Published in final edited form as:

J Electromyogr Kinesiol. 2018 February ; 38: 197–202. doi:10.1016/j.jelekin.2017.03.001.

Carpal Tunnel Syndrome Impairs Index Finger Responses to Unpredictable Perturbations

Emily L. Grandy, MS¹, Kaihua Xiu, PhD¹, Tamara L. Marquardt, BS¹, Chengliu Li, PhD¹, Peter J. Evans, MD, PhD², and Zong-Ming Li, PhD^{1,2,3}

¹Hand Research Laboratory, Department of Biomedical Engineering, Cleveland Clinic, Cleveland, Ohio

²Department of Orthopaedic Surgery, Cleveland Clinic, Cleveland, Ohio

³Department of Physical Medicine and Rehabilitation, Cleveland Clinic, Cleveland, Ohio

Abstract

The fine-tuning of digit forces to object properties can be disrupted by carpal tunnel syndrome (CTS). CTS' effects on hand function have mainly been investigated using predictable manipulation tasks; however, unpredictable perturbations are commonly encountered during manual tasks, presenting situations which may be more challenging to CTS patients given their hand impairments. The purpose of this study was to investigate muscle and force responses of the index finger to unpredictable perturbations in patients with CTS. Nine CTS patients and nine asymptomatic controls were instructed to stop the movement of a sliding plate by increasing index finger force following an unexpected perturbation. The electrical activity of the first dorsal interosseous muscle and forces exerted by the index finger were recorded. CTS patients demonstrated 20.9% greater muscle response latency and 12.0% greater force response latency compared to controls ($p < 0.05$). The duration of plate sliding was significantly different between groups ($p < 0.05$); the CTS group's duration was 142.2 ± 5.8 ms compared to the control group's duration of 133.1 ± 8.4 ms. Although CTS patients had increased muscle and force response durations comparatively, these differences were not statistically significant. Findings from this study suggest CTS-induced sensorimotor deficits interfere with accurate detection, processing and response to unpredictable perturbations. These deficits could be accounted for at multiple levels of the peripheral and central nervous systems. Delayed and decreased responses may indicate inefficient object manipulation by CTS patients and may help to explain why CTS patients tend to drop objects.

Correspondence to: Zong-Ming Li, PhD, Biomedical Engineering/ND20, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195, Phone: (216) 444-1211, Fax: (216) 444-9198, liz4@ccf.org.

Financial Disclosure

We confirm that there are no known conflicts of interest associated with this publication and there was no significant financial support for this work that could have influenced its outcome.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Keywords

Carpal tunnel syndrome; Sensorimotor deficit; Perturbation; Response

Introduction

Healthy individuals dexterously and effortlessly execute manual tasks of daily living with effective integration of sensory information and the motor machinery of the hand. However, dexterity is vulnerable to peripheral nerve disturbances (Cole, Steyers et al. 2003, Nowak and Hermsdorfer 2003) as well as central neurological conditions such as Parkinson's disease (Fellows, Noth et al. 1998) and focal hand dystonia (Nowak, Rosenkranz et al. 2005). Carpal tunnel syndrome (CTS) is a common entrapment neuropathy at the wrist with symptoms including pain, tingling, numbness and weakness of the hand, as well as implications for hand sensorimotor function. For example, patients with CTS experience hand clumsiness while performing daily tasks, including often inexplicably dropping hand held objects (Pazzaglia, Caliandro et al. 2010).

Impairment of hand function associated with CTS has been studied using a variety of manual tasks including grip and pinch strength (Fernandez-de-Las-Penas, Perez-de-Heredia-Torres et al. 2009, Baker, Moehling et al. 2013), precision pinch force (Li, Evans et al. 2015), precision pinch motion (Nataraj, Evans et al. 2014), and thumb opposition (Marquardt, Nataraj et al. 2014). Grip and pinch strength is commonly employed in clinical settings to evaluate hand function. CTS has been shown to be associated with moderate to large deficits in hand strength (Fernandez-de-Las-Penas, Perez-de-Heredia-Torres et al. 2009, Baker, Moehling et al. 2013), although motor capability is preserved (Li, Harkness et al. 2005). CTS patients also demonstrate reduced accuracy and stability of digit forces during sustained precision pinch with submaximal forces, particularly when the produced force is not accompanied by visual feedback of the force outputs (Li, Evans et al. 2015). Additionally, when holding a tool in two-digit precision grip, CTS patients tend to overexert grip force (Lowe and Freivalds 1999). CTS not only effects digit force control during precision pinch, but also impairs digit motion. For example, CTS patients demonstrated greater variability and lack of precision in digit-movement and digit-contact during precision motion tasks (Gehrmann, Tang et al. 2008, Nataraj, Evans et al. 2014). When CTS was simulated by median nerve block at the wrist, the nerve block caused deteriorated performance of precision pinch forces (Dun, Kaufmann et al. 2007), kinematic inaccuracy during precision pinch motion (Li and Nimbarde 2006), and worsened digit coordination and synchronization (Li and Li 2013). In addition to the synergistic actions of the thumb and index finger, independent investigation of thumb opposition and circumduction have shown that CTS patients demonstrate reduced translational and angular kinematics (Marquardt, Nataraj et al. 2014).

The effects of CTS on hand function have been mainly investigated based on predictable manipulation tasks in which the digits either manipulate passive objects or perform anticipatory tasks under predictable experimental conditions. However, manual tasks commonly involve manipulations that encounter unpredictable perturbations (e.g. holding a

fishing pole when a fish struggles against a hook). In unpredictable events, timely sensory feedback and motor responses are required to prevent manipulative failure (Johansson, Hager et al. 1992, Hager-Ross and Johansson 1996). In comparison to predictable tasks, manipulations involving unpredictable perturbations may be more challenging to CTS patients considering the sensory deficits such as significantly elevated detection thresholds (Tucker, White et al. 2007), diminished sensibility to palmar afferents (Szabo and Gelberman 1984), and lack of dexterity (Chen, Jou et al. 2015) associated with the neuromuscular problem. Therefore, the purpose of this study was to investigate muscle and force responses of the index finger to unpredictable perturbations in patients with CTS. It was hypothesized that CTS patients, in comparison to asymptomatic controls, would demonstrate deteriorated EMG and finger responses to unpredictable perturbations, as indicated by prolonged response latency, increased response duration, and decreased response intensity.

Methods

Human Subjects

Nine CTS patients (51.2 ± 11.0 years; 7 female, 2 male) and 9 gender-matched asymptomatic controls (48.0 ± 13.8 years) participated in this study. All subjects were right-hand dominant or ambidextrous, as verified by the Edinburgh Handedness Inventory (Oldfield 1971). Subjects in the CTS group were clinically diagnosed with CTS in the right hand (Keith, Masear et al. 2010) based on satisfying at least three of the following criteria: 1) history of paresthesias, pain, and/or numbness in the median nerve innervated hand territory persisting for at least 3 months; 2) positive provocative maneuvers (i.e. Tinel's sign, Phalen's test, or compression test); 3) abnormal electrodiagnostic testing consistent with median nerve neuropathy at/or distal to the wrist (Stevens, Smith et al. 1999); and 4) an overall CTS Severity Questionnaire score of greater than 1.5 (Levine, Simmons et al. 1993). Eligibility for the control group required absence of CTS-like symptoms. Exclusion criteria for both groups included: 1) history of electrodiagnostic testing indicating ulnar, radial, or proximal median neuropathy; 2) existence of a central nervous system disease (e.g. multiple sclerosis, motor neuron disease, Parkinson's disease, dystonia); 3) pregnancy; 4) history of trauma or surgical intervention to the right hand/wrist; 5) rheumatoid arthritis or osteoarthritis of the right hand/wrist; 6) diabetes; and 7) steroid injection to the hand within 3 months of testing. Prior to the experiment, all subjects signed a consent form approved by the Institutional Review Board.

Experimental setup

A custom experimental set-up was created to induce unexpected perturbations to the index finger and capture the associated muscle and force responses (Figure 1). The set-up included a frictionless linear slide (RS3-2SS, Del-Tron Precision Inc., Bethel, CT) instrumented with a six-component force/torque transducer (Nano17, ATI Industrial Automation, Inc., Apex, NC). An adapter plate covered with 100-grit sandpaper was attached to the top of the transducer to provide an expanded area for finger engagement. Two 100 g weights were attached in series to a wire which was secured to the linear slide and routed over a pulley. One weight served as the baseline load and the other as the perturbation load. The

perturbation weight was initially suspended by a computer-controlled electromagnet (XRN-XP 12VDC, Amico Corp., Birmingham, AL); the unpredictable perturbation was implemented when the electromagnet was turned off causing the perturbation weight to fall 20 cm. The transducers' signals were amplified and multiplexed using a custom ATI interface box (ATI Industrial Automation, Inc., Apex, NC) and digitized using an analog-digital converter (PXI-6289, National Instruments, Austin, TX). To eliminate visual cues of the perturbation, the perturbation weight was concealed from the subject's sight.

A 22-inch computer monitor was positioned 50 cm in front of the subject to display finger force production. Graphically displayed on the monitor was a tank with dimensions of 200 (width) $\times$ 500 (height) pixels, and a vertical scale from 0–6 N. Within the tank, there was a target line at 3 N and a bar that fluctuated in real-time to indicate the normal force exerted by the subject onto the adaptor plate. To record muscle activity, a surface electromyography (EMG) system (MyoSystem 1400, Noraxon USA, Inc., Scottsdale, Arizona, USA) was used. The visual feedback of finger force, control of the electromagnet, and data collection were implemented using a custom *LabVIEW* (National Instruments, Austin, TX) program.

Experimental procedures

Each subject sat in a height adjustable chair by a testing table. A pair of surface electrodes (#272S Dual Electrodes, Noraxon USA Inc., Scottsdale, Arizona, USA) was placed over the belly of the first dorsal interosseous (FDI) muscle in accordance with previously described guidelines (Hislop and Montgomery 2007). Additionally, a ground electrode was placed on the ulnar styloid process. Then, the wrist and forearm were rested on a 20° wedged support in a fully pronated posture. The subject was asked to extend the index finger and position its pulp at the center of the adaptor plate in the proximal-distal direction (x-axis). The position of the wedged support was adjusted to ensure that the index finger was straight and in parallel with the inclination surface of the support (Figure 1). Then, the forearm of the subject was secured to the support with a strap to prevent arm and wrist motion. The subject also donned a pair of earmuffs during the experiment to eliminate auditory cues of the perturbation.

At the beginning of each trial, the subject pressed the adaptor plate with the index finger while maintaining a stable posture. The subject was instructed to match their pressing force as accurately as possible to the 3 N target line displayed on the computer monitor. During the trial, the perturbation weight was randomly released and the subject was instructed to respond to the perturbation as quickly as possible to stop the sliding motion of the plate while maintaining the wrist and finger postures. Each trial lasted 60 s and the perturbation was delivered randomly in the time window of 20–40 s. During this testing period the perturbation signal, force and EMG data were simultaneously collected. A sampling frequency of 1000 Hz was used for data collection. Each subject performed 3 practice trials, followed by 15 formal trials with a 60 s rest between trials.

Data Processing

The EMG and force signals of individual trials were conditioned prior to data quantification. The EMG signals were full-wave rectified and then smoothed using a root mean square

(RMS) technique. A 10 ms moving window RMS was implemented to derive the onset of muscle response for each trial. A 100 ms moving window RMS was applied to determine the time and magnitude of peak muscle response. The force signals were smoothed by a 2nd order low-pass zero-lag Butterworth filter with a cutoff frequency of 20 Hz.

Using the filtered signals, baseline values of the muscle and force signals prior to the perturbation were determined as the mean of each respective signal over a 5 sec period before the release of the perturbation weight. For each trial, the onset of perturbation was determined as the time point when the tangential force (x-direction) exceeded 2 standard deviations (SD) of its baseline. To quantify the muscle response, the conditioned EMG signals from each trial were synchronized at their onsets of perturbation and averaged for each subject. Likewise, the conditioned force signals were similarly synchronized and averaged. A new baseline value of the averaged signal over the 5 sec prior to the synchronization point was determined for subsequent analyses. Fifteen trials were completed by each subject with the first nine successful trials used for data analyses, and every subject had at least nine successful trials. Data processing and analyses were performed using custom *MATLAB* (MathWorks, Natick, MA) programs.

Data Analysis

The onset of muscle response was identified as the initial time point when the EMG signal averaged within a 30 ms moving window continuously exceeded 2 SD of its baseline for 50 ms (Di Fabio 1987). After determining the onset of muscle response, the muscle response latency was calculated as the time period between the onset of perturbation and the onset of muscle response. The peak EMG (muscle) response and the time point of the peak response were also found. The muscle response duration was determined as the time interval between the onset of muscle response and the time point of peak muscle response. Additionally, the muscle response intensity was defined as the ratio of the peak to baseline EMG magnitudes.

The force response parameters were determined similarly to the parameters of the muscle response. The force response latency was quantified as the time duration between the onset of perturbation and the onset of force response. The force response duration was determined as the time interval between the onset of force response and the time point of peak force response. The force response intensity was defined as the ratio of the peak to baseline normal force magnitudes.

As an additional response measure, the moving duration of the slide was determined to quantify the consequence of the finger's response on the object. First, the instantaneous center of pressure of the index finger on the adapter plate was obtained in the moving direction of the slide (x-direction). The center of pressure (P) was calculated using the torque about the y-axis (M_y), the tangential force in the x-direction (F_x), and the normal force (F_z) as $P = -(M_y + d \cdot F_x) / F_z$. The plate thickness, d , was 6.35 mm. After the instantaneous center of pressures were determined, the data was filtered using a 2nd order low-pass Butterworth filter with a cutoff frequency of 20 Hz (Li, Hogrel et al. 2012) and the slide's moving velocity was obtained by first-order differentiation of the instantaneous center of pressures. Accordingly, the moving duration of the slide was quantified as the time

interval between the onset of perturbation and the time instant when the plate stopped sliding (i.e. when the velocity of the index finger's center of pressure was zero).

Statistical Analyses

Statistical analyses were performed using *SigmaStat 3.5* (Systat Software Inc, San Jose, CA). Normality of all variables was verified using the Kolmogorov-Smirnov test. Independent t-tests were performed on variables between groups (CTS versus control). The Mann-Whitney Rank Sum test was used as a surrogate method when data failed normality. A p-value of less than 0.05 was considered statistically significant.

Results

Subjects in both the control and CTS groups were able to use their index finger to stop the sliding plate in response to unpredictable perturbations. In general, finger responses were characterized by activation of the FDI muscle followed by increased normal force application for both groups; however, the CTS group had slower force and EMG responses to unexpected perturbation in comparison to the control group (Figure 2). In addition to slower responses, the CTS group tended to have shorter response durations, lower response intensities, as well as a longer time to stabilize the perturbed sliding plate.

The muscle and force response latencies of the index finger to unpredictable perturbations were significantly longer in the CTS group than in the control group ($t(8) = 2.71$, $p < 0.05$ for muscle; $t(8) = 2.31$, $p < 0.05$ for force, Figure 3). In addition, the force latency was significantly greater than muscle latency for both control and CTS groups ($t(8) = 9.62$, $p < 0.001$ for controls; $t(8) = 4.12$, $p < 0.001$ for CTS). For the control group, the muscle and force response latencies were 75.1 ± 8.0 ms and 103.4 ± 10.5 ms, respectively. The CTS group demonstrated 20.9% greater muscle response latency and 12.0% greater force response latency in comparison to the control subjects. Relative to muscle latency, force latency was prolonged by 28.3 ± 11.4 ms for the control subjects and 25.1 ± 10.2 ms for CTS patients.

The response durations of the index finger for the control and CTS groups to unpredictable perturbations were 178.2 ± 20.0 ms and 185.6 ± 61.4 ms, respectively. The force response duration for the control and CTS groups were 257.9 ± 47.0 ms and 275.6 ± 69.3 ms, respectively. There was no significant difference in muscle response duration or force response duration between the control and CTS groups ($t(8) = 0.34$, $p = 0.74$ and $t(8) = 0.64$, $p = 0.54$, respectively).

For the control group, the muscle and force response intensities, normalized to baseline values, were 11.8 ± 6.9 and 7.6 ± 3.5 , respectively. For the CTS group, the muscle and force response intensities were 9.1 ± 4.8 and 5.8 ± 2.6 , respectively. Although the CTS group demonstrated a decrease of 22.4% in muscle intensity and 23.4% in force intensity relative to the controls, these differences were not significant ($t(8) = 0.97$, $p = 0.36$ and $t(8) = 1.26$, $p = 0.24$, respectively). The duration of plate sliding was significantly different between groups ($t(8) = 2.96$, $p < 0.05$); the control group's duration was 133.1 ± 8.4 ms in comparison to the CTS group's duration of 142.2 ± 5.8 ms.

Discussion

This study investigated the effects of CTS on finger muscle and force responses to unpredictable perturbations applied to the index finger by examining muscle and force response latencies, durations, intensities, as well as motion of the perturbed object. The primary findings of this study were that CTS subjects demonstrated prolonged muscle and force latencies in response to the perturbation.

Prolonged response latencies associated with CTS could be accounted for by sensorimotor deficits at multiple levels of the peripheral and central nervous systems. At the peripheral level, cutaneous sensory feedback resulting from stimulation at the digit-object interface is essential to trigger appropriate reactive digit motor responses to perturbations (Johansson, Hager et al. 1992, Macefield, Hager-Ross et al. 1996). However, in patients with sensory deficits such as numbness, tingling, and chronic pain, which are primary symptoms of CTS, motor processing can be impaired, resulting in delayed motor responses. Previous studies demonstrated that responses to unpredictable perturbations were delayed in individuals who underwent digital anesthesia (Cole and Abbs 1988, Johansson, Hager et al. 1992) and in the elderly (Cole and Rotella 2001). In healthy individuals, cutaneous afferent input in response to a load force perturbation of a grasped object facilitates a timely adjustment of grip force to prevent slips (Johansson, Hager et al. 1992). In precision pinch, the grip/load force ratio can be adjusted within 75 ms after the onset of slip (Johansson and Westling 1987) and within 80–175 ms between the onset of grip force response and subsequent load force increases (Johansson, Hager et al. 1992). The current study had consistent results with a force response latency of approximately 100 ms for control subjects. However, patients with CTS demonstrated 12.4 ms longer response latency when reacting to the perturbation. The task in the current study relied primarily on sensory input from the index finger, which may have been disrupted by neuropathy of the median nerve in CTS. Compression of the median nerve affects the sensory conduction function of the index finger thereby disturbing the process of sensorimotor integration. It is well documented that CTS is associated with decreased median nerve sensory conduction velocity for the index finger (Keith, Masear et al. 2010). As chronic median nerve compression may contribute to degradation of stimulus encoding for the mechanoreceptors at the fingertips in CTS patients, this could further contribute to a lack of sensitive responses.

In addition to peripheral factors, the postponement of sensory information transduction at central sites for CTS patients may also have contributed to the increased response latency observed in this study. In CTS, median nerve impairment has been shown to alter afferent processing which, in turn, modifies somatotopic organization (Dhond, Ruzich et al. 2012). Although the effects of CTS on the motor cortex are still relatively unknown, similar maladaptations are expected to occur because of the continuous S1-M1 communications required to complete manual tasks (Wiestler, McGonigle et al. 2011, Ejaz, Hamada et al. 2015) and because continuous pain – such as in CTS – is associated with attenuated motor cortex reactivity (Kirveskari, Vartiainen et al. 2010). Compared to the more distinct cortical representations of individual digits in asymptomatic controls (Napadow, Kettner et al. 2006), CTS patients have diffuse, enlarged and overlapping cortical representations thought to be caused by abnormal deafferentation due to chronic paresthesia and pain (Tecchio, Padua et

al. 2002). In CTS, blurred cortical representations for median nerve innervated digits are maladaptive, as blurring compromises fine motor skill and the ability to discriminate between inputs corresponding to adjacent digits; this has also been linked to paresthesia severity in CTS patients (Maeda, Kettner et al. 2014). By impacting sensorimotor integration at the central level, sensory and motor cortical remodeling may contribute to functional deficits associated with the ability of CTS patients to effectively respond to unexpected perturbations.

Whilst decreased distinctiveness of cortical representations for individual digits may be the central manifestation of CTS within the CNS, changes in volumetric gray matter (Maeda, Kettner et al. 2013) and reductions in sensory and motor cortical thickness corresponding to pain and paresthesia severity (Maeda, Kettner et al. 2016) have also been demonstrated for CTS patients. Morphometric changes in the brain as a result of chronic pain states have been widely reported (Apkarian, Sosa et al. 2004, Kuchinad, Schweinhardt et al. 2007, Maeda, Kettner et al. 2016). In CTS, gray matter volume in the sensory cortex correlated with median nerve conduction velocity; the slower the conduction, the more pronounced the volumetric reduction (Maeda, Kettner et al. 2013). These additional morphological expressions can negatively influence subsequent processing of sensorimotor information, with repercussions for hand function and dexterity, including an interference with normal sensory perception and thus a patient's ability to manipulate objects in a predictive and reactive manner.

Sensory information is supplied to the index finger via the median nerve; however, the FDI muscle is innervated by the ulnar nerve. As CTS is predominantly a median nerve problem, sensory input may be more susceptible to disruption than muscle force production in patients with CTS. Our results indeed demonstrate that response latency related to sensory conduction for CTS patients deteriorates, but motor outcomes of response duration and intensity were relatively preserved. This is consistent with a previous study showing that motor strength was relatively preserved in CTS patients with mild and moderate severity (Li, Harkness et al. 2005). However, the results of the current study are in contrast with the findings of previous studies in which CTS patients (Lowe and Freivalds 1999) and asymptomatic subjects who underwent digital anesthesia (Dun, Kaufmann et al. 2007) displayed increased grip force during a precision pinch task. This discrepancy may be attributable to the more severe motor impairment of anesthesia and the different strategies used to complete each task. Precision pinch tasks rely predominantly on anticipatory mechanisms from previous sensorimotor memories, whereas unpredictable perturbation tasks depend on instantaneous sensory feedback (Cole and Abbs 1988). Moreover, thenar muscles of the thumb are innervated by the median nerve, and therefore functional impairments in thumb-finger precision tasks are likely different from those in the index finger-only task in the current study.

The moving duration of the slide was 9.1 ms longer for the CTS group. The duration of slide movement resulted from the combined effects of muscle and force response latencies, durations and intensities. Movement duration was determined to indicate effects of the finger's response on the sliding object after the perturbation. In particular, CTS patients' significantly longer response times following the onset of object perturbation likely is the

contributing factor to the sliding duration. Subject specific examination revealed that those participants with the longest sliding durations also exhibited the greatest force response latency to perturbation, meaning the longer it took to react to the movement of the plate the longer the plate was permitted to slide. The longer object moving duration is suggestive of a higher risk of object drop, which may help explain why CTS patients tend to drop objects (Pazzaglia, Caliandro et al. 2010).

There are a few limitations to consider for this study. First, the experimental protocol involved the perturbation of only the index finger. This specific condition permitted the well-controlled investigation of muscle and force responses of one digit to unpredictable perturbations in patients with CTS. More research is needed to understand how CTS patients react to unpredictable perturbations that are encountered during manual tasks involving multiple digit manipulations. Furthermore, due to the effects of muscle enslaving on adjacent digits in CTS, it would be worthwhile to investigate muscle and force latency, intensity and duration for all digits during an unpredictable task to determine the extent to which single digits recruit neighboring fingers. Second, the same baseline and perturbation weights were used for all subjects; the weights were not adjusted based on physical characteristics (e.g. weight, strength) of individual subjects, and future studies may investigate how subjects respond to varying perturbation intensities.

Acknowledgments

Funding Sources: National Institutes of Health (NIH/NIAMS R01AR056964)

Research reported in this publication was supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health under Award Number R01AR056964. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

- Apkarian AV, Sosa Y, Sonty S, Levy RM, Harden RN, Parrish TB, Gitelman DR. Chronic back pain is associated with decreased prefrontal and thalamic gray matter density. *The Journal of neuroscience : the official journal of the Society for Neuroscience*. 2004; 24(46):10410–10415. [PubMed: 15548656]
- Baker NA, Moehling KK, Desai AR, Gustafson NP. Effect of carpal tunnel syndrome on grip and pinch strength compared with sex- and age-matched normative data. *Arthritis care & research*. 2013; 65(12):2041–2045. [PubMed: 23925936]
- Chen PT, Jou IM, Lin CJ, Chieh HF, Kuo LC, Su FC. Is the Control of Applied Digital Forces During Natural Five-digit Grasping Affected by Carpal Tunnel Syndrome? *Clinical Orthopaedics and Related Research*. 2015; 473(7):2371–2382. [PubMed: 25690168]
- Cole KJ, Abbs JH. Grip force adjustments evoked by load force perturbations of a grasped object. *Journal of neurophysiology*. 1988; 60(4):1513–1522. [PubMed: 3193168]
- Cole KJ, Rotella DL. Old age affects fingertip forces when restraining an unpredictably loaded object. *Experimental brain research*. 2001; 136(4):535–542. [PubMed: 11291734]
- Cole KJ, Steyers CM, Graybill EK. The effects of graded compression of the median nerve in the carpal canal on grip force. *Experimental brain research*. 2003; 148(2):150–157. [PubMed: 12520402]
- Dhond RP, Ruzich E, Witzel T, Maeda Y, Malatesta C, Morse LR, Audette J, Hamalainen M, Kettner N, Napadow V. Spatio-temporal mapping cortical neuroplasticity in carpal tunnel syndrome. *Brain : a journal of neurology*. 2012; 135(Pt 10):3062–3073. [PubMed: 23043143]

- Di, Fabio RP. Reliability of computerized surface electromyography for determining the onset of muscle activity. *Physical Therapy*. 1987; 67(1):43–48. [PubMed: 3797476]
- Dun S, Kaufmann RA, Li ZM. Lower median nerve block impairs precision grip. *Journal of electromyography and kinesiology : official journal of the International Society of Electrophysiological Kinesiology*. 2007; 17(3):348–354. [PubMed: 16616519]
- Ejaz N, Hamada M, Diedrichsen J. Hand use predicts the structure of representations in sensorimotor cortex. *Nature Neuroscience*. 2015; 18(7):1034–+. [PubMed: 26030847]
- Fellows SJ, Noth J, Schwarz M. Precision grip and Parkinson's disease. *Brain*. 1998; 121(Pt 9):1771–1784. [PubMed: 9762964]
- Fernandez-de-Las-Penas C, Perez-de-Heredia-Torres M, Martinez-Piedrola R, de la Llave-Rincon AI, Cleland JA. Bilateral deficits in fine motor control and pinch grip force in patients with unilateral carpal tunnel syndrome. *Exp Brain Res*. 2009; 194(1):29–37. [PubMed: 19066868]
- Gehrmann S, Tang J, Kaufmann RA, Goitz RJ, Windolf J, Li ZM. Variability of precision pinch movements caused by carpal tunnel syndrome. *J Hand Surg Am*. 2008; 33(7):1069–1075. [PubMed: 18762099]
- Hager-Ross C, Johansson RS. Nondigital afferent input in reactive control of fingertip forces during precision grip. *Exp Brain Res*. 1996; 110(1):131–141. [PubMed: 8817264]
- Hislop, HJ., Montgomery, J. Daniels and Worthingham's muscle testing : techniques of manual examination. St. Louis, Mo: Saunders/Elsevier; 2007.
- Johansson RS, Hager C, Backstrom L. Somatosensory control of precision grip during unpredictable pulling loads. III. Impairments during digital anesthesia. *Experimental brain research*. 1992; 89(1):204–213. [PubMed: 1601098]
- Johansson RS, Hager C, Riso R. Somatosensory control of precision grip during unpredictable pulling loads. II. Changes in load force rate. *Experimental brain research*. 1992; 89(1):192–203. [PubMed: 1601097]
- Johansson RS, Westling G. Signals in tactile afferents from the fingers eliciting adaptive motor responses during precision grip. *Experimental brain research*. 1987; 66(1):141–154. [PubMed: 3582528]
- Keith MW, Masear V, Chung KC, Amadio PC, Andary M, Barth RW, Maupin K, Graham B, Watters WC 3rd, Turkelson CM, Haralson RH 3rd, Wies JL, McGowan R. American Academy of Orthopaedic S. American Academy of Orthopaedic Surgeons clinical practice guideline on the treatment of carpal tunnel syndrome. *J Bone Joint Surg Am*. 2010; 92(1):218–219. [PubMed: 20048116]
- Kirveskari E, Vartiainen NV, Gockel M, Forss N. Motor cortex dysfunction in complex regional pain syndrome. *Clin Neurophysiol*. 2010; 121(7):1085–1091. [PubMed: 20185362]
- Kuchinad A, Schweinhardt P, Seminowicz DA, Wood PB, Chizh BA, Bushnell MC. Accelerated brain gray matter loss in fibromyalgia patients: premature aging of the brain? *The Journal of neuroscience : the official journal of the Society for Neuroscience*. 2007; 27(15):4004–4007. [PubMed: 17428976]
- Levine DW, Simmons BP, Koris MJ, Daltroy LH, Hohl GG, Fossel AH, Katz JN. A self-administered questionnaire for the assessment of severity of symptoms and functional status in carpal tunnel syndrome. *The Journal of bone and joint surgery. American volume*. 1993; 75(11):1585–1592. [PubMed: 8245050]
- Li K, Evans PJ, Seitz WH Jr, Li ZM. Carpal tunnel syndrome impairs sustained precision pinch performance. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*. 2015; 126(1):194–201. [PubMed: 24877682]
- Li K, Hogrel JY, Duchene J, Hewson DJ. Analysis of fatigue and tremor during sustained maximal grip contractions using Hilbert-Huang Transformation. *Med Eng Phys*. 2012; 34(7):832–840. [PubMed: 22177573]
- Li K, Li ZM. Cross recurrence quantification analysis of precision grip following peripheral median nerve block. *J Neuroeng Rehabil*. 2013; 10:28. [PubMed: 23453041]
- Li ZM, Harkness DA, Goitz RJ. Thumb strength affected by carpal tunnel syndrome. *Clin Orthop Relat Res*. 2005; 441:320–326. [PubMed: 16331021]

- Li ZM, Nimbarte AD. Peripheral median nerve block impairs precision pinch movement. *Clin Neurophysiol.* 2006; 117(9):1941–1948. [PubMed: 16887386]
- Lowe BD, Freivalds A. Effect of carpal tunnel syndrome on grip force coordination on hand tools. *Ergonomics.* 1999; 42(4):550–564. [PubMed: 10204420]
- Macefield VG, Hager-Ross C, Johansson RS. Control of grip force during restraint of an object held between finger and thumb: responses of cutaneous afferents from the digits. *Experimental brain research.* 1996; 108(1):155–171. [PubMed: 8721164]
- Maeda Y, Kettner N, Holden J, Lee J, Kim J, Cina S, Malatesta C, Gerber J, McManus C, Im J, Libby A, Mezzacappa P, Morse LR, Park K, Audette J, Tommerdahl M, Napadow V. Functional deficits in carpal tunnel syndrome reflect reorganization of primary somatosensory cortex. *Brain : a journal of neurology.* 2014; 137(Pt 6):1741–1752. [PubMed: 24740988]
- Maeda Y, Kettner N, Kim J, Kim H, Cina S, Malatesta C, Gerber J, McManus C, Libby A, Mezzacappa P, Mawla I, Morse LR, Audette J, Napadow V. Primary somatosensory/motor cortical thickness distinguishes paresthesia-dominant from pain-dominant carpal tunnel syndrome. *Pain.* 2016; 157(5):1085–1093. [PubMed: 26761384]
- Maeda Y, Kettner N, Sheehan J, Kim J, Cina S, Malatesta C, Gerber J, McManus C, Mezzacappa P, Morse LR, Audette J, Napadow V. Altered brain morphometry in carpal tunnel syndrome is associated with median nerve pathology. *NeuroImage Clinical.* 2013; 2:313–319. [PubMed: 23799199]
- Marquardt TL, Nataraj R, Evans PJ, Seitz WH Jr, Li ZM. Carpal tunnel syndrome impairs thumb opposition and circumduction motion. *Clinical orthopaedics and related research.* 2014; 472(8):2526–2533. [PubMed: 24777728]
- Napadow V, Kettner N, Ryan A, Kwong KK, Audette J, Hui KK. Somatosensory cortical plasticity in carpal tunnel syndrome—a cross-sectional fMRI evaluation. *NeuroImage.* 2006; 31(2):520–530. [PubMed: 16460960]
- Nataraj R, Evans PJ, Seitz WH Jr, Li ZM. Effects of carpal tunnel syndrome on reach-to-pinch performance. *PloS one.* 2014; 9(3):e92063. [PubMed: 24632925]
- Nataraj R, Evans PJ, Seitz WH Jr, Li ZM. Pathokinematics of precision pinch movement associated with carpal tunnel syndrome. *Journal of orthopaedic research : official publication of the Orthopaedic Research Society.* 2014; 32(6):786–792. [PubMed: 24536036]
- Nowak DA, Hermsdorfer J. Selective deficits of grip force control during object manipulation in patients with reduced sensibility of the grasping digits. *Neuroscience research.* 2003; 47(1):65–72. [PubMed: 12941448]
- Nowak DA, Rosenkranz K, Topka H, Rothwell J. Disturbances of grip force behaviour in focal hand dystonia: evidence for a generalised impairment of sensory-motor integration? *Journal of neurology, neurosurgery, and psychiatry.* 2005; 76(7):953–959.
- Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia.* 1971; 9(1):97–113. [PubMed: 5146491]
- Pazzaglia C, Caliendo P, Granata G, Tonali P, Padua L. “Dropping objects”: a potential index of severe carpal tunnel syndrome. *Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology.* 2010; 31(4):437–439.
- Stevens JC, Smith BE, Weaver AL, Bosch EP, Deen HG Jr, Wilkens JA. Symptoms of 100 patients with electromyographically verified carpal tunnel syndrome. *Muscle & nerve.* 1999; 22(10):1448–1456. [PubMed: 10487914]
- Szabo RM, Gelberman RH. Peripheral nerve compression: etiology, critical pressure threshold, and clinical assessment. *Orthopedics.* 1984; 7(9):1461–1466. [PubMed: 24823179]
- Tecchio F, Padua L, Aprile I, Rossini PM. Carpal tunnel syndrome modifies sensory hand cortical somatotopy: a MEG study. *Human brain mapping.* 2002; 17(1):28–36. [PubMed: 12203686]
- Tucker AT, White PD, Kosek E, Pearson RM, Henderson M, Coldrick AR, Cooke ED, Kidd BL. Comparison of vibration perception thresholds in individuals with diffuse upper limb pain and carpal tunnel syndrome. *Pain.* 2007; 127(3):263–269. [PubMed: 17030439]
- Wiestler T, McGonigle DJ, Diedrichsen J. Integration of sensory and motor representations of single fingers in the human cerebellum. *Journal of Neurophysiology.* 2011; 105(6):3042–3053. [PubMed: 21471398]

Biographies

Emily L. Grandy, MS, obtained her bachelor's degree in Exercise Science from the Department of Human Sciences from The Ohio State University in 2009, and her master's degree from the Department of Life Sciences at Roehampton University, London, in 2013. She is currently the Research Coordinator in the Hand Research Laboratory at Cleveland Clinic.

Kaihua Xiu, PhD, obtained a Bachelor's in 2003 and a Master's degrees in 2006, respectively, from Sichuan University, China. She received her PhD degree in Biomedical Engineering in 2011 from Beihang University, China. She worked as a postdoctoral fellow in the Hand Research Laboratory at Cleveland Clinic in 2015.

Tamara L. Marquardt, BS, received a Bachelor's degree in Biomedical Engineering with a specialization in Biomechanics and a Minor in Mathematics from the University of Cincinnati in 2011. She worked as a senior research engineer in the Hand Research Laboratory at Cleveland Clinic.

Chengliu Li, MS, obtained a Bachelor of Science degree in 2004 in Electrical Engineering from Yanshan University, China and a master's degree in 2008 in Electrical Engineering from Beijing Jiaotong University, China. He also received a master's degree in Electrical Engineering in 2011 at the University of Pittsburgh. In 2014, he was a visiting student in the Hand Research Laboratory at Cleveland Clinic.

Peter J. Evans, MD, PhD, is an orthopedic surgeon and the Director of the Upper Extremity Center at Cleveland Clinic. He received his BA in 1983 from Harvard College, MD in 1987 from University of Calgary, and PhD in 1993 from University of Toronto. His research focuses on peripheral nerve injury and repair.

Zong-Ming Li received his Ph.D. from the Pennsylvania State University in 1998. He is currently Full Staff in the Departments of Biomedical Engineering, Orthopaedic Surgery, and Physical Medicine & Rehabilitation at Cleveland Clinic. Dr. Li's research interest is in biomechanical translation to solve clinical problems related to the hand and upper extremity.

Figure 1. Schematic of experimental setup: (1) transducer, (2) linear slide, (3) baseline weight, (4) perturbation weight, and (5) electromagnet

Figure 2.

Muscle and force responses for representative control and CTS subjects. Indicated are the onsets of perturbation (a), muscle response for the control subject (b), muscle response for the CTS subject (c), force response for the control (d), and force response for the CTS subject (e).

Figure 3. Muscle and force response latencies (ms) for control and CTS groups (mean $\pm$ standard deviation, * $p < 0.05$)