at which point the participant was asked to report which position they felt was further from the start position. The second measure entailed an ipsilateral remembered active matching task using a wrist joint bimanual manipulandum. The use of these two devices provided a comprehensive assessment of wrist joint position sense in adults with chronic stroke (≥6 months) and healthy age-matched controls.

2. METHODS

Participants

Behavioral data was collected from 8 adults with stroke participating in a study conducted by Dr. Ann Van de Winckel, PhD, MSPT, PT, titled "Functional Correlational Analysis and Functional Connectivity between Brain Lesions and Sensorimotor Impairments in Individuals with Stroke", whose protocol has been approved by the IRB. In this study, approximately 40 patients will be enrolled who have experienced a stroke 6 or more months prior to time of enrollment (patients in chronic stage of stroke). Additionally, behavioral data was collected from 8 age- and gender-matched healthy volunteers who were recruited as controls. Recruitment of patients with stroke was facilitated through an existing database of participants with stroke of the Brain Body Mind Lab (Dr Van de Winckel) and via recruitment from the outpatient populations in rehabilitation centers and hospitals in the Twin Cities. The recruitment of patients with stroke embodied no restrictions regarding race, age, sex or socio- economic status. Patients with stroke and healthy participants attended a screening visit with Dr. Van de Winckel and underwent a full clinical assessment to detect their current sensory and motor function, as well as their current performance in daily life and well-being.

Inclusion criteria for the healthy group and people with stroke included medical stability, between 18-99 years of age, achievement of a score greater than 13/16 on the Mini-Mental State Exam-2 Brief version, and reliable exteroceptive and proprioceptive sensibility, assessed by a crude clinical test of finger and wrist position and motion sense. All patients with stroke were in the chronic stage of recovery (≥6 months post-stroke) and had experienced a cortical infarct (ischemic stroke) affecting the right Middle Cerebral Artery. Demographic information as well as lesion location are detailed in Table 1. Healthy adults were excluded if they had ever experienced a stroke or another brain injury or illness related to the brain that has had lasting effects or effects experienced at the time of recruitment. Furthermore, healthy participants were excluded if they had any interfering comorbidities that would hinder their participation and accurate scoring during the clinical assessment, such as a bone fracture, cancer, or peripheral neuropathy. Patients with stroke were excluded if they exhibited unilateral spatial neglect, as identified by the Bell's test, (Gauthier et al., 1989). Additionally, patients with stroke were excluded if they exhibited aphasia, apraxia, severe sensory impairments such that movements of the finger, hand, or wrist were not reliability felt, or other interfering comorbidities.

Table 1. Stroke patient demographic information and lesion location.

PATIENT ID	AGE	SEX	TIME SINCE STROKE	BRAIN LESION
S01	73	M	3 years 3 months	R MCA lesion
S02	52	M	7 years	R MCA lesion
S03	54	F	7 years	Bilateral MCA lesion (watershed infarcts)
S05	70	M	1 year 6 months	R MCA lesion
S09	46	F	1 year	R MCA lesion
S10	45	F	7 months	R MCA lesion
S12	28	M	4 years 7 months	R MCA lesion
S13	45	F	1 year	R MCA lesion

Setting

Proprioceptive data was collected in the Human Sensorimotor Control Laboratory, 400 Cooke Hall, 1900 University Ave. SE, Minneapolis, MN 55455.

Description of apparatus and experimental protocol with each device

Wrist Bimanual Manipulandum

A body-scalable, bimanual wrist position sense device with one degree of freedom in the horizontal plane was used to measure proprioceptive acuity of the wrist. The lever arms of the device are adjustable to fit the length of the hands, and the width of the two lever arms also adjusts to accommodate the participants' anthropometric differences. The proprioceptive acuity task involved horizontal rotation of the hand. Due to the extent of the impairment in the majority of the patients with stroke, the participants in this group were unable to complete the task with the hemiplegic hand. As such, they were all tested with their unaffected side, which was the right side, and matched the remembered position ipsilaterally. Healthy adults used their non-dominant hand for this task.

An ipsilateral matching task was employed to measure proprioceptive acuity. The participant's hand was passively moved to 15° of wrist flexion (reference position) from a starting position of 0°. Participants were then asked to actively match the reference position with respectively the same hand. Encoder data were transmitted to a laptop and stored for data analysis. Participants performed 5 trials, preceded by a one-minute practice session. This assessment required ~5 minutes.

3-D wrist robot

The second device utilized in the present research was a Wrist robot, developed for motor control studies and rehabilitation. The robot has three degrees of freedom: flexion/extension, ab/adduction, and pronation/supination. The corresponding rotation axes meet at a single point. The range of motion (ROM) values through which the device can move the wrist approximately match the ROM of a typical wrist movement . The participants were instructed to hold a handle connected to the robot while his or her forearm rested in a padded holder so that the biomechanical rotation axis was as close as possible to the robot's. Small misalignments were compensated for by means of a sliding connection between the handle and the robot. The wrist robot protocol measured the joint position discrimination threshold, or just noticeable difference (JND) threshold of the left wrist, which was the hemiplegic side for the participants with stroke. Healthy subjects completed this task with their non-dominant hand. During each trial, the participant's wrist was moved to two different positions. The participant was then asked to report which of the two positions he or she thought was further from the starting position. The psi-marginal algorithm employs an adaptive algorithm that adjusts the stimulus size difference contingent on the participant's response to the previous trial. The participants completed 30 trials of the discrimination task. The psi-marginal method inferred the individual's threshold based on their pattern of responses, the size of the stimulus difference, and their individual lapse rate (Prins, 2013). The task entailed forced choice with two options, so the guess rate of 50% is factored into the method. The psi-marginal algorithm finds the participant's threshold using the maximum likelihood of the correct response for each trial while taking into account the nuisance parameters and the guess rate, which corresponds to roughly 75-80% of the correct response rate (Prins, 2013). This assessment required ~30 minutes.

Statistical analysis

Behavioral assessment of proprioceptive acuity via the active protocol yielded measurements of bias, or position error (PE), and precision, or the standard deviation of position error (SDPE). Bias was operationally defined as the mean of the absolute value of the difference between the final position of the manipulandum and the target position. Descriptive statistics were performed to analyze the joint position matching error and variability for the active matching protocol and the just noticeable difference (JND) threshold and for the passive protocol. To investigate the differences between participants with stroke and healthy controls, Mann Whitney U tests were performed for bias, precision, and just noticeable difference threshold. To investigate the relationship between proprioceptive and motor function, a Spearman's rank correlation was computed between proprioceptive variables and the motor variables Total Left Arm score, Total Left Hand score, and Total Left Side score (MESUPES-ARM-L, MESUPES-TOTH-L, and MESUPES-TOT-L) for all participants (Healthy, Stroke) and for the participants in each group (Healthy or Stroke). The significance level was set to α = 0.05.

3. RESULTS

Table 2. Scores for each participant on each of the proprioceptive variables and MESUPES ARM L, HAND L, and TOT L. IDs. A01-A19 are healthy volunteer IDs.

SUBJECT ID	JND THRESHOLD	BIAS	PRECISION	MESUPES ARM L	MESUPES HAND L	MESUPES TOT L
A01	3.12	2.08	1.92	40	9	58
A02	1.19	6.39	2.06	40	1	57
A04	0.82	4.59	3.85	40	18	58
A05	1.94	2.26	1.58	40	5	58
A09	2.19	1.09	1.44	40	9	56
A12	2.42	2.60	2.12	40	0	58
A13	1.22	6.52	2.31	40	0	58
A19	2.65	3.73	3.37	40	12	57
S01	2.10	23.02	7.30	32	18	41
S02	1.57	13.12	3.08	18	17	19
S03	3.46	7.00	2.84	40	18	58
S05	4.63	7.65	2.30	36	18	41
S09	3.54	2.72	5.50	27	16	36
S10	2.71	0.32	5.43	12	18	12
S12	7.16	5.29	4.20	0	18	0
S13	2.92	10.69	5.68	39	17	51

Legend: A01-A19 are IDs from healthy volunteers; S01-S13 are IDs from patients with stroke.

Table 3. Group means, medians and standard deviations for each of the proprioceptive variables.

GROUP	MEAN JND THRESHOLD	MEDIAN JND THRESHOLD	JND STD DEV.	MEAN BIAS	MEDIAN BIAS	BIAS STD DEV.	MEAN PRECISION	MEDIAN PRECISION	PRECISION STD DEV.
HEALTHY	1.93	2.07	0.80	3.66	3.17	2.02	2.33	2.09	0.85
STROKE	3.51	3.19	1.75	9.32	7.32	6.41	4.54	4.82	1.74

Position sense acuity based on ipsilateral joint position matching

The protocol assessed the ability to proprioceptively perceive the position of the wrist joint and then match this experienced degree of flexion by actively moving the hand to the remembered position. The median position error, or bias, was significantly higher in the stroke group compared to the healthy controls (z = -2.36, $p < 0.01$) (see Fig. 1 & Table 3). The computed effect size was large (Cohen's $d = 1.19$). Additionally, the spread of bias values for the group of patients with stroke was considerably larger than that of the group of healthy controls (see Table 2).

Furthermore, analysis of the standard deviation of position error, or precision, revealed that patients with stroke performed significantly more variably than healthy controls (z = -2.57, $p < 0.01$), indicating that perceptual precision was lower in the group of participants with stroke (see Fig. 2 & Table 3). The computed effect size was large (Cohen's $d = 1.61$).

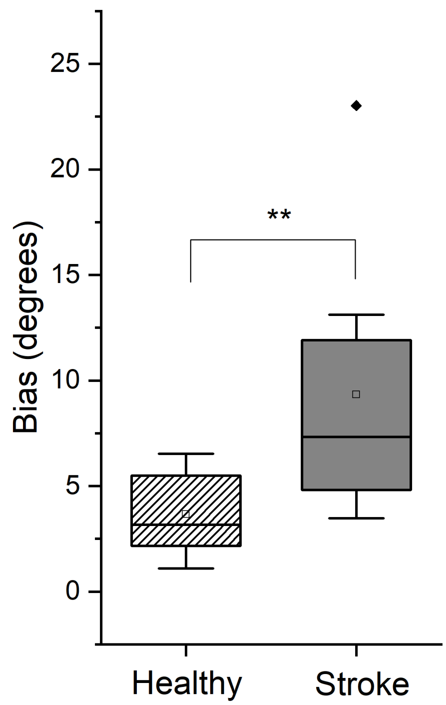

Figure 1. Boxplots of position sense bias or position error (PE) in degrees for both groups during the ipsilateral joint position-matching task.

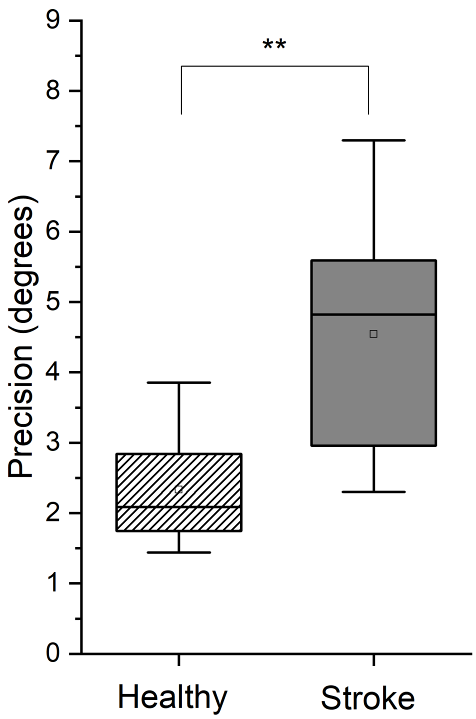

Figure 2. Boxplots of precision or standard deviation of position error (SDPE) in degrees for both groups during the ipsilateral joint position matching task.

Position sense acuity based on the psychophysical discrimination threshold testing

The present protocol assessed wrist joint position sense acuity of the left wrist based on a passive joint rotation without muscle activation. As a group, patients with stroke had significantly elevated JND thresholds (*Median*: 3.19°, *IQR*: 2.13°) when compared to the healthy control group (*Median*: 2.07°, *IQR*: 1.39°) ($z = -2.15$, $p < .05$) (see Fig. 3, Fig. 4, & Table 3). The computed effect size was large (Cohen's $d = 1.15$).

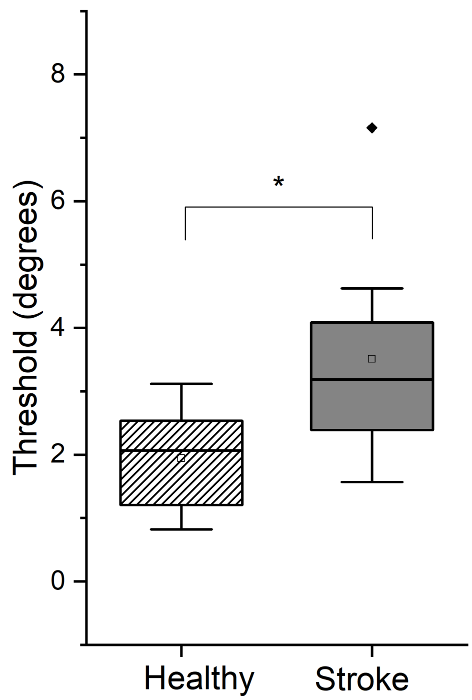

Figure 3. Boxplots of position sense JND thresholds in degrees for both groups for the psychophysical discrimination threshold task.

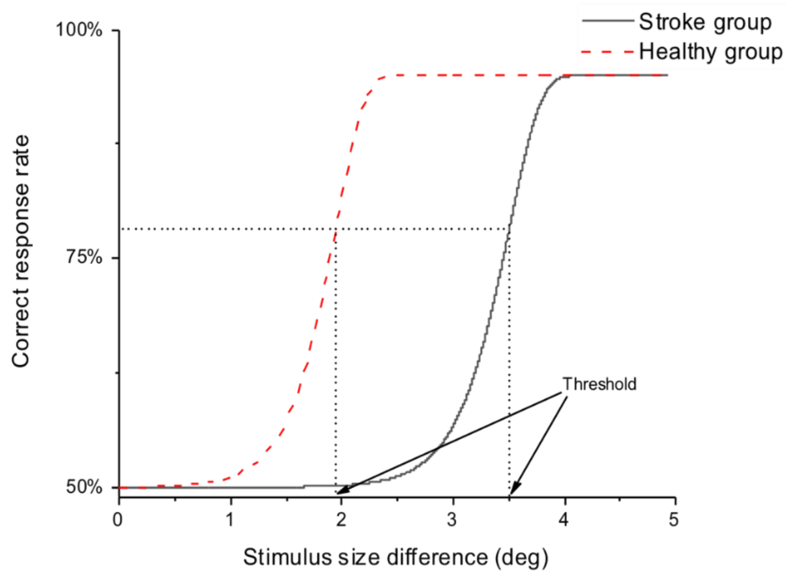

Figure 4. Psychophysical sensitivity functions for both groups. The psi-marginal method determined the threshold to be between 75-80% of the correct response rate based on the psi-marginal algorithm. The curve for the stroke group is shifted to the right, giving rise to an elevated threshold.

Relationship between wrist proprioception and motor function as measured by MESUPES

I examined the extent to which wrist position sense acuity correlated with motor ability as measured by MESUPES arm, hand, and total scores for the left side, which was the hemiplegic side for the patients with stroke. Individual scores on the MESUPES assessments are detailed in Table 2. Spearman correlations were first performed for the combined group, including both patients with stroke and healthy controls, which revealed no significant relationship between MESUPES Total-L score and JND threshold (ρ = -0.40, p = .12) (see Fig. 5). Additionally, MESUPES Arm-L score did not correlate significantly with JND thresholds (ρ = -0.35, p = .18) (see Fig. 6). MESUPES-TOTH-L score, which is a combined score for two clinical assessments of the left hand (active movements, and scoring of orientation of hand and wrist towards objects while moving the object) was not significantly correlated with JND threshold (ρ = -0.32, p = .22). The same correlational analysis was then performed between the measure of position sense acuity and motor function for each group to understand if measures of proprioceptive acuity predict motor ability within the group of patients with stroke and the group of healthy controls, respectively. For each group, the results yielded no significant correlation between just noticeable difference threshold and any of the MESUPES scores (p's > .05)

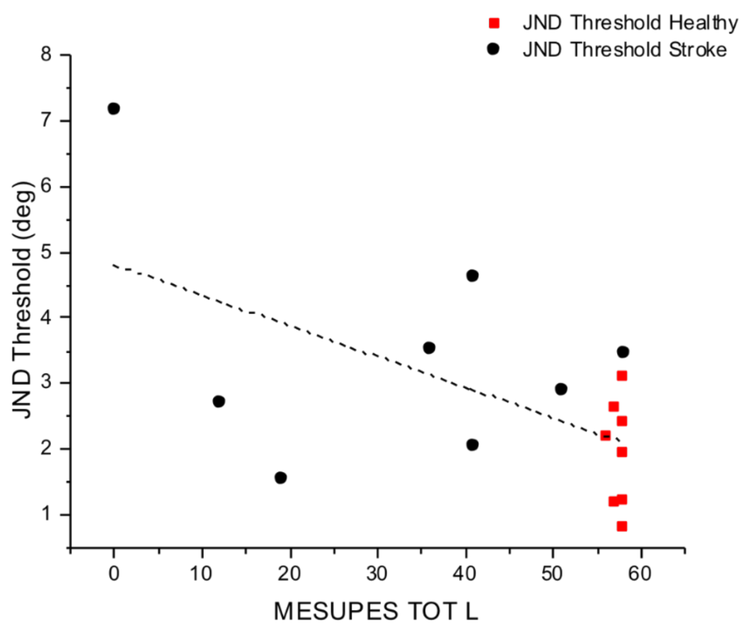

Figure 5. Correlation between proprioceptive acuity and motor function of the left arm and hand as measured by the MESUPES.

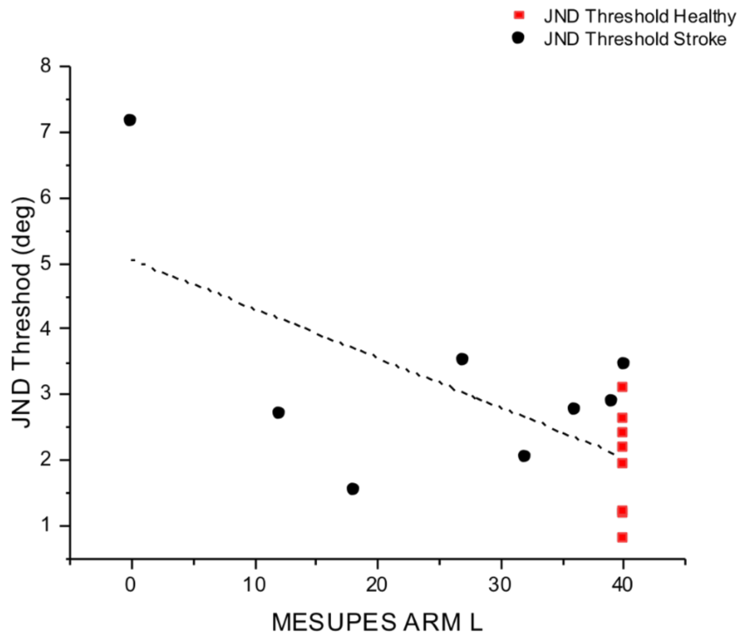

Figure 6. Depicts the correlation between proprioceptive acuity and motor function of the arm as measured by the MESUPES.

4. DISCUSSION

This research sought to elucidate the extent of the proprioceptive deficit in patients with stroke with left hemiplegia compared to healthy age- and gender-matched controls using two novel measures of wrist proprioception. Although it is understood that upper extremity function is often affected by cortical stroke, the present research sought to understand if wrist proprioception is systematically affected and how well the measures of proprioception map on to the MESUPES, which is a clinical measure of the quality of movement of patients with stroke (Van de Winckel et al., 2006). We employed one test protocol that utilized the wrist bimanual manipulandum and one that used the 3-d wrist robot. The 3-d wrist robot protocol tested proprioceptive limb position sense more purely, in which the wrist joint was passively moved and no volitional movement of the participant was required. The other procedure required the participant to actively match a previously assumed joint position. Position sense acuity thresholds based on the passive displacement of the hand were significantly elevated in the group of patients with stroke. Active joint position matching in the unaffected side showed a systematic increase in bias in the stroke group. Furthermore, the standard deviation of the position error during active matching was significantly higher in the stroke group compared to healthy controls, indicating that active position sense of the stroke group was systematically less precise. Lastly, just noticeable difference threshold did not correlate significantly with MESUPES-TOT-L, MESUPES-TOT-H-L, and MESUPES-TOT-ARM-L scores of the affected side in participants with stroke and in healthy adults.

Wrist position sense acuity is reduced in stroke

It is established in the literature that stroke is associated with somatosensory impairments (Meyer et al., 2014, 2016a, 2016b). Relatively few studies, however, have investigated the relationship between proprioceptive acuity at the wrist joint and chronic stroke (Vlaar et al, 2017; Turk et al., 2008). The present research provides objective evidence of the somatosensory deficit in patients with stroke as measured by just noticeable difference threshold. As expected, the just noticeable difference threshold for patients with stroke was significantly elevated in the affected hand when compared to healthy controls. Utilization of the 3-d wrist robot allowed for pure assessment of proprioception, as no voluntary or volitional movement was required of the participant to complete the task. To date, relatively little is known about the specific association between the location of brain lesions and proprioceptive dysfunction. This, unfortunately, makes it difficult to posit a precise locus or a mechanism that underlies the observed differences between patients with stroke and healthy controls on this measure of proprioceptive acuity. Likely, the lesion damaged regions that are integral to somatosensory processing of afferent information arising from peripheral proprioceptors, diminishing the patients' ability to accurately perceive the slight differences in the stimulus movements.

Abnormal precision and bias during active joint position matching with the ipsilesional limb

The group of patients with stroke showed both an elevated perceptual bias as well as significantly higher error variability during the active joint position matching task in the unaffected hand. This implies that both perceptual response accuracy and repeatability are affected by cortical stroke. Due to the nature of the motor deficit, the participants in the stroke group were unable to perform the task with the contralesional limb, and as such, the active matching task was performed on the ipsilesional side. These results demonstrate that there is a systematic sensorimotor deficit on the unaffected or “good” side in patients with stroke in addition to diminished proprioceptive acuity on the hemiplegic or affected side. Our results are in alignment with a previous study where 64% of patients had sensory deficits in the ipsilateral side, as depicted by Semmes-Weinstein monofilaments, Sensory Fugl-Meyer assessment and the Nottingham sensory Assessments in the wrist and hand (Lima et al. 2015). Previous studies have posited the mechanism for the ipsilesional sensorimotor deficit to arise from damage to uncrossed corticospinal tracts, which may disrupt one’s ability to perceive and interpret somatosensory information from ipsilateral inputs (Ziemann et al., 1999). Furthermore, ipsilesional sensorimotor deficit post-stroke may arise from a disruption of interhemispheric transcallosal transfer of somatosensory information (Shimizu et al., 2002). With the administration of the present active matching protocol, this suggests that activation of the ipsilateral hemisphere during unilateral upper-limb movements might be related to excitatory or inhibitory effects in the contralateral hemisphere. It is plausible that these mechanisms underlie the observed sensorimotor deficits in the group of patients with stroke.

Relationship between proprioceptive acuity and motor function

Motoric deficits are among the most prominent in individuals post-stroke. Given that there is a moderate association between proprioceptive function and motor control in chronic patients with stroke, when tested with clinical scales, the extent to which wrist proprioceptive acuity as defined by JND threshold correlates with measures of quality of motor function in the affected arm and hand as evaluated by the Motor Evaluation Scale for Upper Extremity in Stoke Patients (MESUPES) was examined. Results show that the MESUPES Total Left Arm, Left Hand, and Total Left Side scores on the affected side in people with stroke did not significantly correlate with JND threshold.

Limitations of the study and future directions

Several limitations of this study need to be acknowledged. First and foremost, data was collected from only 8 patients with stroke and 8 age- and sex matched healthy adults. Although very large effect sizes were calculated for each of the statistical tests (except for the correlations), the low n limits the generalizability of the study.

Additionally, there are methodological limitations that should be addressed. The experimental protocol was limited to one reference position (15º of wrist flexion). It would have been desirable, but not logistically possible, to examine wrist position sense acuity at several different joint positions, mapping the complete joint workspace.

5. CONCLUSION

This study documents that chronic stroke following a lesion to the right middle cerebral artery is associated with proprioceptive deficit at the wrist joint, which likely contributes to the observed motor deficits in this population. Assessment of pure proprioception via the psychophysical discrimination threshold protocol revealed significantly elevated discrimination thresholds in the group of patients with stroke. Furthermore, assessment of wrist position sense acuity via the ipsilateral active joint position matching protocol revealed elevated bias and reduced precision in the group of patients with stroke in the “unaffected” wrist. While sensory deficits in the affected side and unaffected side have previously been reported, the use of the devices employed in this research could improve the assessment of efficacy of a given physical therapeutic regimen on proprioceptive recovery by quantitatively assessing proprioceptive improvement in populations of patients with stroke or neurodegenerative diseases with a high degree of precision. Moreover, our 3-D robot provides objective feedback to a participant’s performance and therefore could be used as individualized therapeutic protocol to improve proprioceptive performance.

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