Regional specificity in the hand area of the primary motor cortex for healthy individuals and individuals with focal hand dystonia

A DISSERTATION
SUBMITTED TO THE FACULTY OF THE GRADUATE SCHOOL
OF THE UNIVERSITY OF MINNESOTA
BY

Kristen Alexis Pickett

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
Doctor of Philosophy

Adviser: Jürgen Konczak, Ph.D., Dr. rer. nat. habil.

Co-adviser: Teresa Jacobson Kimberley, PhD, PT

July 2010

Acknowledgements

I owe a great deal of thanks and gratitude to many people without whom I would not have been able to finish this dissertation.

My deepest gratitude is to my two advisors. Dr. Jürgen Konczak has been my mentor and guide through eight long years of training and education. He has brought me a long way toward learning how to be a scientist. Dr. Teresa Kimberly has taken me from a fledgling scientist and convinced me that there is quite literally no limit to the things that I can accomplish. She has allowed me the freedom to explore on my own but has always been close by watching over me. Allowing me to lead when possible but always willing to guide when necessary. As I go forward toward the next phase of this great adventure, she will serve as a model of how to be a great researcher but more importantly a big, bright shining light to all of the lives I will touch. I am a different person than the one who arrived here in 2002 and I owe so much of that to these two individuals.

To Mom, Dad, Abbie, Ethan and McKenzie, it has been a long trek and I know I have missed out on some important moments in order to do this crazy thing, but I hope you know that not a day went by that I did not think of you and how much I love you. I cannot put into words what it has meant to know that you are always there, supporting me, thinking of me and loving me.

Additionally, my extended family, Grandma Eileen, Uncle Greg, Aunt Loraine and Grandpa Havlik, have provided so much support and love through the years. I am forever in debt to all of you. I love you all very much.

Jeff Withers saw me though many long nights and early mornings and worked to help me accomplish all that I have. No matter what happens, you will always hold a special place in my heart.

To my friend and colleague, Heidi Vander Velden, who has quite literally stood by my side through many long hours and has been willing to ebb and flow with me through this entire journey.

Megan Luce, our paths seem to be inexorably intertwined and each day I become more appreciative of that fact. As the world continues to grow and challenge us I hope we can always have each other's ear for the big and the small stuff.

To the BPL members and especially Michael Borich and Kuan-yi Li, even though we are all going our separate ways, we must remember to reunite on occasion. The BPL has served so much more than its original purpose and has, on numerous occasions, been my saving grace.

A special thanks to my committee member who were willing to work with me to get this done and out on time.

And to Marta, Carol, Jonathan and all of the other folks that worked thanklessly to help me and countless others accomplish their goals, thank you, thank you, thank you. The world is a better place because of wonderful supportive folks like yourselves.

Many friends have helped me to maintain some level of sanity along the way and I am eternally grateful to all of you.

And finally to Jeanne, without your guidance all those years ago, I would have never arrived at this point.

Dedication

This dissertation is dedicated to three of the most amazing women I have ever known. My Grandma Havlik who did not survive long enough to see me finish but who was one of my biggest supporters and who has been with me all along. My Aunt Loraine who has always been and will always be a source of strength and support. And finally to Grandma Pickett who has overcome every obstacle placed in her path and continues, on a daily basis to surprise and amaze me with her strength, determination and optimism.

Abstract

Idiopathic focal hand dystonia is a movement disorder characterized by abnormal postures and loss of motor control of the affected limb. Currently, the underlying pathophysiology responsible for these motor manifestations is not fully understood. Recent empirical evidence suggests a link between deficits of cortical inhibition, maladaptive plasticity and abnormal sensory and motor processing in individuals with dystonia. These factors may contribute to an atypical organization of the hand knob area of the primary motor cortex. The current literature lacks a well designed method to clearly define and quantify healthy cortical activation. The purpose of this study was to first establish a definition of healthy cortical activation in the primary motor cortex during a finger tapping task and then use this baseline for comparison to a group of participants with focal hand dystonia. **Methods**. Functional magnetic resonance imaging was used to compare the cortical activation of six participants diagnosed with idiopathic focal hand dystonia to eight healthy individuals during a randomly ordered finger tapping task. Quantification of the cortical activation was performed with GLM beta weight analysis to examine for main effects and through a 'Selectivity Index' that allowed for activation of a single digit (in the hemisphere contralateral to the moving digit) to be measured relative to the activation of the four other digits of the hand. **Results**. In the beta weight analysis differences in cortical activation was found at the group, finger and hemisphere levels ($p < 0.05$). Significant interaction effects were found in activation for group

x finger x hemisphere ($p = 0.02$). The analysis demonstrated less selectivity of individual finger activation in both hemispheres for the dystonic group compared to the healthy group (right: $p = 0.0017$, left $p = 0.0105$). **Discussion.** This study is the first to define a method for determining the degree to which a cortical area is associated with the movement of one digit related to another. Importantly, it elucidates a potential neuropathophysiological substrate related to individual finger activation in the primary motor cortex in humans with focal dystonia.

Table of Contents

List of Tables

List of Figures

List of Appendices

.

CHAPTER 1

INTRODUCTION

Idiopathic focal task specific hand dystonia (FHD) is a movement disorder in which individuals present with abnormal postures of the affected hand due to co-contractions of the agonist and antagonist muscles as well as spastic activity of associated muscles. Hyperactivity of these muscles causes a twisting or spasmodic movement of the limb drastically decreasing the functional range of motion during dystonic episodes (Hallett 2006a; Pullman and Hristova 2005; Rona, et al. 1998). Initially the presentation of symptoms is localized to a single body segment (focal) and manifests only during specific fine motor skills (task specific). However, the disease can be progressive in that symptoms can begin to onset during related fine motor tasks, present in the opposite limb and eventually can be disabling in their systemic presentation (Hallett 2006b; Sheehy and Marsden 1982).

There is currently no known cure for dystonia and the treatment options are limited in their efficacy and in the duration of their effect. To date, the cause of dystonia has not been isolated. Various regions of the brain have been studied in an attempt to isolate the pathophysiology including the somatsensory cortex (Bara-Jimenez, et al. 1998; Baumer, et al. 2007; Blake, et al. 2002a; Byl, et al. 1996a; Byl, et al. 2000; Byl, et al. 1997; Byl, et al. 1996b), motor cortex (Altenmuller 2003; Curra, et al. 1998) and basal ganglia (Berardelli, et al. 1998; Peller, et al. 2006; Rona, et al. 1998). However, these studies focus on the location rather than the mechanism of the disease.

Current research has focused on three plausible causative neural mechanisms for FHD; deficits of cortical inhibition, maladaptive plasticity and abnormal sensory and motor processing (Lin and Hallett 2009). The combination of these factors may then lead to abnormal associations between sensory inputs and motor outputs, thereby leading to abnormal, unwanted connections and subsequent impairment of motor control. The presence of each of these three components has been reported previously in the dystonic patient population (Berardelli, et al. 1998; Curra, et al. 1998; Garraux, et al. 2004; Rona, et al. 1998) and shall be explored herein; however, the extent to which all three may in fact be interrelated has not yet be elucidated.

Neuroplasticity is a known phenomenon in the nervous system which can be generally defined as alterations in the allocation of cortical regions, usually in response to altered homeostasis. This phenomenon has been widely studied both in healthy individuals (Berlucchi and Buchtel 2009; Buonomano and Merzenich 1998; Cooke and Bliss 2006; Hlustik, et al. 2004) as well in cases of clinical pathology such as stroke (Caramia, et al. 1996; Kopp, et al. 1999). The vastly individualistic and plastic quality of the human brain itself poses a clear challenge in rendering a definition of “normal.” Similarly, understanding aberrant cortical inhibition, particularly in the motor cortex, requires knowledge of not only the inhibitory mechanism but also the facilitation of the related motor output. That said, in order to quantify the extent to which a patient population is pathological, we must first be able to clearly define and quantify healthy cortical activation. In

the hand area of the primary motor cortex, defining unique areas for individual finger activation has not yet been successfully accomplished or has been thought to be unfeasible due to the nature of the physiology. Thus, the first component of this work was to establish a definition of healthy cortical activation on the primary motor cortex during individuated finger tapping. This baseline was then used for comparison to the dystonic patient population.

REVIEW OF RELEVANT LITERTURE

Activation of Primary Motor Area during finger tapping

Since the early work of J. Hughlings Jackson in 1863 with epileptic individuals, the primary motor (M1) area of the human brain has been understood to exhibit an anatomically defined regional specificity known as somatotopic organization (Jackson 1873/1931). That is, for a given anatomical component, there exists a definable region of the cerebral cortex that is related to movement of that component. This conjecture was later support via electrical stimulation studies in both animals (Ferrier 1874; Fritsch and Hitzig 1870) and humans (Foerster 1936; Penfield and Boldrey 1937). This somatotopic pairing of the motor components of the body to the neural components of the brain does not imply a proportional distribution based upon size, but rather a distribution based upon finite control. Thus a motor area necessitating a greater level of fine motor control will be allotted a relatively greater number of neurons as compared to a gross motor region. This may impart be related to the number of small muscles needed for fine motor control (Devanne, et al. 2006). For example the hand is controlled by 29 intrinsic and extrinsic muscles while nine muscles control shoulder motion (Alexander 1992) thus the fact that the hand area of M1 is considerably larger than the shoulder area may in fact imply that a similar cortical space is necessary for each muscle being controlled.

Evidenced by the somatotopic organization of the homunculus (figure 1), localization of M1 theoretically allows for movements of unique anatomical areas

to be controlled by localized groups of cortical neurons on the precentral gyrus (Penfield and Rasmussen 1950). That is, movement of the index finger of the left hand is correlated to activation of one region of M1 while movement of the left ankle is associated with activation of a different region. While this does not suggest exclusive control of the movement, it does suggest a primary area of control. To what extent cortical regions can be uniquely correlated to individual, finite motor output is a topic of much interest.

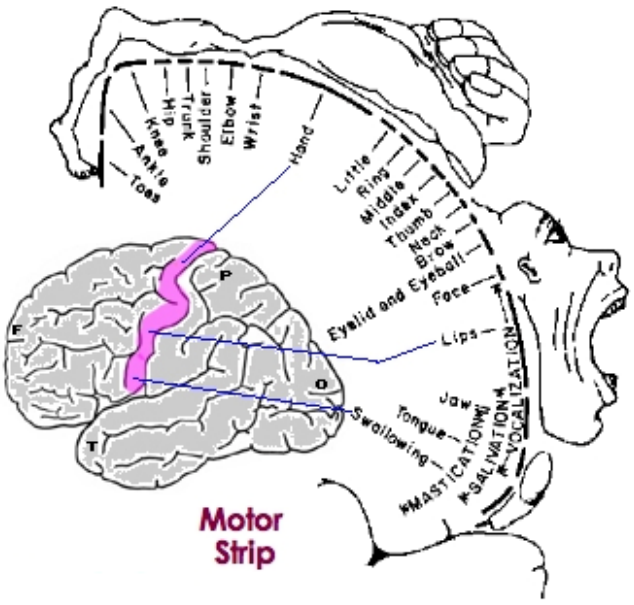


Figure 1. Homunculus imposed on the motor cortex (M1) highlighted in pink. (homunculus depictions adapted from Penfiled and Rasmussen 1950)

The organization of the cortical neurons is not as clearly localized and identifiable as the cartoon depiction of the homunculus's organization portrays. The somatopic organization of M1 does not exhibit perfectly definable and localized areas of activation. Indeed, "large" regions of disperse activity allowing for overlap between anatomically defined cortical areas have been found in

primates (Andersen, et al. 1975; Asanuma and Rosen 1972; Gould, et al. 1986; Nudo, et al. 1992; Sato and Tanji 1989; Schieber and Hibbard 1993) as well as in humans (Plow, et al. 2010; Sanes, et al. 1995; Sanes and Schieber 2001; Schieber 1999; Schieber 2001). The disperse nature of the organization of M1 was illustrated by Gould et al. (1986) across the entire motor system of the owl monkey during microstimulation. This work examined not only the anatomical region but the specific joint motion caused by the motoric output. This allowed for mapping of not only the anatomy (elbow) but of precise moments (flexion or extension). In figure 2, which depicts only the upper limb motor distribution, we are able to see not only the cortical regions assigned to wrist, but the wrist flexion, wrist extension, wrist abduction and wrist adduction areas. As can be seen by the imposed red circles, regions associated with wrist motion are found in eleven separate areas which range in both size and geometry (Gould, et al. 1986).

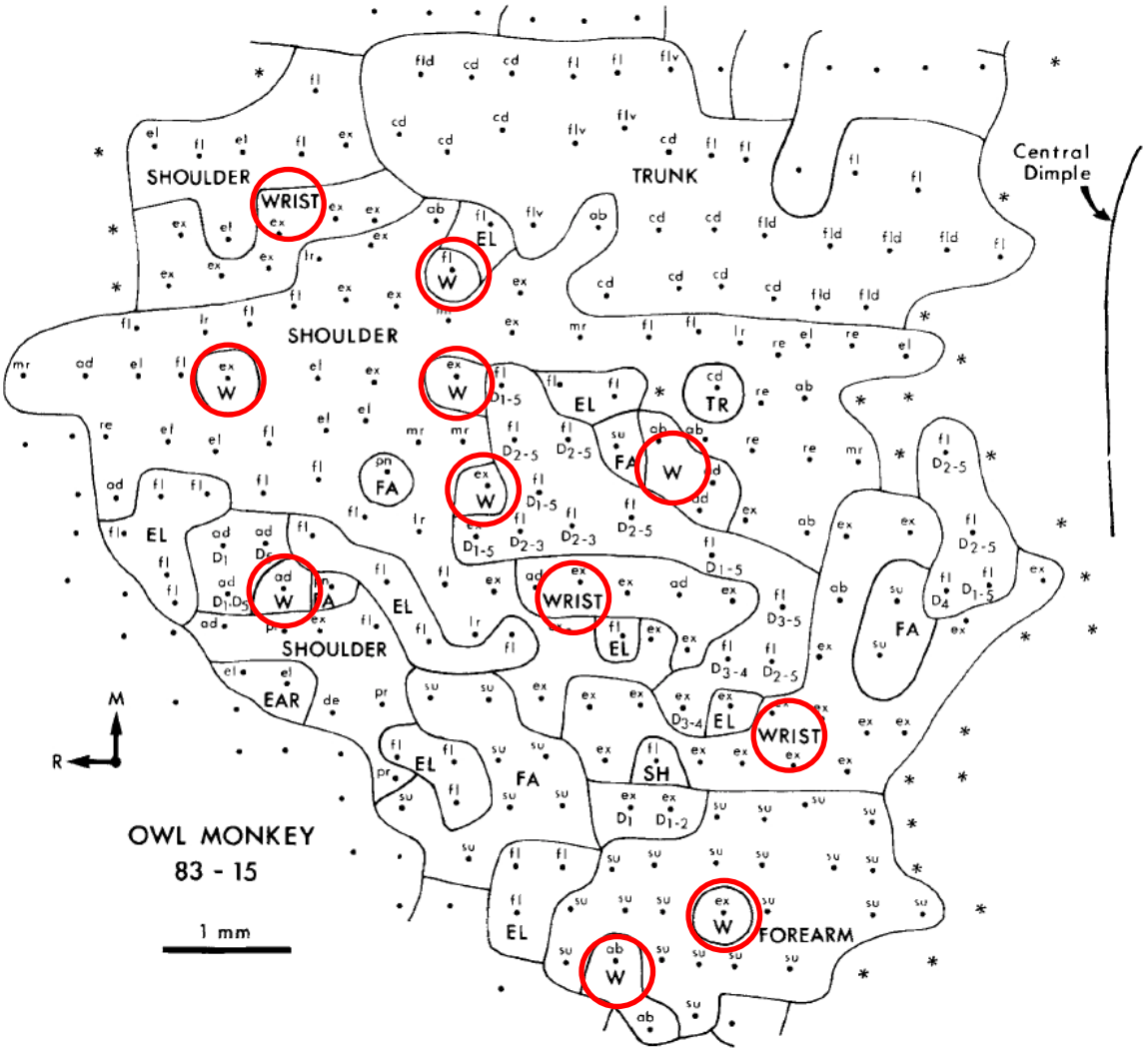


Figure 2. Distribution of upper limb movement location and type during microstimulation of the cortex of the owl monkey. Red circles indicate the eleven separate areas associated with wrist motion. fld = trunk flexion (ventral muscles relaxed; flv = trunk flexion (ventral muscles engaged); D_1 = thumb; D_s-D_5 = digits 2 – digit 5; FA = forearm; EL = elbow; TR = trunk; SH = shoulder; W = wrist. (Gould, et al. 1986)

There is evidence to support cortical region overlap, it is also possible to identify specific somatotopically defined regions within M1 in monkey models

(Asanuma and Rosen 1972) and in humans (Beisteiner, et al. 2001; Dechent and Frahm 2003; Kleinschmidt, et al. 1997; Lotze, et al. 2000; Plow, et al. 2010). Much of the science supporting the presence of a somatotopic distribution of M1 has utilized novel mechanism for either the data acquisition or statistical analysis. Lotze et al (2000) used a 2D-projection reconstruction method and demonstrated differentiated areas of M1 in a group of healthy subjects performing foot, elbow, fist, thumb, index finger, and lip movements. This methodology allowed for normalization of individual variance in the shape and size or the precentral gyrus to an extent beyond that of typical Talairach transformation. Functional data were assessed using a 95% confidence interval band rather than finite activation points and both the center of gravity and activation maxima were used during the initial data analysis. When individual data points were collapsed and all 30 participants combined, a somatopically organized motor cortex emerged with uniquely defined regions for movement of the lips, foot, elbow fist, thumb and index finger. Overlap of the activation areas was present, but within this, a somatotopy was still elucidated. Similarly, Plow et al (2010) used a subtraction method to show the presence of definable cortical regions of M1(2010). Here the authors used high resolution (1.5 mm x 1.5 mm x 1. 5mm) functional magnetic resonance imaging (fMRI) to find cortical activation during a finger, elbow and ankle tracking task. Again, both center of mass and the peak activation area were used during data analysis. This study differed in its design in that a subtraction method was used to isolate specific cortical regions. This was

accomplished by first calculating the percentage of overlapping voxels between the finger and elbow motions. Second, the location of both the center of gravity and the peak area of activation were determined in Talairach space. Finally, the percent signal intensity was found for each condition by comparing the intensity during the tracking task to the intensity during the rest phase. These three components allowed for a subtraction based model to be used. The authors found that, on average, an overlap of 35.10% +/- 15.95% was demonstrated across all subjects. However, localized regions of activation were able to be determined as shown in figure 3 (Plow, et al. 2010).

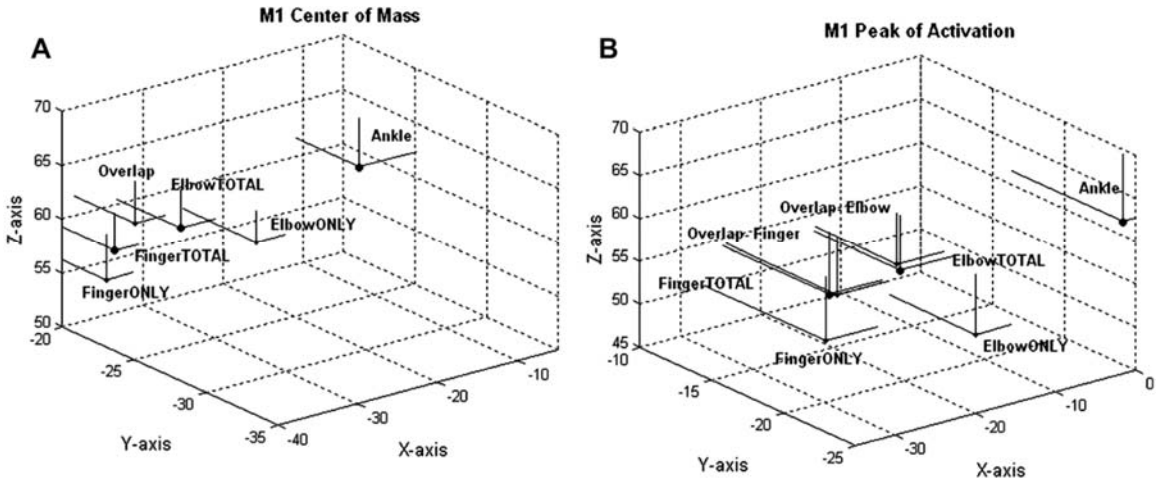


Figure 3. Three-dimensional location of Ankle, Elbow and Finger activation. (A) Center of Mass (COM) locations for each of the 3 unique locations (Ankle, Elbow ONLY, Finger ONLY) plus the COM location of the overlap area of elbow and finger, Elbow TOTAL which includes all Elbow activation regardless of overlap and Finger TOTAL which includes all Finger activation. (B) Peak Activation loci for each of the previously defined areas sans the general overlap area and plus unique areas for Overlap Finger and Overlap Elbow which are defined as the areas with only overlapping activation during the respective tracking task (Plow, et al. 2010).

Mapping of the hand region or of individual finger motion of M1 has proven to be particularly challenging. "Individuation" is a term used to describe the degree to which one cortical location can be correlated to a specific anatomical location. For example, overlapping cortical control of the index (d2) and middle finger (d3) exists; however, the amount to which each finger can be correlated to activation of a specific area of M1 and the dispersion of this activation, addresses the individuation of each finger. The area of M1 associated with hand and finger movements is commonly referred to as the "hand knob" and has been found to be organized with the thumb most lateral and each of the successive fingers progressing medially toward the midline (Grafton, et al. 1993; Kleinschmidt, et al. 1997; Penfield and Rasmussen 1950).

Individuation of individual fingers has been widely investigated with vastly differing results. A number of studies indicate that the somatotopic arrangement of M1, while present, cannot be proven to be more than a gross estimate of actual location. The presiding contention from this vantage is that M1 is defined by a large amount of functional and anatomical overlap. Additionally, M1 and particularly the hand knob, cannot be individuated due to large scale variability between individuals as well as interhemispheric asymmetries both within and between individuals (Nudo, et al. 1992; Poliakov and Schieber 1999; Rao, et al. 1995; Sanes, et al. 1995; Sanes and Schieber 2001; Schieber and Hibbard 1993). This hypothesis is due, in part, to the complex physiology of the hand. One confounding variable associated with many of the studies investigating

activation of unique digits is the likely coactivation of adjacent digits during finger flexion or extension movements in healthy individuals (Watson 2006). The issue of mechanical coupling, defined as related motion of two adjacent fingers due to the anatomical architecture of the hand, was specifically addressed by Lang and Schieber (2004). In this study, both passive and active individuated finger movements were used to examine the mechanical coupling and the central nervous system's role in these movements. The authors concluded that the mechanical coupling of the hand had the greatest impact on limiting the individuation of digits 2, 3 and 4 and placed little limitation on the thumb. Notably, the central nervous system was found to limit the individuation of digits 4 and 5 during large movements. These results indicate a mechanical limit to the amount of individuation of the human digits. From a research perspective, any study designed to report on individual finger activation must account for the mechanical coupling in the research paradigm and/or in the analysis of the subsequent data.

While overlap of cortical activation is known to be present, especially with dexterous motor control such as finger tapping, two additional factors must be considered: 1) the overlap is necessary to allow for more complex movements to be highly coordinated between digits; 2) some level of independence is also present for each area. These two components place a greater focus on the function of the anatomy thus the term 'functional somatotopy' has recently been coined. Much of the evidence for shifting to a functional somatotopy has come from recent studies that have capitalized on improvements to imaging

techniques. Technological improvements have allowed for better viewing of the functional somatotopy within the overlapping activation and include increased spatial resolution and magnetic strength of fMRI studies, more accurate transcranial magnetic stimulation protocols and improvements in the means employed for statistical exploration of the data. As argued by Plow et al. (2010) and support by Dechent and Frahm (2003) perhaps the coarse spatial resolution (2.5 x 2.5 x 8 mm) and weak 1.5 T MRI machine employed by Sanes et al (1995) which resulted in the diffuse and overlapping activation of M1. In contrast, studies using higher spatial resolution (Hlustik, et al. 2001) and stronger magnets (Beisteiner, et al. 2001) have been successful in identifying areas of individuation despite the overlap.

Dechent and Frahm (2003) established a functional somatotopy paradigm with their investigation of individual finger activation of M1 in a 2T MRI. The investigators found significant overlap of individual fingers with direct mapping of 'finger-specific' activation versus rest; however, when a single finger was contrasted against another finger, individuation of each digit was observed. Furthermore, when center of mass coordinates were computed, statistically significantly different locations were isolated for each finger (see figure 4).

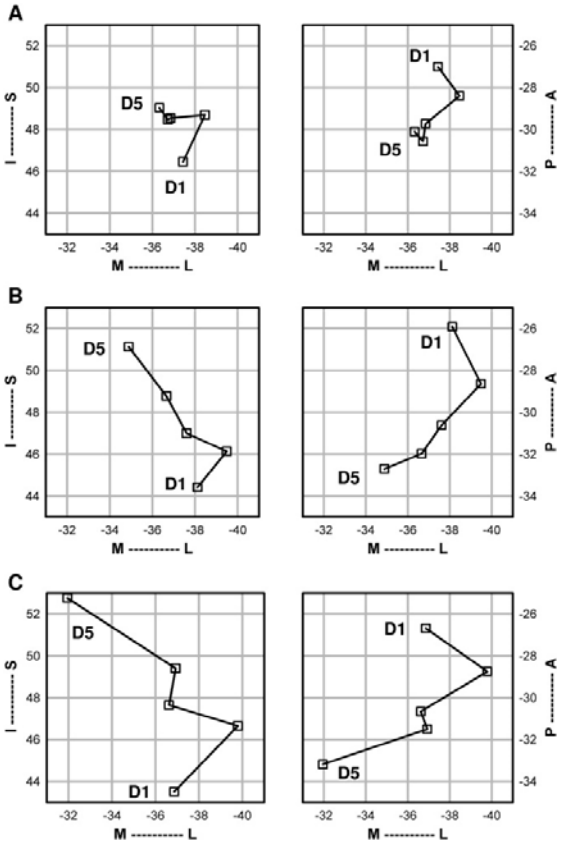


Figure 4. Mean center of mass based Somatotopy of left M1 hand area during use of different examination techniques. Left image were created using a posterior-anterior projection. Right images created with inferior-superior projection. (A) Direct paradigm, (B) differential paradigm using all other digits for contrast, (C) differential paradigm using only the directly neighboring digits. (Dechent and Frahm 2003)

Lateralization of Cortical Motor Control

The interaction between hemispheres during individual hand movements is an important issue in understanding M1 dysfunction in FHD. It is well understood that the primary descending signal from the central nervous system that allows for control of volitional movement originates in the contralateral hemisphere (Jackson 1873/1931). That is, when we want to tap the right index finger, the signal to initiate and later to control the movement comes from the hand knob of M1 on the left side of the brain. This contralateral control is possible because approximately 90% of the neurons responsible for carrying the

descending motor signal cross over from the side on which they originate. 75% of the descending corticospinal neurons decussate in the medulla and approximately 15% more decussate within the spinal cord. In monkeys it has been demonstrated that the remaining 10% of the ipsilateral neurons do not cross at any point but rather innervate the ipsilateral muscles of the shoulder complex (Liu and Chambers 1964; Ralston and Ralston 1985). Brinkman and Kuypers (1973) used macaque monkeys with split brains to demonstrate this phenomenon. In this study the monkeys were presented with a desired food object that could be viewed by only one eye. In that the hemispheres were no longer interconnected, the hemisphere that viewed the target also controlled any subsequent motor manifestations. The movements of both forelimbs were then examined. The “seeing hemisphere” was able to control reaching and grasping of the contralateral arm but only reaching in the ipsilateral arm (Brinkman and Kuypers 1973). This study clearly indicates that most but not all motor control is accomplished contralaterally.

Focal Hand Dystonia

In seminal work that advanced our understanding of dystonia, disorganization of the cortical representation of the sensory cortex was demonstrated using a monkey model (Byl, et al. 1997; Byl, et al. 1996b). Byl et al (1997) had monkeys learn and excessively perform a task requiring articulated, fine motor control of the distal limb. In these animals, some developed clinical

signs of dystonia. It was found that there was disorganization of the sensorimotor map in the subjects with dystonia. These results demonstrated that faulty neuroplastic cortical changes are associated with dystonic symptom development. Interestingly, the maps tended to normalize after monkeys were trained on a task requiring gross, proximal movements.

Indeed, FHD has an increased propensity among people whose occupation requires mastery of a defined set of fine motor skills (Altenmuller 2003; Braun, et al. 2003). It has been hypothesized that the requisite level of sensorimotor control needed by this group of professionals may be linked to one or multiple levels of neuropathology (Byl 2003; Byl 2006; Byl, et al. 1997; Byl, et al. 1996b; Classen 2003; Curra, et al. 1998). Two subtypes of FHD have been established based upon the task that induces the dystonic postures; writers' cramp and musician's dystonia. Highly trained musicians appear to be particularly at risk for dystonia (Altenmuller 2003; Jabusch, et al. 2005; Nutt, et al. 1988; Pullman and Hristova 2005; Schuele and Lederman 2004). Abnormal levels of cortical plasticity are reported in individuals with musician's focal hand dystonia (Byl 2004; Classen 2003; Garraux, et al. 2004; Quartarone, et al. 2008; Quartarone, et al. 2005) as are impairments of inhibition (Bara-Jimenez, et al. 2000; Sohn and Hallett 2004; Tamura, et al. 2008; Tinazzi, et al. 2000). The extent to which these two phenomenon are related is yet unknown.

Bara-Jimenez et al (1998) reported abnormal humuncular organization of the somatosensory cortex in individuals with FHD during a sensory stimulation

task. Results of this study indicated closer cortical representations of the finger in the patient population, as well as a degrading of the medial fifth digit to lateral first digit organization of the normal somotosensory cortex. Of particular note, a correlation was reported between the extent of degraded organization of the digit representation and the motor dysfunction severity.

Individual finger representation has also been studied in subjects with dystonia. In a functional magnetic resonance imaging study utilizing a modified classical guitar neck, Pujol et al (2000) attempted to compare cortical function of dystonic individuals with that of an age and musical experience matched control group. Five individuals with FHD performed exercises designed to reproduce each individual's specific dystonic posture. In the dystonia group, activation of the cortex during tasks performed utilizing the non-affected hand revealed cortical activation similar to that of the control group. However, during tasks performed with the affected hand the contralateral sensorimotor cortex showed increased activation while the premotor cortex revealed a reduction in activation as compared with both the control group and the non-affected hand (Pujol et al., 2000). This study in particular illustrates the cortical changes associated with Focal Task Specific dystonia and the usefulness of fMRI technology in the understanding of these changes.

Summary

FHD has been shown to be associated with a variety of potential pathophysiological changes, but a true understanding of the neurological underpinnings remains unknown. Central to this issue is the need to quantify the cortical organization associated with hand and finger movement in FHD. This may allow for the development of more efficient diagnostic techniques, elucidate mechanisms that address the nature of the disease, and serve as a method for monitoring neural substrates associated with interventions. To this end, this study used fMRI to quantify the cortical activation of the primary motor area during a finger tapping task in healthy individuals. The normative data was then used as a basis for comparison to a group of individuals with focal hand dystonia to establish both hand and finger activation differences during the same finger tapping task.

CHAPTER 2

PURPOSE

There remains controversy regarding the degree of cortical activation that can be associated with an individual finger movement. Measurement of that phenomenon is critical to be able to determine potential differences between the cortical control of finger movement in healthy people and those with focal hand dystonia. The purpose of these experiments were to determine if there were differences in activation based on individual finger movement, then to develop a method of visualizing and quantifying the activation and finally, to compare activation differences based on group.

Aim 1: Quantification of cortical activation during finger tapping in healthy individuals.

In order to render a decision about the abnormality of any patient population a working definition of “normal” must first be established. To this end, part one of this study sought to define the level of selectivity of finger movement in the primary motor cortex within the healthy population during a finger tapping task using a 3 Tesla MRI. In healthy subjects:

Hypothesis 1: Cortical activation associated with individual finger movements is different.

Hypothesis 2: Cortical activation can be quantified during finger tapping according to preferential finger activation relative to the activation associated with other fingers.

Aim 2: Determine the difference in cortical activation during finger tapping between healthy subjects and subjects with dystonia

Once the methodology had been established in the healthy subjects, individuals with FHD were evaluated both at the group and individual level to determine differences from healthy.

Hypothesis 3: Cortical activation related to finger movement will be different between groups.

Hypothesis 4: Subjects with dystonia will demonstrate less selectivity of individual digit activation compared to healthy subjects.

CHAPTER 3

METHODOLOGY

Aim 1: Quantification of cortical activation during finger tapping in healthy individuals.

Subjects

Eight healthy individuals (4 females, means age 30.3 yrs +/- 5.59 yrs) with no history of pathology participated in the study. All inclusion and exclusion criteria (Appendix I) were approved by the Center for Magnetic Resonance Imaging as well as the Internal Review Board of the University of Minnesota (IRB study number 0705M07221). Informed consent was obtained from all participants as described in the IRB.

Procedure

Prior to beginning the fMRI recording, participants were instructed how to perform the finger tapping task and were instructed to practice the task until both the experimenter and the participant were comfortable with the individual's performance. Participants were directly observed to determine if they understood and were able to complete the task.

In the MRI, a visual presentation of the cueing sequence was visualized on a mirror mounted directly in front of the individual's face on the head coil. The mirror reflected an image that was projected (Sony projector with custom lens made by Navitar) onto a screen which was located above the participant's head. The finger tapping task consisted of a self paced, three second, pseudo-

randomly ordered, individuated finger tap. Cues were presented in blocks of 10, where each block consisted of one cue of each of the ten digits. Ten total blocks were presented during each scanning sequence (Figure 5). Presentation of the cues was controlled with Matlab (Mathworks, Inc., Natick, MA) Participants were instructed to self pace their tapping but to continue tapping for the entire duration indicated by the visual stimulus. In order to monitor the movements performed in the MRI, a custom made keyboard device was engineered. This device provided a rigid surface that allowed tactile feedback to the participant about both finger placement and task completion. Any trial resulting in less than 95% accuracy was removed from the analysis.

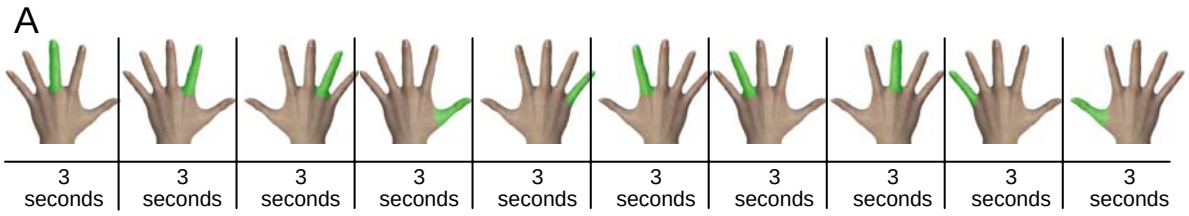


Figure 5. Finger cueing and design matrix. (A) Participants were cued to tap a given finger when the finger was highlighted in green. All 10 digits were cued 10 total times in one scanning sequence. The order of the cueing sequence was randomly determined but all participants perfomed the same randomly ordered task. (B) The resulting experimental design of the finger cueing series. Here 2 cycles of the finger cueing sequence is shown. The white areas represent a tapping cue for the given finger.

MRI

Data collection was done in a 3 Tesla magnet (Magnex Scientific, UK) with a Siemens console (Erlangen, German) and a Siemens Avanto body gradient set. Eco-planar imaging (EPI) data acquisition was accomplished with an eight channel, receiver-only head coil. The visual cue for the finger tapping task changed every 3 seconds and was temporally linked to the 3 second scanning cycle of the MRI. Thus data were collected at a rate of 3 seconds per volume (TR = 3000 ms, TE = 300 ms.). The field of view of the functional scans was centered on areas the pre and post central gyrus with scans directed parallel to the central sulcus (figure 5). Slice orientation was oblique coronal. The focus on a specified cortical area compromised the understanding of the neuronal activity of areas not included in the selected zone; however, the resolution of the cortical activity in the area of interest is improved. Within the indicated area, 36 individual 2.0 mm slices were collected. This allowed for voxel resolution of 2.0 mm x 2.0 mm x 2.0 mm.

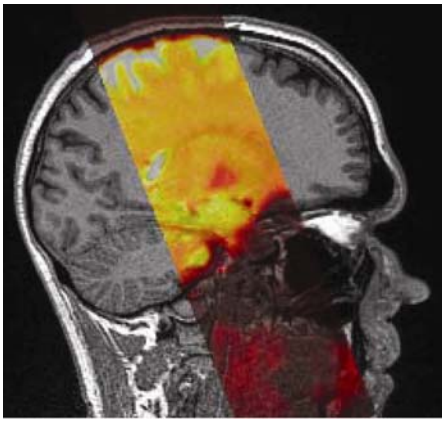


Figure 6. Location and orientation of EPI. Functional scanning sequences were collected at a oblique coronal orientation. Scans were centered on M1 and S1 and aligned parallel to the central sulcus.

Each participant completed a minimum of six scanning sequences; a localizer to allow for positioning, three separate functional EPI sequences, an anatomical scan and a field map. This anatomical scan imaged the entire skull and allowed for alignment of the functional scan data to the participant's brain. The field map sequence was used for motion compensation during one of the analysis techniques. The first two of the EPI scans collected without complication during the previously mentioned finger tapping task were used for initial data analysis. All scanning sequences completed without complication were used in the post hoc analysis.

fMRI data preprocessing

3D motion correction of the EPI, transformation of t1 weighted scans into Talairach space (Talairach and Tournoux 1988) and alignment of the EPI and anatomical data was completed in Brain Voyager QX (Brain Innovation, Maastricht, The Netherlands). Post hoc comparisons of EPI were completed using a separate analysis package. Motion correction of the EPI images for Post hoc analysis was completed using FSL's McFLIRT (www.fmrib.ox.ac.uk/fsl/) followed by a fieldmap-based distortion compensation using FSL. This technique allowed for optimum alignment of the EPI to the anatomical scan in the M1 area of the cortex (figure 7).

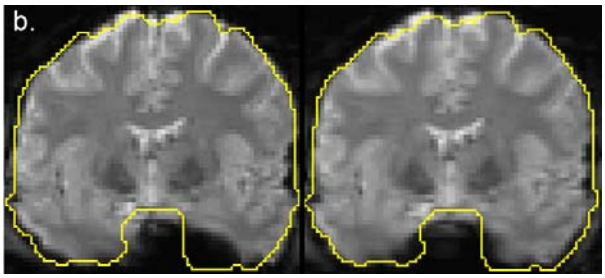


Figure 7. Fieldmap Based Distortion Compensation. EPI image A) before and B) after distortion compensation.

Brain Voyager was used to apply a general linear model (GLM) to the EPI data and account for the hemodynamic response function. A General Linear Model GLM with 16 predictors and a model constant was applied to the data (figure 7). The predictors included all ten digits, X translation (mm), Y translation (mm), Z translation (mm), X rotation (mm), Y rotation (mm) and Z rotation (mm). The data were then exported to Matlab 2009b (Mathworks, Inc., Natick, MA) where a custom made Matlab filter was applied to focus the analysis on voxels in the hand knob area of M1 and the data were reconditioned for analysis in SPSS Statistics 17.0 (© 2010 SPSS Inc., an IBM Company, Chicago, IL).

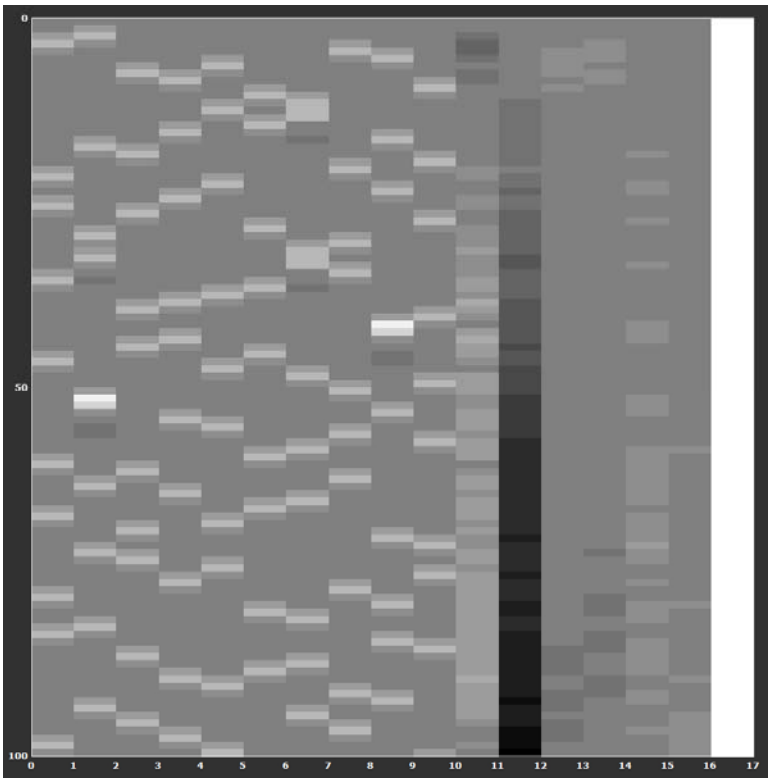


Figure 8. General Linear Model used in data analysis. 16 total model predictors are shown on the x axis with the 10 digits represented in the first 10 columns. 100 total scans are on the y axis. The HRF can be seen in the first 10 column as the dark gray area above and below the light gray cue area.

Statistical analysis

Hypothesis 1: Cortical activation associated with individual finger movements is different.

Group statistical comparisons for main effects were calculated and visualized on the cortical surface in Brain Voyager. Beta weights for all subjects were then exported to SPSS for further analysis. Univariate GLM analysis of variance (ANOVA) with a two-tailed a priori significance threshold of alpha = 0.05 was used to determine significant differences in finger activation within each hemisphere and group.

Hypothesis 2: Cortical activation can be quantified during finger tapping according to preferential finger activation relative to the activation associated with other fingers.

"Winner take all" region of interest

Due to limitations in Brain Voyager's ability to perform a post hoc analysis that allows for exploration of individual voxels at the group level, the entire post hoc comparison was completed outside of Brain Voyager. This phase of the analysis included data from all intact scans with accuracy scores of at least 95% to increase the BOLD response estimation (the application of the 95% accuracy threshold resulted in the removal of 2 scans). The hemodynamic response function was estimated using custom Matlab code (spm_hrf.m, www.fil.ion.ucl.ac.uk/spm/software/spm5). Individual voxel significance was estimated using a 1000 iteration permutation analysis to control for multiple comparisons (Nichols and Holmes 2002). Each significantly modulated voxel was then assigned to a digit based upon a winner-take-all algorithm in which the digit with the highest positive BOLD response "wins" the voxel. All voxels assigned to a particular digit were grouped together and defined as the region of interest (ROI) for that particular digit.

The defined winner-take-all responses were then visualized on flattened cortical patches that were individually cut from the full flattened hemisphere in order to focus on only the primary motor area. Center of mass and activation

area calculations were done on the ROIs at this level. Any ROI cluster with an area of less than 4 mm^2 was excluded from further analysis.

Selectivity

To examine the extent to which any given area was truly associated with only one given finger, a Selectivity Index was calculated. This number compared the BOLD response for the ROI's defining finger to that of the other four fingers of the given hand by assigning a percentage of total activation ratio to each finger. Thus, if all five of the fingers were equally responsible for a voxel's modulation, each digit would have a value of 0.2 and if only one digit related to an individual voxel, that digit would have a value of 1.0 and the other digits would each assume a value of 0.0. The SI was calculated for a given digit (D) as

$$SI_{D/R} = \frac{BOLD_R(D)}{\sum_{d=1}^{5} \left| BOLD_R(d) \right|}$$

Where R is the given ROI for D and BOLD() is the magnitude of the BOLD response during cueing of D. SI's were calculated for each digit both contralaterally and ipsilaterally.

Aim 2: Determine the difference in cortical activation during finger tapping between healthy subjects and subjects with dystonia

Subjects

Nine individuals diagnosed with idiopathic, focal, task specific hand dystonia participated in this component of the study. Due to technical complications with the MRI, data from only 6 of these individuals (3 females, mean age 48.8 yrs, std +/- 9.33 yrs) was able to be used for data analysis. Individuals with FHD had received a differential diagnosis of FHD at least six months prior to participation and had not received a botulinum injection for at least six months (Table 1). All inclusion and exclusion criteria (for a full review of inclusion criteria see appendix I) were approved by the Center for Magnetic Resonance Imaging as well as the Internal Review Board of the University of Minnesota (IRB study number 0705M07221). Informed consent was obtained from all participants as described in the IRB.

Table 1: *Clinical and demographic information and subjective symptom report for subjects with dystonia*

Sex	Age	Preferred Hand	Duration of symptoms	Diagnosis	Symptom report	Botox treatment
M	42	R	14 yr	MD R	2nd/3rd digit spasm during typing and classical guitar playing	No
M	55	L	9 yr	MD L	L 2nd digit flexion playing piano	No
F	55	R	12 yr	WC R	R hand abnormal flexion/tremor during writing/mousing/pinching	No
F	38	R	7 mo	WC R	R hand abnomal posturing during writing	No
F	61	R	25 yr	WC R	R hand abnormal posturing/cramping during writing/carpentry	Yes, 14 yr prior
M	42	R	3 yr	WC R	R hand abnormal posturing/fatigue during writing and typing	Yes, 6 mo prior

Procedure

During the training session, each participant with dystonia was instructed to tap the cued finger for the entire time the cue appeared and to tap at a comfortable rate; however, the frequency at which the individual tapped should, at no time, cause their dystonic symptoms to manifest. These individuals were visually monitored and asked at the completion of each EPI scanning sequence if any symptoms occurred during the scan. Any scan completed with dystonic symptoms present was removed from the final analysis. All additional procedures were the same as the procedures used with the healthy group.

MRI

The same 3T MRI and 8 channel head coil was used for data acquisition as stated above.

Statistical Analysis

Hypothesis 3: Cortical activation related to finger movement will be different between groups.

For this hypothesis, the primary data analysis was identical to that completed for the healthy data set. Statistical comparison of group differences between the healthy participants to those with FHD was completed in SPSS Statistics 17.0. Univariate GLM ANOVA was performed for all variables of interest. Interaction effects were assessed for group and finger by hemisphere.

Hypothesis 4: Subjects with dystonia will demonstrate less selectivity of individual digit activation compared to healthy subjects.

The selectivity index was calculated and used to compare the mean contralateral and ipsilateral selectivity of activation of the defining digit in each ROI. Independent t-tests were conducted.

CHAPTER 4

RESULTS

Aim 1: Quantification of cortical activation during finger tapping in healthy individuals

Hypothesis 1: Cortical activation associated with individual finger movements is different in the healthy population.

In the healthy participants, significant differences in the BOLD signal related to both hand (figure 9) and individual digit were found in Brain Voyager using a multi-subject random effects GLM. Figure 9 shows the strength of the beta weights for contralateral and ipsilateral hemisphere activation at the p < 1.7680e-24 level with a contrast specifying all digits of the right hand as positive and the left hand as negative (Bonferroni corrected, p<0.0001).

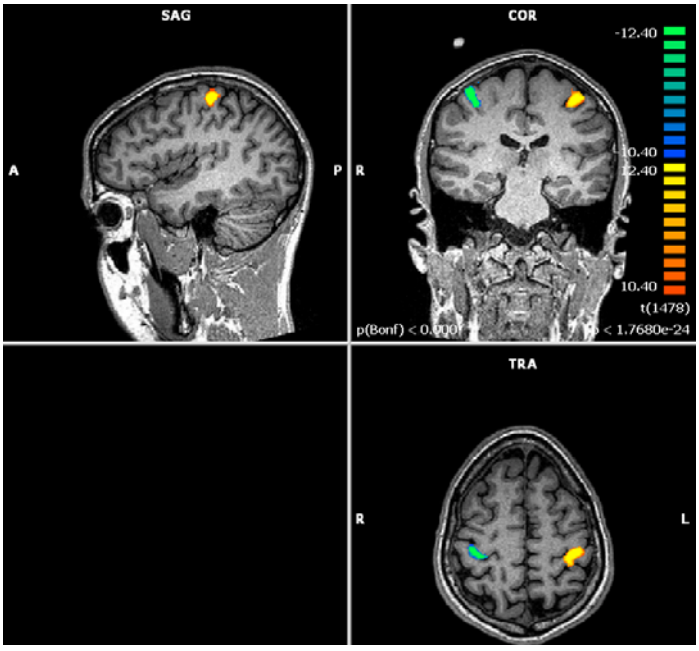


Figure 9. Multisubject analysis of hand activation in healthy subjects. Brain Voyager based visualization of activation uniquely activated during movement of the right hand in all healthy subjects.

GLM indicated a main effect of age ($p < 0.0001$). The effect of age on cortical activation is unknown; therefore it was used as a covariate during subsequent analyses. A univariate within-group GLM analysis revealed a significant main effect of hemisphere, finger, and a hemisphere by finger interaction (Table 2). Further post hoc analysis of the observed differences between the individual digits was then performed as per Hypothesis 2.

Table 2. Group level statistics for comparison of main effect within the healthy population.

Tests of Between-Subjects Effects

Dependent Variable:beta

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	1902.635[a]	20	95.132	57.952	.000
Intercept	1165.809	1	1165.809	710.178	.000
age	1634.622	1	1634.622	995.766	.000
Hemisphere	94.554	1	94.554	57.600	.000
finger	133.175	9	14.797	9.014	.000
Hemisphere * finger	40.604	9	4.512	2.748	.003
Error	121868.789	74239	1.642		
Total	124888.667	74260			
Corrected Total	123771.424	74259			

a. R Squared = .015 (Adjusted R Squared = .015)

Hypothesis 2: Cortical activation can be quantified during finger tapping according to preferential finger activation relative to the activation associated with other fingers.

Post hoc analysis of the beta weight measures for cortical activation using the winner-take-all method described above revealed that distinct cortical regions are preferentially associated with cueing of each digit. The mean number of activated voxels of all healthy participants for each cued digit is shown in figure 10. Cueing of both the right and left thumbs ($D1_R$ and $D1_L$ respectively) resulted in more than two times the volume of significantly modulated voxels. Additionally, strong contralateral activation patterns are clearly depicted as few voxels were assigned to corresponding ipsilateral digits.

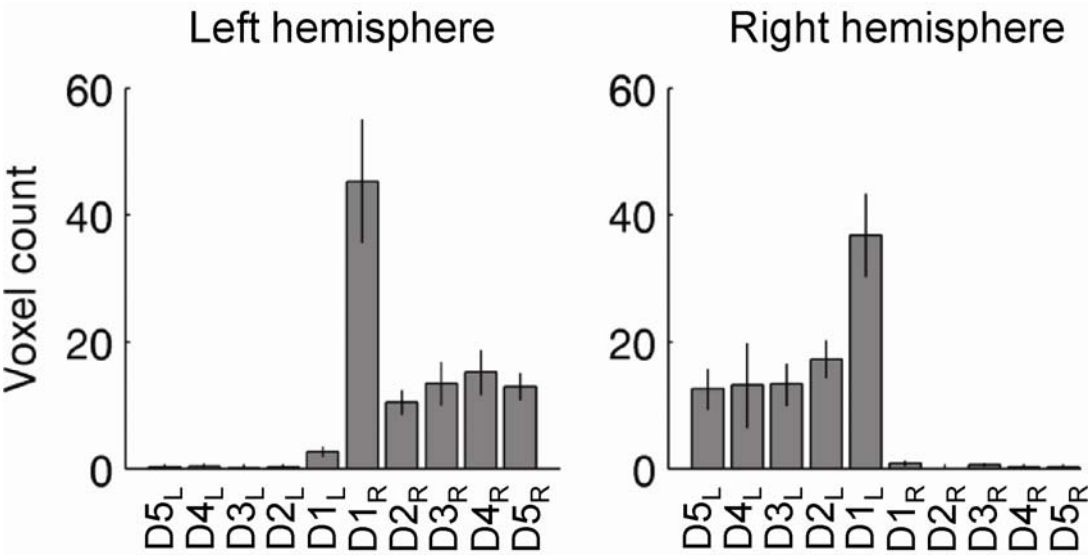


Figure 10. Average number of significantly modulated voxels for each cued digit in healthy subjects. Each bar represents the mean number of voxels assigned to each digit's respective cue for each participant. Both thumbs show more than double the voxel volume as compared to the other eight digits.

The percent change in BOLD response (beta weight) measure for each digit ROI (defined by the finger that displayed the greatest activation) for both the ipsilateral and contralateral activation is shown in figure 11. This figure illustrates the preference for a given finger, but in addition, the relative contribution that defined region activates during the cuing of the non-defining (preferred) digit.

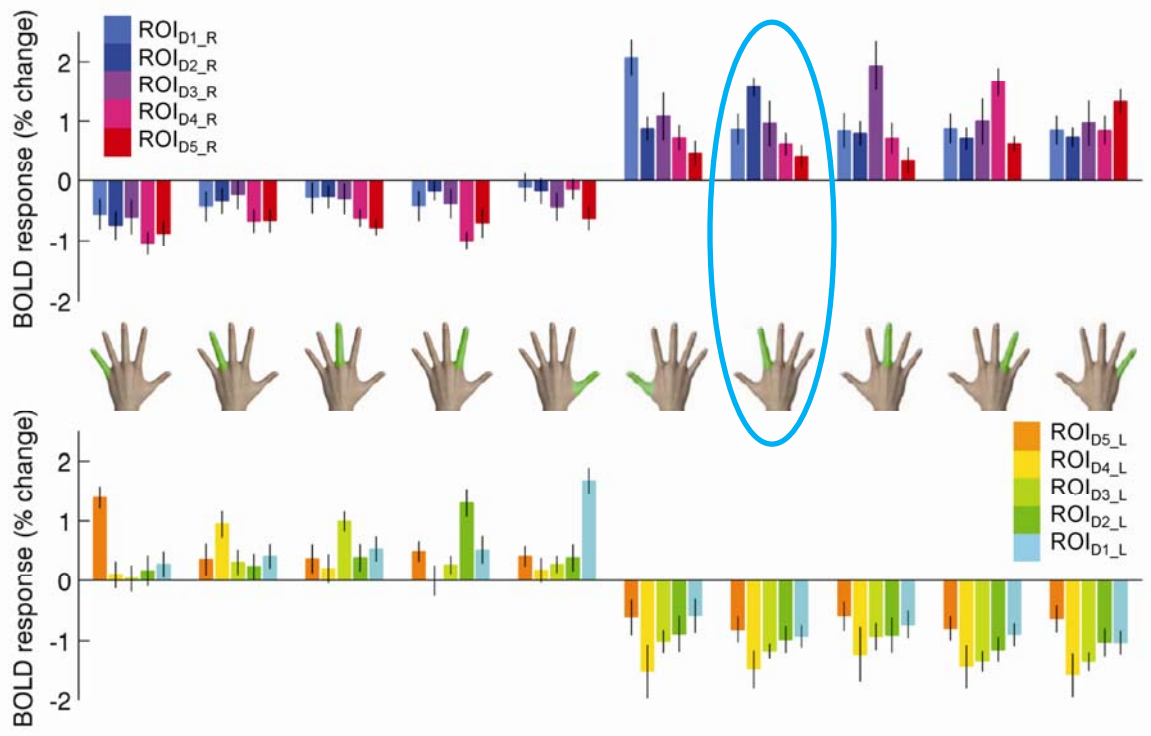


Figure 11. Winner-Take-All ROI clusters for each cue in each hemisphere. Left (top) and right (bottom) hemisphere ROI clusters. Each positive ROI cluster is defined by the winner-take-all method for the cued digit. For example the cluster circled in blue is the ROI_{D2_R} cluster in the left hemisphere. By definition the activation of D2 has the longest bar in the group. The activation of all of the remaining digits of the right hand are shown immediately to the left (D1) and right (D3, D4 and D5).

Selectivity

The mean selectivity index values, reported for the primary digit within each ROI, varied between the right and left hemisphere for the healthy group. Mean selectivity values ± SD were highest in the non-dominant (right) hemisphere (SI=0.57 ± 0.04) and significantly lower in the dominant hemisphere [SI=0.43 ± 0.04 ($t = 2.4749$, $p = 0.0267$)]. For comparison, the selectivity indices for ipsilateral activation of the contralaterally defined ROIs is shown in figure 12b. The ipsilateral selectivity demonstrates the lack of ipsilaterally defined voxels in the hand knob.

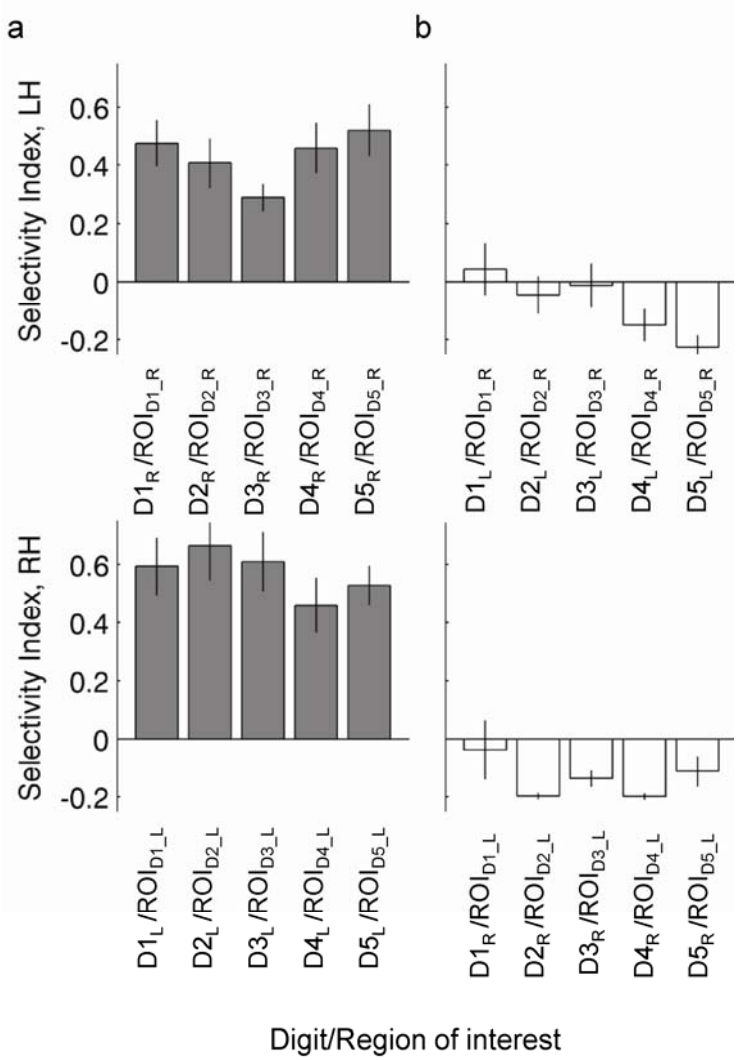


Figure 12. Mean selectivity indexes for the primary digit in each digit ROI in healthy subjects. A) Contralaterally defined digit ROI's for each of the 10 cued fingers. B) Ipsilaterally defined ROI's. The mean right hemisphere selectivity was higher than the left hemisphere (p=0.0267). Suggests variable selectivity across digits and differences between hemispheres.

Aim 2: Determine the difference in cortical activation during finger tapping between healthy subjects and subjects with dystonia

In the dystonic participants, as with the healthy population, significant differences in the BOLD signal related to the cued hand were observed in Brain Voyager (figure 13) using a multi-subject random effects GLM. Figure 13 shows the strength of the beta weights for contralateral and ipsilateral hemisphere

activation at the p < 1.7680e-24 level with a contrast specifying all digits of the right hand as positive and the left hand as negative (Bonferroni corrected, p<0.0001).

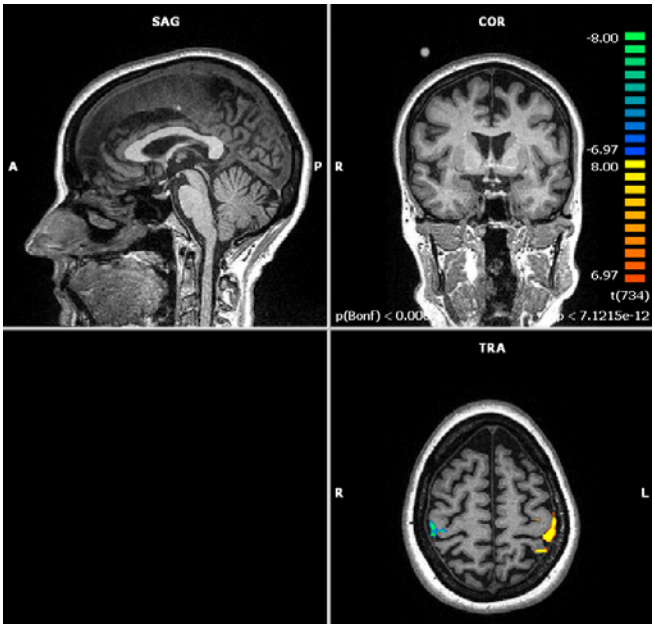


Figure 13. Multisubject analysis of finger activation in subjects with dystonia. Brain Voyager based visualization of activation uniquely activated during movement of the right hand in all subjects with dystonia.

Hypothesis 3: Cortical activation related to finger movement will be different between groups.

Group level analysis revealed significant differences between the healthy and dystonic groups (table 3). Groups were not matched regarding age (p< 0.0001) and the effect of age on brain activation is not fully understood, therefore age was used as a covariate. A 3-way GLM ANOVA examined for finger x group x hemisphere interactions. A significant interaction was found [group x finger x hemisphere (F = 2.114 and p-value < 0.020)] (Table 3). Additional comparisons were performed within each group, within each hemisphere, to determine if there were differences between fingers (table 4).

Table 3. Between group analysis for comparison of FHD and healthy group.

Tests of Between-Subjects Effects

Dependent Variable:beta

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	753.605[a]	40	18.840	10.384	.000
Intercept	55.248	1	55.248	30.451	.000
age	267.832	1	267.832	147.622	.000
group	43.561	1	43.561	24.009	.000
Hemisphere	9.265	1	9.265	5.107	.024
finger	166.115	9	18.457	10.173	.000
group * Hemisphere	81.570	1	81.570	44.959	.000
group * finger	34.516	9	3.835	2.114	.025
Hemisphere * finger	47.250	9	5.250	2.894	.002
group * Hemisphere * finger	35.658	9	3.962	2.184	.020
Error	219276.113	120859	1.814		
Total	222508.735	120900			
Corrected Total	220029.717	120899			

a. R Squared = .003 (Adjusted R Squared = .003)

Table 4. Comparison of Hemisphere by Hand effect between groups.

Group	Hemisphere	Hand	F	p-value
Dystonia	Left	Left	1.24	0.292
Healthy	Left	Left	0.202	0.938
Dystonia	Right	Right	1.333	0.255
Healthy	Right	Right	3.758	0.005
Dystonia	Left	Right	0.418	0.796
Healthy	Left	Right	1.792	0.127
Dystonia	Right	Left	4.116	0.003
Healthy	Right	Left	3.008	0.017

As with the healthy individuals, analysis of the beta weight measures for cortical activation revealed that distinct cortical regions are preferentially associated with cueing of each digit. The mean number of activated voxels for the group with dystonia is illustrated in figure 15. The strong contralateral activation patterns shown in the healthy group are also demonstrated in the FHD group as few voxels were assigned to corresponding ipsilateral digits.

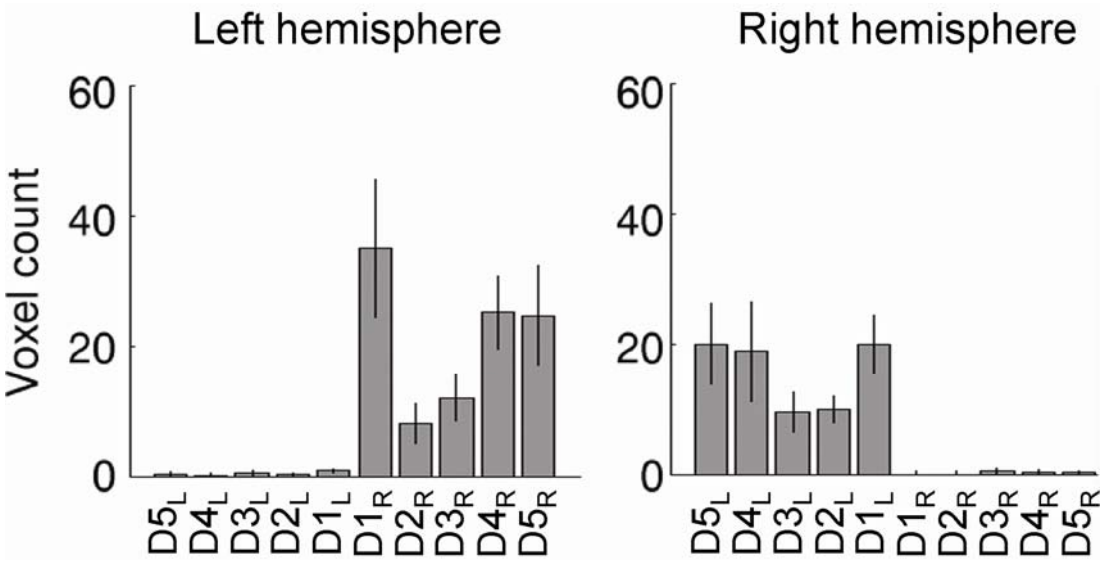
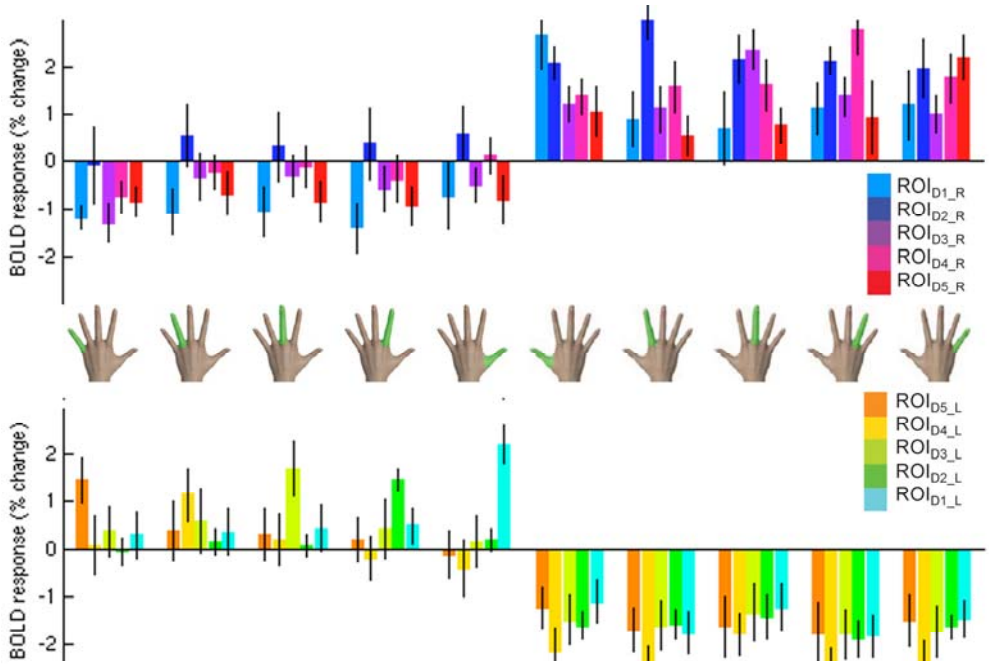


Figure 14. Mean number of significantly modulated voxels for each cued digit in the subjects with dystonia. Each bar represents the mean number of voxels assigned to each digit's respective cue for each dystonic participant via the winner-take-all method. This figure can be compared to figure 11 to illustrate the differences between the healthy and dystonic populations.

The percent change in BOLD response (beta weight) measure for each digit ROI for both the ipsilateral and contralateral activation was also calculated for the subjects with dystonia and is shown in figure 16 with the healthy data repeated for comparison.

A. Dystonia



B. Healthy

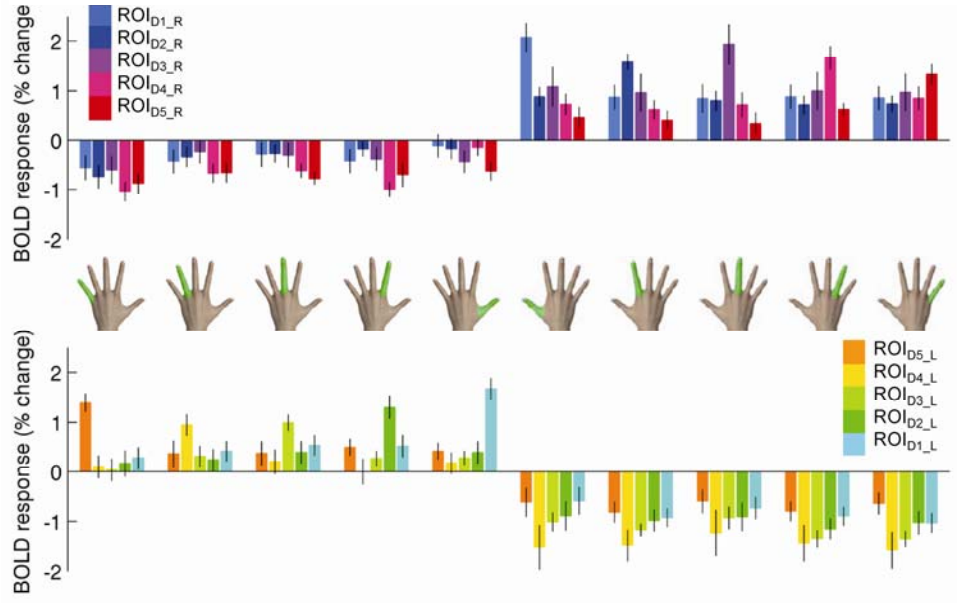


Figure 15. Dystonic (A) and Healthy (B) Winner-Take-All ROI clusters for each cue in each contralateral hemisphere and Ipsilateral activation of contralateral ROI. Left (top) and right (bottom) hemisphere ROI clusters. Each positive ROI cluster is defined by the winner-take-all method for the cued digit.

Hypothesis 4: Subjects with dystonia will demonstrate less selectivity of individual digit activation compared to healthy subjects.

The mean selectivity values ± SD in the non-dominant (right) hemisphere of the dystonia group was SI=0.3515 ± 0.13, which was significantly less than in the healthy group SI=0.57 ± 0.04 (t = 3.5921, p=0.0071). In the dominant (left) hemisphere, the group with dystonia was also significantly lower in mean SI values (healthy: 0.43 ± 0.04, dystonia: 0.346 ± 0.04, t = 3.3204, p=0.0105).

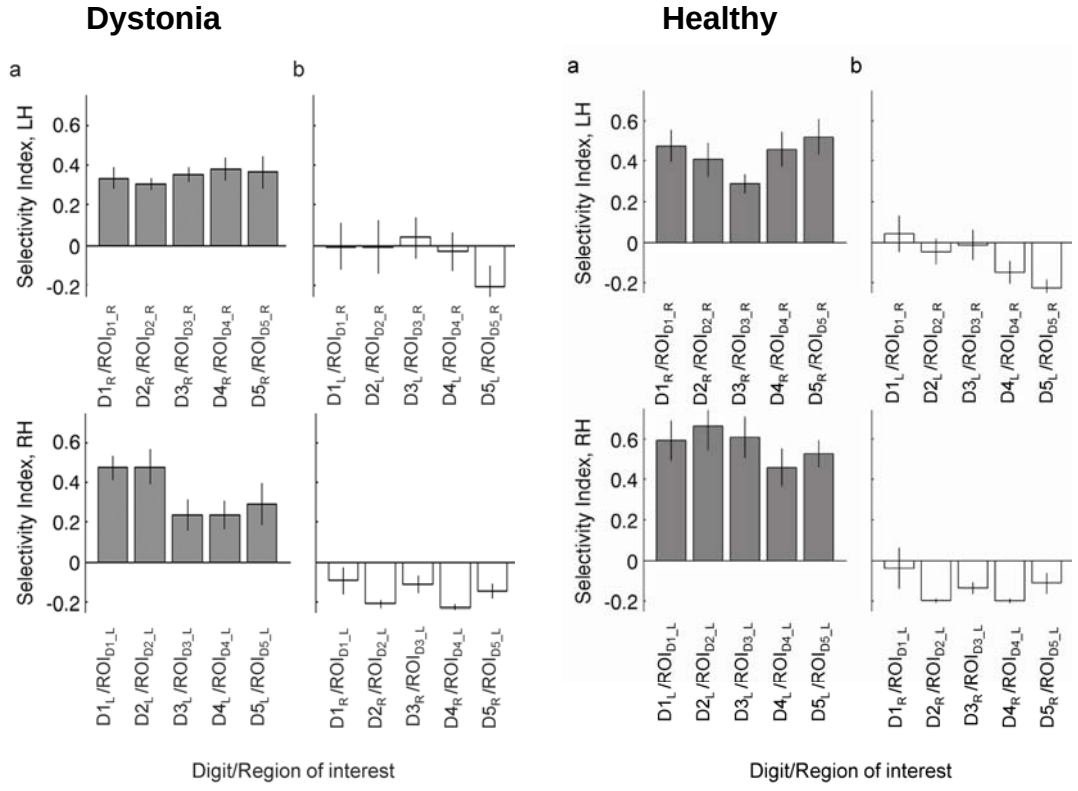


Figure 16. Selectivity Index for both groups, both hemispheres. Selectivity Index in the hemisphere (A) contralateral and (B) ipsilateral to the cued digit for each group; dystonia (left) and healthy (right). The bar graph represents the selectivity index for the digit that defined the ROI. In the left hemisphere, the group with dystonia displays uniform selectivity across ROIs. The dystonia group has significantly lower selectivity in both hemispheres compared to the healthy group. This suggests less “preference” for the defining digit compared to the other digits of the same hand.

Summary

In summary, the significant findings of these data are that cortical activation can be determined and differentiated according to a preference for individual finger movement. This is not demonstrating an exclusive association of given finger movement within a region, but rather a preference. The degree of preference can also be quantified as it relates to the movement of other fingers on either hand. In the comparison between groups, there are significant differences in finger activation between groups. The group with dystonia had significantly less selectivity in both hemispheres compared to healthy subjects.

CHAPTER 5

DISCUSSION

The primary purpose of the initial phase of the study was to define a digit dependent voxel assignment method that would allow for the quantitative measure of regionally defined selectivity in the hand knob of the primary motor cortex. This task has been explored before with various levels of success (Acharya, et al. 2008; Aggarwal, et al. 2008; Aggarwal, et al. 2009; Beisteiner, et al. 2001; Chen, et al. 1997; Dechent and Frahm 2003; Georgopoulos, et al. 1999; Hamed, et al. 2007; Kleinschmidt, et al. 1997; Plow, et al. 2010; Rao, et al. 1995; Sanes, et al. 1995; Schieber 1990; Schieber 1991; Schieber and Hibbard 1993) but to date there has been no method published that allows for the visualization and quantification of the degree to which one cortical area contributes to single digit movement relative to movement of the other digits. To this end, our a priori assumption was not that individual cortical regions were solely associated with movement of a specific digit, but rather our goal was to determine if preferentially defined regions could be identified and measure the extent to which each area was ‘selective.’

This study revealed a measureable difference in the BOLD signal activation between the groups, hemispheres and individual fingers. Thus, we rejected the null hypothesis of no difference in cortical activation between individual finger movements in healthy subjects (Hypothesis 1).

Using the selectivity index for comparison of the BOLD responses within a given ROI to motion of the other four digits on the contralateral hand, we demonstrated a pattern of selectivity in the right hemisphere that was significantly greater than the selectivity measured in the left hemisphere. This finding supported our Hypothesis 2 and suggests that the control of dominant vs. non-dominant hand is associated with a different mechanism of control.

These results support the findings of Dechent and Frahm (2003) and indicate a likely functional somatotopic organization of the primary motor cortex, in which the underlying organization is based more upon motor function than on an anatomically based somatotopic organization. A functional organization would necessitate both a high level of individual finger independence to allow for individual control of the digits as well as an overlapping control of multiple fingers to allow for dexterous control of all of the digits of the hand. The results also support work conducted by Georgopoulos and colleagues (1999) that indicates a distributed population of neurons are responsible for movement of individual joints.

Our findings in Aim 2 demonstrate several differences in cortical activation between subjects with dystonia and healthy subjects, whether evaluated by beta weight (percent change in BOLD signal) or selectivity. The group with dystonia displayed less selectivity, indicating a more distributed control of individual digits. One theory surrounding the causative mechanism of task specific focal hand dystonia relates to deficits of cortical inhibition, maladaptive plasticity and

abnormal sensory and motor processing (Lin and Hallett 2009). The combination of these factors may then lead to abnormal associations between sensory inputs and motor outputs leading to maladaptive plastic changes in the brain. Previous studies have shown that the sensory area of the brain is atypically organized in individuals with focal dystonia (Bara-Jimenez, et al. 1998; Blake, et al. 2002a; Blake, et al. 2002b; Braun, et al. 2003; Byl 2004; Byl, et al. 1997; Hallett 2006a; Lim, et al. 2001; Lin and Hallett 2009)

A much smaller body of literature has addressed changes in the motor cortex (Garraux, et al. 2004; Hallett 2009; Pujol, et al. 2000; Quartarone, et al. 2005). Our findings support this body of work in that the group with dystonia displayed significantly different patterns of cortical activation as compared to the healthy group on multiple levels of comparison including hemisphere and finger. Of particular note is the significant difference in the cortical selectivity displayed by each hemisphere. This finding indicates that not only does the dystonia group have abnormal levels of activation related to cueing or motor control of each finger, they also are not able to individuate or “select” the desired finger to the same extent as healthy individuals. This may account for the hyperactivity observed in adjacent digits by individuals with dystonia during the finger tapping task. Indeed other findings confirm a more global maladaptive control, rather than a problem with only the dystonic muscles. This is supported by reports of widespread impairment of cortical inhibition as measured by transcranial

magnetic stimulation across the sensorimotor system, even in muscles without any symptoms of dystonia (Cakmur, et al. 2004; Quartarone, et al. 2008).

The most significant limitation of the current study is the lack of age matched control subjects and in the case of the musicians, age and experienced matched control subjects. It has been documented in the motor control literature that experience at a given motor task alters the cortical organization of the primary motor cortex (Berlucchi and Buchtel 2009; Buonomano and Merzenich 1998). Additionally, a larger sample size in both the patient and the healthy populations may allow for more robust selectivity mapping results. Finally, an additional exploratory technique that allows for mapping of the cortical activation on the flattened cortical image will be explored in the next round of data processing.

In conclusion, these experiments have shown that cortical activation can be quantified regarding preferential activation for a single digit's movement relative to other digit. A maladaptive pattern of activation has been found in the dystonic patient population for both digits that manifest dystonic postures and for those digits that appear to be unaffected. This result was found in both hemispheres of the patient population. These findings help to elucidate the neuropathophysiological mechanisms in focal dystonia and have application in both clinical and translational dystonia research as will in broader studies of motor control.

CHAPTER 6

BIBLIOGRAPHY

Acharya S, Tenore F, Aggarwal V, Etienne-Cummings R, Schieber MH, Thakor NV. (2008): Decoding individuated finger movements using volume-constrained neuronal ensembles in the M1 hand area. IEEE Trans Neural Syst Rehabil Eng 16(1):15-23.

Aggarwal V, Acharya S, Tenore F, Shin HC, Etienne-Cummings R, Schieber MH, Thakor NV. (2008): Asynchronous decoding of dexterous finger movements using M1 neurons. IEEE Trans Neural Syst Rehabil Eng 16(1):3-14.

Aggarwal V, Tenore F, Acharya S, Schieber MH, Thakor NV. (2009): Cortical decoding of individual finger and wrist kinematics for an upper-limb neuroprosthesis. Conf Proc IEEE Eng Med Biol Soc 2009:4535-8.

Alexander RM. (1992): The human machine. New York: Columbia University Press. 176 p. p.

Altenmuller E. (2003): Focal dystonia: advances in brain imaging and understanding of fine motor control in musicians. Hand Clin 19(3):523-38, xi.

Andersen P, Hagan PJ, Phillips CG, Powell TP. (1975): Mapping by microstimulation of overlapping projections from area 4 to motor units of the baboon's hand. Proc R Soc Lond B Biol Sci 188(1090):31-6.

Asanuma H, Rosen I. (1972): Topographical organization of cortical efferent zones projecting to distal forelimb muscles in the monkey. Exp Brain Res 14(3):243-56.

Bara-Jimenez W, Catalan MJ, Hallett M, Gerloff C. (1998): Abnormal somatosensory homunculus in dystonia of the hand. Ann Neurol 44(5):828-31.

Bara-Jimenez W, Shelton P, Sanger TD, Hallett M. (2000): Sensory discrimination capabilities in patients with focal hand dystonia. Ann Neurol 47(3):377-80.

Baumer T, Demiralay C, Hidding U, Bikmullina R, Helmich RC, Wunderlich S, Rothwell J, Liepert J, Siebner HR, Munchau A. (2007): Abnormal plasticity of the sensorimotor cortex to slow repetitive transcranial magnetic stimulation in patients with writer's cramp. Mov Disord 22(1):81-90.

Beisteiner R, Windischberger C, Lanzenberger R, Edward V, Cunnington R, Erdler M, Gartus A, Streibl B, Moser E, Deecke L. (2001): Finger somatotopy in human motor cortex. Neuroimage 13(6 Pt 1):1016-26.

Berardelli A, Rothwell JC, Hallett M, Thompson PD, Manfredi M, Marsden CD. (1998): The pathophysiology of primary dystonia. Brain 121 (Pt 7):1195-212.

Berlucchi G, Buchtel HA. (2009): Neuronal plasticity: historical roots and evolution of meaning. Exp Brain Res 192(3):307-19.

Blake DT, Byl NN, Cheung S, Bedenbaugh P, Nagarajan S, Lamb M, Merzenich M. (2002a): Sensory representation abnormalities that parallel focal hand dystonia in a primate model. Somatosens Mot Res 19(4):347-57.

Blake DT, Byl NN, Merzenich MM. (2002b): Representation of the hand in the cerebral cortex. Behavioural Brain Research 135(1-2):179-184.

Braun C, Schweizer R, Heinz U, Wiech K, Birbaumer N, Topka H. (2003): Task-specific plasticity of somatosensory cortex in patients with writer's cramp. NeuroImage 20(2):1329-1338.

Brinkman J, Kuypers HG. (1973): Cerebral control of contralateral and ipsilateral arm, hand and finger movements in the split-brain rhesus monkey. Brain 96(4):653-74.

Buonomano DV, Merzenich MM. (1998): Cortical Plasticity: From Synapses to Maps. Annual Review of Neuroscience 21(1):149-186.

Byl N, Wilson F, Merzenich M, Melnick M, Scott P, Oakes A, McKenzie A. (1996a): Sensory dysfunction associated with repetitive strain injuries of tendinitis and focal hand dystonia: a comparative study. J Orthop Sports Phys Ther 23(4):234-44.

Byl NN. (2003): What can we learn from animal models of focal hand dystonia? Rev Neurol (Paris) 159(10 Pt 1):857-73.

Byl NN. (2004): Focal hand dystonia may result from aberrant neuroplasticity. Adv Neurol 94:19-28.

Byl NN. (2006): Aberrant learning in individuals who perform repetitive skilled hand movements: Focal hand dystoniaâ€”Part 1. 10(3):227-247.

Byl NN, McKenzie A, Nagarajan SS. (2000): Differences in somatosensory hand organization in a healthy flutist and a flutist with focal hand dystonia: a case report. J Hand Ther 13(4):302-9.

Byl NN, Merzenich MM, Cheung S, Bedenbaugh P, Nagarajan SS, Jenkins WM. (1997): A primate model for studying focal dystonia and repetitive strain injury: effects on the primary somatosensory cortex. Phys Ther 77(3):269-84.

Byl NN, Merzenich MM, Jenkins WM. (1996b): A primate genesis model of focal dystonia and repetitive strain injury: I. Learning-induced dedifferentiation of the representation of the hand in the primary somatosensory cortex in adult monkeys. Neurology 47(2):508-20.

Cakmur R, Donmez B, Uzunel F, Aydin H, Kesken S. (2004): Evidence of widespread impairment of motor cortical inhibition in focal dystonia: a transcranial magnetic stimulation study in patients with blepharospasm and cervical dystonia. Adv Neurol 94:37-44.

Caramia MD, Iani C, Bernardi G. (1996): Cerebral plasticity after stroke as revealed by ipsilateral responses to magnetic stimulation. Neuroreport 7(11):1756-60.

Chen R, Cohen LG, Hallett M. (1997): Role of the ipsilateral motor cortex in voluntary movement. Can J Neurol Sci 24(4):284-91.

Classen J. (2003): Focal hand dystonia--a disorder of neuroplasticity? Brain 126(Pt 12):2571-2.

Cooke SF, Bliss TV. (2006): Plasticity in the human central nervous system. Brain 129(Pt 7):1659-73.

Curra A, Berardelli A, Rona S, Fabri S, Manfredi M. (1998): Excitability of motor cortex in patients with dystonia. Adv Neurol 78:33-40.

Dechent P, Frahm J. (2003): Functional somatotopy of finger representations in human primary motor cortex. Hum Brain Mapp 18(4):272-83.

Devanne H, Cassim F, Ethier C, Brizzi L, Thevenon A, Capaday C. (2006): The comparable size and overlapping nature of upper limb distal and proximal muscle representations in the human motor cortex. Eur J Neurosci 23(9):2467-76.

Ferrier D. (1874): Experiments on the Brain of Monkeys.--No. I. Proceedings of the Royal Society of London 23:409-430.

Foerster O. (1936): The motor cortex in man in the light of hughlings jackson's doctrines. Brain 59(2):135-159.

Fritsch G, Hitzig E. (1870): Electric excitability of the cerebrum (Uber die elektrische Erregbarkeit des Grosshirns). Epilepsy Behav 15(2):123-30.

Garraux G, Bauer A, Hanakawa T, Wu T, Kansaku K, Hallett M. (2004): Changes in brain anatomy in focal hand dystonia. Ann Neurol 55(5):736-9.

Georgopoulos AP, Pellizzer G, Poliakov AV, Schieber MH. (1999): Neural coding of finger and wrist movements. J Comput Neurosci 6(3):279-88.

Gould HJ, 3rd, Cusick CG, Pons TP, Kaas JH. (1986): The relationship of corpus callosum connections to electrical stimulation maps of motor, supplementary motor, and the frontal eye fields in owl monkeys. J Comp Neurol 247(3):297-325.

Grafton ST, Woods RP, Mazziotta JC. (1993): Within-arm somatotopy in human motor areas determined by positron emission tomography imaging of cerebral blood flow. Exp Brain Res 95(1):172-6.

Hallett M. (2006a): Pathophysiology of dystonia. J Neural Transm Suppl(70):485-8.

Hallett M. (2006b): Pathophysiology of writer's cramp. Hum Mov Sci 25(4-5):454-63.

Hallett M. (2009): Dystonia: a sensory and motor disorder of short latency inhibition. Ann Neurol 66(2):125-7.

Hamed SB, Schieber MH, Pouget A. (2007): Decoding M1 neurons during multiple finger movements. J Neurophysiol 98(1):327-33.

Hlustik P, Solodkin A, Gullapalli RP, Noll DC, Small SL. (2001): Somatotopy in human primary motor and somatosensory hand representations revisited. Cereb Cortex 11(4):312-21.

Hlustik P, Solodkin A, Noll DC, Small SL. (2004): Cortical plasticity during three-week motor skill learning. J Clin Neurophysiol 21(3):180-91.

Jabusch HC, Zschucke D, Schmidt A, Schuele S, Altenmuller E. (2005): Focal dystonia in musicians: treatment strategies and long-term outcome in 144 patients. Mov Disord 20(12):1623-6.

Jackson JH. (1873/1931): On the anatomical and physiological location of movement in the brain. In: J. Taylor, Editor, Selected writings of John Hughlings Jackson. London: Hodder and Stoughton.

Kleinschmidt A, Nitschke MF, Frahm J. (1997): Somatotopy in the human motor cortex hand area. A high-resolution functional MRI study. Eur J Neurosci 9(10):2178-86.

Kopp B, Kunkel A, Muhlnickel W, Villringer K, Taub E, Flor H. (1999): Plasticity in the motor system related to therapy-induced improvement of movement after stroke. Neuroreport 10(4):807-10.

Lang CE, Schieber MH. (2004): Human finger independence: limitations due to passive mechanical coupling versus active neuromuscular control. J Neurophysiol 92(5):2802-10.

Lim VK, Altenmuller E, Bradshaw JL. (2001): Focal dystonia: current theories. Hum Mov Sci 20(6):875-914.

Lin PT, Hallett M. (2009): The Pathophysiology of Focal Hand Dystonia. Journal of Hand Therapy 22(2):109-114.

Liu CN, Chambers WW. (1964): An Experimental Study of the Cortico-Spinal System in the Monkey (Macaca Mulatta). The Spinal Pathways and Preterminal Distribution of Degenerating Fibers Following Discrete

Lesions of the Pre- and Postcentral Gyri and Bulbar Pyramid. J Comp Neurol 123:257-83.

Lotze M, Erb M, Flor H, Huelsmann E, Godde B, Grodd W. (2000): fMRI Evaluation of Somatotopic Representation in Human Primary Motor Cortex. NeuroImage 11(5):473-481.

Nichols TE, Holmes AP. (2002): Nonparametric permutation tests for functional neuroimaging: a primer with examples. Hum Brain Mapp 15(1):1-25.

Nudo R, Jenkins W, Merzenich M, Prejean T, Grenda R. (1992): Neurophysiological correlates of hand preference in primary motor cortex of adult squirrel monkeys. J. Neurosci. 12(8):2918-2947.

Nutt JG, Muenter MD, Melton LJ, 3rd, Aronson A, Kurland LT. (1988): Epidemiology of dystonia in Rochester, Minnesota. Adv Neurol 50:361-5.

Peller M, Zeuner KE, Munchau A, Quartarone A, Weiss M, Knutzen A, Hallett M, Deuschl G, Siebner HR. (2006): The basal ganglia are hyperactive during the discrimination of tactile stimuli in writer's cramp. Brain 129(Pt 10):2697-708.

Penfield W, Boldrey E. (1937): Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain 60(4):389-443.

Penfield W, Rasmussen T. (1950): The cerebral cortex of man; a clinical study of localization of function. New York,: Macmillan. xv, 248 p. p.

Plow B, Arora P, Pline MA, Binenstock MT, Carey JR. (2010): Within-limb somatotopy in primary motor cortex - revealed using fMRI. Cortex 46(3):310-321.

Poliakov AV, Schieber MH. (1999): Limited functional grouping of neurons in the motor cortex hand area during individuated finger movements: A cluster analysis. J Neurophysiol 82(6):3488-505.

Pujol J, Roset-Llobet J, Rosines-Cubells D, Deus J, Narberhaus B, Valls-Sole J, Capdevila A, Pascual-Leone A. (2000): Brain cortical activation during guitar-induced hand dystonia studied by functional MRI. Neuroimage 12(3):257-67.

Pullman SL, Hristova AH. (2005): Musician's dystonia. Neurology 64(2):186-7.

Quartarone A, Morgante F, Sant'angelo A, Rizzo V, Bagnato S, Terranova C, Siebner HR, Berardelli A, Girlanda P. (2008): Abnormal plasticity of sensorimotor circuits extends beyond the affected body part in focal dystonia. J Neurol Neurosurg Psychiatry 79(9):985-90.

Quartarone A, Rizzo V, Bagnato S, Morgante F, Sant'Angelo A, Romano M, Crupi D, Girlanda P, Rothwell JC, Siebner HR. (2005): Homeostatic-like plasticity of the primary motor hand area is impaired in focal hand dystonia. Brain 128(8):1943-1950.

Ralston DD, Ralston HJ, 3rd. (1985): The terminations of corticospinal tract axons in the macaque monkey. J Comp Neurol 242(3):325-37.

Rao SM, Binder JR, Hammeke TA, Bandettini PA, Bobholz JA, Frost JA, Myklebust BM, Jacobson RD, Hyde JS. (1995): Somatotopic mapping of the human primary motor cortex with functional magnetic resonance imaging. Neurology 45(5):919-24.

Rona S, Berardelli A, Vacca L, Inghilleri M, Manfredi M. (1998): Alterations of motor cortical inhibition in patients with dystonia. Mov Disord 13(1):118-24.

Sanes JN, Donoghue JP, Thangaraj V, Edelman RR, Warach S. (1995): Shared neural substrates controlling hand movements in human motor cortex. Science 268(5218):1775-7.

Sanes JN, Schieber MH. (2001): Orderly somatotopy in primary motor cortex: does it exist? NeuroImage 13(6 Pt 1):968-74.

Sato KC, Tanji J. (1989): Digit-muscle responses evoked from multiple intracortical foci in monkey precentral motor cortex. J Neurophysiol 62(4):959-70.

Schieber MH. (1990): How might the motor cortex individuate movements? Trends Neurosci 13(11):440-5.

Schieber MH. (1991): Individuated finger movements of rhesus monkeys: a means of quantifying the independence of the digits. J Neurophysiol 65(6):1381-91.

Schieber MH. (1999): Rethinking the motor cortex. Neurology 52(3):445-6.

Schieber MH. (2001): Constraints on somatotopic organization in the primary motor cortex. J Neurophysiol 86(5):2125-43.

Schieber MH, Hibbard LS. (1993): How somatotopic is the motor cortex hand area? Science 261(5120):489-92.

Schuele S, Lederman RJ. (2004): Long-term outcome of focal dystonia in string instrumentalists. Mov Disord 19(1):43-8.

Sheehy MP, Marsden CD. (1982): Writers' cramp-a focal dystonia. Brain 105 (Pt 3):461-80.

Sohn YH, Hallett M. (2004): Disturbed surround inhibition in focal hand dystonia. Ann Neurol 56(4):595-9.

Talairach J, Tournoux P. (1988): Co-planar stereotaxic atlas of the human brain : 3-dimensional proportional system : an approach to medical cerebral imaging. Stuttgart ; New York, New York: G. Thieme ; Thieme Medical Publishers. viii, 122 p. p.

Tamura Y, Matsuhashi M, Lin P, Ou B, Vorbach S, Kakigi R, Hallett M. (2008): Impaired intracortical inhibition in the primary somatosensory cortex in focal hand dystonia. Mov Disord 23(4):558-65.

Tinazzi M, Priori A, Bertolasi L, Frasson E, Mauguiere F, Fiaschi A. (2000): Abnormal central integration of a dual somatosensory input in dystonia. Evidence for sensory overflow. Brain 123 (Pt 1):42-50.

Watson AH. (2006): What can studying musicians tell us about motor control of the hand? J Anat 208(4):527-42.

Appendix I

Inclusion Criteria

General Inclusion Criteria:

- Male or Female subjects, 30 to 65 years of age.
- No other preexisting neurological or orthopedic diagnosis.
- Full range of motion of both upper extremities.

Patient Group Inclusion Criteria (all of the above criteria must be met in addition to the following):

- Idiopathic focal hand dystonia
- Symptomatic for no less than 2 years
- No dystonia medicaiton
- No botulinum toxin in previous 4 months

Exclusion:

- Females who are pregnant, breast-feeding, or planning a pregnancy during the study or who think that they may be pregnant at the start of the study.
- Any non-titanium metal in body.
- Pacemaker, shrapnel, indwelling pump, clips, cholear implant, or other non-compatible metal
- Known, uncontrolled systemic disease.
- Known neurologic and psychiatric disorders.
- Any condition or situation that, in the investigator's opinion, may put the subject at significant risk, confound the study results, or interfere significantly with the subject's participation in the study.
- Claustrophobia

Appendix II

Cortical mapping of sensory and motor areas in healthy individuals and individuals with focal hand dystonia during a finger tapping task.

You are invited to be in a research study involving brain imaging and sequential finger tapping. You were selected as a possible participant for this study because (1) you are between the ages of 30 and 65 years of age, (2) you have been affected by focal hand dystonia for at least two years and (3) you have no history of any associated neural or muscular deficits in your affected hands. Please read this form and ask any questions you may have before agreeing to be in this study.

Introduction

This study is being conducted by Teresa Kimberley PhD, PT in the Program in Physical Therapy and Cheryl Olman, PhD, from the Department of Psychology at the University of Minnesota. The purpose of this study is to determine how dystonia affects the brain when performing and sensing movement. We are also doing this work with healthy people in order to compare your results to those of someone your same age and gender that has not been diagnosed with dystonia. The information gained from this study may be helpful in developing future treatment approaches as well as gaining a better understanding of the role brain organization plays in dystonia.

Procedures

If you agree to participate in this study, we will ask you to do the following:

Answer questions about your medical history and current health.

Complete a battery of tests assessing your proprioceptive sensitivity (awareness of your limbs in space relative to your own body), motor ability and your sensory ability.

While lying down in a functional magnetic resonance imaging (fMRI) machine, you will perform a battery of tasks involving active movements of your fingers. There will be a screen visible while you are inside the fMRI and this screen will prompt you to perform the selected movement. The entire fMRI portion of the experiment will last approximately 45 minutes. You will be in contact with the researchers throughout this time.

The MRI is a technique used to look at the brain and is commonly used in hospitals and clinics. During the MRI scan, a strong magnet makes the

hydrogen atoms in your body send out a signal. This signal is received by a coil around your head and sends a picture of your brain to the computer. The computer pictures show which parts of your brain were active when the scan was performed. You will hear loud noises during the scanning, but will be given earplugs and headphones to dampen the sound. The FDA has approved the magnetic strength (3 Tesla) of this device; however, the long-term risks of this strength are not yet known. This procedure will last approximately 45 minutes.

During the scan and while in the device, you will be able to communicate with the researchers and leave the scanner at any time if you wish.

Risks and Benefits

Most people do not experience any ill effects from the large magnetic field, but some people do report dizziness, mild nausea, headache, a metallic taste in their mouth, or a sensation of flashing lights. These symptoms, if present, subside shortly after leaving the magnet. No serious ill effects have been reported to date at any site operating at this magnetic field strength, which is twice the strength of typical hospital MRIs. However, there could be adverse effects that we do not yet know about.

If you have had any surgeries or have any metal implants such as aortic valve replacements, joint implants, metal sutures, or a cardiac pacemaker, we need to know about them as it may not be safe for you to go into the MRI. Also, if you are pregnant or could be pregnant you should not participate in the MRI. During the MRI, you will be in a semi-enclosed, dark area for about one hour. This may not be a suitable environment for a person who has experienced bouts of claustrophobia.

There is no known benefit directly to you for your participation in this study; however, we hope to gain important information to aid the development of future treatments as well as a better understanding of how the brain is affected by dystonia.

Costs

You will not receive payment for participating in this study. Parking will be provided at the testing session. You will not be charged for any tests. The University of Minnesota Physical Therapy Department or the Center for Magnetic Resonance Research will be paying for the MRI.

Research Related Injury

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury, please let the researchers know right away.

Confidentiality

The records of this study will be kept private. In any reports that are produced, we will not include any information that will make it possible to identify you as a subject.

Voluntary Nature of the Study

Your decision whether or not to participate will not affect your current or future relations with the University of Minnesota. If you decide to participate, you are free to withdraw at any time without affecting those relationships.

Contacts and Questions

You may ask any questions you have now. If you have questions later, you may call Teresa Kimberley (612) 626-4096.

If you have any questions or concerns regarding the study and would like to talk to someone other than the researcher(s), contact the Helpline at telephone number 612-672-7692 or toll free at 866-508-6961. You may also contact this office in writing or in person at University of Minnesota Medical Center, Fairview-Riverside Campus, #815 Professional Building, 2200 Riverside Avenue, Minneapolis, MN 55454. You will be given a copy of this form to keep for your records.

Statement of Consent

I have read the above information. I have asked questions and have received answers. I consent to participate in this study.

Print Name_____

Signature_____

Date_____

Signature of Investigator_____

Date_____

Appendix III

Name:_____ Date:_____ DOB: _____ (mm/dd/yy) Weight: ____lbs

For staff only:		
Session #:	IRB #:	Operator #:

CMRR Safety Screening Form

1. Do you have a problem with claustrophobia (fear of closed spaces?)
   No_____ A little _____ Pretty much _____ Severe _____

2. Do you have a heart pacemaker or defibrillator or other implanted devices?
   No _____ Yes _____

3. Have you ever had an operation? If yes, Investigator to fill out Page 2.
   No _____ Yes _____

4. Have you ever been injured by metallic foreign body which was not removed?
   No _____ Yes _____

5. Do you wear braces on your teeth? Do you have removable bridgework or false teeth?
   No _____ Yes _____

6. Do you have any tattoos or unremovable body piercings? If so, indicate where.
   No _____ Yes _____

7. Do you wear a hearing aid? If yes, it will need to be removed for the scan.
   No _____ Yes _____

8. (Females only): *It is recommended that you not wear underwire bras for the scanning session, due to possible discomfort when the metal is attracted by the field, and a small risk of heating in the wire.*
   Do you have any reason to believe that you are pregnant? No _____ Yes _____
   Are you currently using (wearing) an IUD or diaphragm? No _____ Yes _____

9. Please list medications you took today or are taking regularly.
   (try to include the name of the medicine, dose, how often, and time of last dose).

10. Have you ever had any previous studies (MRI, CT or other)? If yes circle on list.
    No _____ Yes _____

11. Do you have a breathing disorder or movement disorder? If yes describe.
    No _____ Yes _____

_____ Date:_____/_____/_____
Signature of Person Completing Page 1

Investigator to complete if Item #3 on Page 1 is Yes.

Some of the following items may be hazardous to your safety and some can interfere with the MRI examination. Please check the correct answer for each of the following. Do you have any of the following:

☐ Yes ☐ No	Cardiac pacemaker
☐ Yes ☐ No	Implanted cardiac defibrillator
☐ Yes ☐ No	Carotid artery vascular clamp
☐ Yes ☐ No	Intravascular stents, filters, or coils
☐ Yes ☐ No	Aortic clip
☐ Yes ☐ No	Internal pacing wires
☐ Yes ☐ No	Vascular access port and/or catheter
☐ Yes ☐ No	Swan-Ganz catheter
☐ Yes ☐ No	Shunt (spinal or intraventricular)
☐ Yes ☐ No	Aneurysm clip(s)
☐ Yes ☐ No	Neurostimulator
☐ Yes ☐ No	Electrodes (on body, head, or brain)
☐ Yes ☐ No	Heart valve prosthesis
☐ Yes ☐ No	Any type of prosthesis (eye, penile, etc.)
☐ Yes ☐ No	Artificial limb or joint replacement
☐ Yes ☐ No	Bone growth/fusion stimulator
☐ Yes ☐ No	Bone/joint pin, screw, nail, wire, plate
☐ Yes ☐ No	Metal rods in bones
☐ Yes ☐ No	Harrington rods (spine)
☐ Yes ☐ No	Metal or wire mesh implants
☐ Yes ☐ No	Wire sutures or surgical staples
☐ Yes ☐ No	Insulin pump or infusion device
☐ Yes ☐ No	Transdermal delivery system (Birth Control/Nicotine/Nitro)
☐ Yes ☐ No	Any implant held in place by a magnet
☐ Yes ☐ No	Cochlear, otologic, or ear implant

NOTE: YOU ARE REQUIRED TO WEAR EARPLUGS OR EARPHONES DURING THE MRI EXAMINATION.

_____ Date:_____/_____/_____

Signature of Investigator Completing Page 2

Appendix IV - SPSS output for hand by hemisphere by group

Appendix V

```
UNIANOVA beta BY finger WITH age
  /METHOD=SSTYPE(3)
  /INTERCEPT=INCLUDE
  /PLOT=PROFILE(finger)
  /CRITERIA=ALPHA(0.05)
  /DESIGN=age finger.
```

Univariate Analysis of Variance
- finger x contralateral hemisphere

[DataSet1] G:\06252010_beta weights for final ana.sav

group = Dystonia

Between-Subjects Factors[a]

		N
finger	1	452
	2	536
	3	567
	4	519
	5	524

a. group = Dystonia

Tests of Between-Subjects Effects[b]

Dependent Variable:beta

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	54.525[a]	5	10.905	15.888	.000
Intercept	229.156	1	229.156	333.877	.000
age	42.956	1	42.956	62.586	.000
finger	11.211	4	2.803	4.083	.003
Error	1779.020	2592	.686		
Total	4697.509	2598			
Corrected Total	1833.546	2597			

a. R Squared = .030 (Adjusted R Squared = .028)

b. group = Dystonia

Profile Plots

Appendix IV

```
USE ALL.
COMPUTE filter_$=(trial = 2 & group = 0 & Hemisphere = 0).
VARIABLE LABEL filter_$ 'trial = 2 & group = 0 & Hemisphere = 0 (FILTER
)'.
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.
T-TEST GROUPS=hand(0 1)
  /MISSING=ANALYSIS
  /VARIABLES=beta
  /CRITERIA=CI(.95).
```

T-Test

[DataSet1] G:\06252010_beta weights for final ana.sav

group = Dystonia

Group Statistics[a]

67

	hand	N	Mean	Std. Deviation	Std. Error Mean
beta	right	5820	-.256874490	1.35571339E0	.0177707761
	left	5820	-.159977304	1.38739510E0	.0181860619

a. group = Dystonia

Independent Samples Test[a]

		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.	t	df
beta	Equal variances assumed	3.337	.068	-3.811	11638
	Equal variances not assumed			-3.811	11631.795

a. group = Dystonia

Appendix IV

Independent Samples Test[a]

		t-test for Equality of Means		
		Sig. (2-tailed)	Mean Difference	Std. Error Difference
beta	Equal variances assumed	.000	-.0968971865	.0254270197
	Equal variances not assumed	.000	-.0968971865	.0254270197

a. group = Dystonia

Independent Samples Test[a]

		t-test for Equality of Means	
		95% Confidence Interval of the Difference	
		Lower	Upper
beta	Equal variances assumed	-.1467384129	-.0470559600
	Equal variances not assumed	-.1467384157	-.0470559572

a. group = Dystonia

```
USE ALL.
COMPUTE filter_$=(trial = 2 & group = 0 & Hemisphere = 1).
VARIABLE LABEL filter_$ 'trial = 2 & group = 0 & Hemisphere = 1 (FILTER
)'.
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.
T-TEST GROUPS=hand(0 1)
  /MISSING=ANALYSIS
  /VARIABLES=beta
  /CRITERIA=CI(.95).
```

T-Test

```
[DataSet1] G:\06252010_beta weights for final ana.sav
```

group = Dystonia

Appendix IV

Group Statistics[a]

	hand	N	Mean	Std. Deviation	Std. Error Mean
beta	right	5840	-.140909107	1.39196753E0	.0182147277
	left	5840	-.132651412	1.43751051E0	.0188106848

a. group = Dystonia

Independent Samples Test[a]

		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.	t	df
beta	Equal variances assumed	6.600	.010	-.315	11678
	Equal variances not assumed			-.315	11665.917

a. group = Dystonia

Independent Samples Test[a]

		t-test for Equality of Means		
		Sig. (2-tailed)	Mean Difference	Std. Error Difference
beta	Equal variances assumed	.752	-.0082576944	.0261843115
	Equal variances not assumed	.752	-.0082576944	.0261843115

a. group = Dystonia

Independent Samples Test[a]

		t-test for Equality of Means	
		95% Confidence Interval of the Difference	
		Lower	Upper
beta	Equal variances assumed	-.0595833215	.0430679327
	Equal variances not assumed	-.0595833271	.0430679382

a. group = Dystonia

```
USE ALL.
COMPUTE filter_$=(trial = 2 & group = 1 & Hemisphere = 0).
```

Appendix IV

```
VARIABLE LABEL filter_$ 'trial = 2 & group = 1 & Hemisphere = 0 (FILTER
)'.
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.
T-TEST GROUPS=hand(0 1)
  /MISSING=ANALYSIS
  /VARIABLES=beta
  /CRITERIA=CI(.95).
```

T-Test

```
[DataSet1] G:\06252010_beta weights for final ana.sav
```

group = Healthy

Group Statistics[a]

	hand	N	Mean	Std. Deviation	Std. Error Mean
beta	right	9245	-.180805617	1.24836238E0	.0129833635
	left	9245	-.147189700	1.27827352E0	.0132944489

a. group = Healthy

Independent Samples Test[a]

		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.	t	df
beta	Equal variances assumed	1.967	.161	-1.809	18488
	Equal variances not assumed			-1.809	18477.645

a. group = Healthy

Appendix IV

Independent Samples Test[a]

		t-test for Equality of Means		
		Sig. (2-tailed)	Mean Difference	Std. Error Difference
beta	Equal variances assumed	.070	-.0336159179	.0185825213
	Equal variances not assumed	.070	-.0336159179	.0185825213

a. group = Healthy

Independent Samples Test[a]

		t-test for Equality of Means	
		95% Confidence Interval of the Difference	
		Lower	Upper
beta	Equal variances assumed	-.0700393749	.0028075391
	Equal variances not assumed	-.0700393763	.0028075404

a. group = Healthy

```
USE ALL.
COMPUTE filter_$=(trial = 2 & group = 1 & Hemisphere = 1).
VARIABLE LABEL filter_$ 'trial = 2 & group = 1 & Hemisphere = 1 (FILTER
)'.
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.
T-TEST GROUPS=hand(0 1)
  /MISSING=ANALYSIS
  /VARIABLES=beta
  /CRITERIA=CI(.95).
```

T-Test

```
[DataSet1] G:\06252010_beta weights for final ana.sav
```

group = Healthy

Appendix IV

Group Statistics[a]

	hand	N	Mean	Std. Deviation	Std. Error Mean
beta	right	9320	-.155628442	1.24378658E0	.0128836201
	left	9320	-.179397013	1.25661960E0	.0130165495

a. group = Healthy

Independent Samples Test[a]

		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.	t	df
beta	Equal variances assumed	3.193	.074	1.298	18638
	Equal variances not assumed			1.298	18636.037

a. group = Healthy

Independent Samples Test[a]

		t-test for Equality of Means		
		Sig. (2-tailed)	Mean Difference	Std. Error Difference
beta	Equal variances assumed	.194	.0237685715	.0183144268
	Equal variances not assumed	.194	.0237685715	.0183144268

a. group = Healthy

Independent Samples Test[a]

		t-test for Equality of Means	
		95% Confidence Interval of the Difference	
		Lower	Upper
beta	Equal variances assumed	-.0121293767	.0596665197
	Equal variances not assumed	-.0121293769	.0596665200

a. group = Healthy

```
USE ALL.
COMPUTE filter_$=(trial = 2 ).
VARIABLE LABEL filter_$ 'trial = 2  (FILTER)'.
```

Appendix IV

```
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.
SORT CASES  BY group.
SPLIT FILE SEPARATE BY group.
UNIANOVA beta BY hand Hemisphere
  /METHOD=SSTYPE(3)
  /INTERCEPT=INCLUDE
  /POSTHOC=hand(BTUKEY)
  /PLOT=PROFILE(Hemisphere*hand)
  /CRITERIA=ALPHA(0.05)
  /DESIGN=hand Hemisphere hand*Hemisphere.
```

Univariate Analysis of Variance

```
[DataSet1] G:\06252010_beta weights for final ana.sav
```

group = Dystonia

Between-Subjects Factors[a]

		Value Label	N
hand	0	right	11660
	1	left	11660
Hemisphere	0	right	11640
	1	left	11680

a. group = Dystonia

Tests of Between-Subjects Effects[b]

Dependent Variable:beta

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	57.447[a]	3	19.149	9.861	.000
Intercept	694.743	1	694.743	357.781	.000
hand	16.116	1	16.116	8.300	.004
Hemisphere	29.926	1	29.926	15.411	.000
hand * Hemisphere	11.451	1	11.451	5.897	.015
Error	45275.288	23316	1.942		

a. R Squared = .001 (Adjusted R Squared = .001)

b. group = Dystonia

Appendix IV

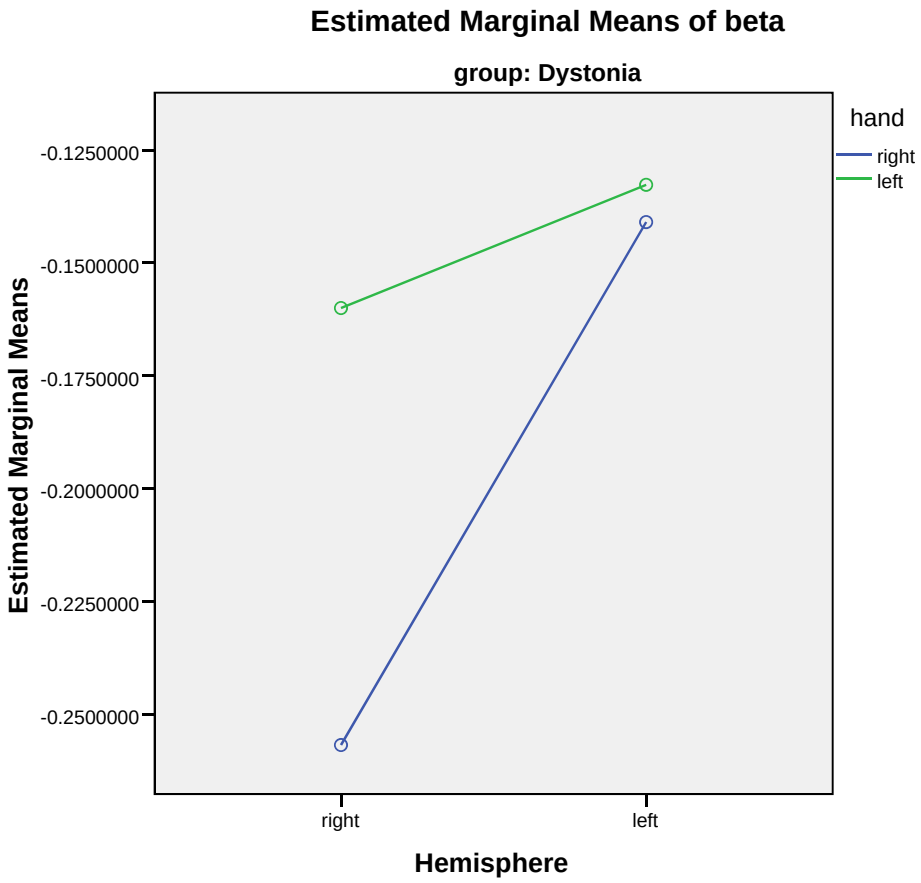
Tests of Between-Subjects Effects[b]

Dependent Variable:beta

Source	Type III Sum of Squares	df
Total	46026.986	23320
Corrected Total	45332.735	23319

b. group = Dystonia

Profile Plots



group = Healthy

Appendix IV

Between-Subjects Factors[a]

		Value Label	N
hand	0	right	18565
	1	left	18565
Hemisphere	0	right	18490
	1	left	18640

a. group = Healthy

Tests of Between-Subjects Effects[b]

Dependent Variable:beta

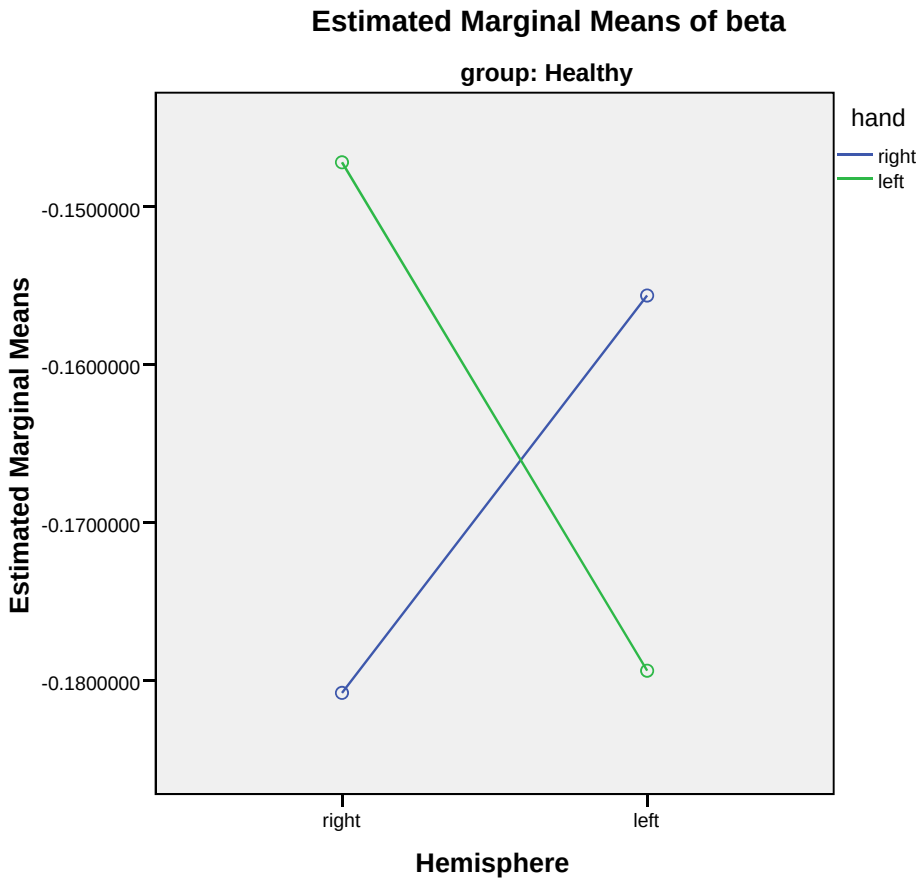
Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	7.971[a]	3	2.657	1.682	.168
Intercept	1020.122	1	1020.122	645.829	.000
hand	.225	1	.225	.142	.706
Hemisphere	.115	1	.115	.073	.788
hand * Hemisphere	7.642	1	7.642	4.838	.028
Error	58642.577	37126	1.580		
Total	59670.774	37130			
Corrected Total	58650.547	37129			

a. R Squared = .000 (Adjusted R Squared = .000)

b. group = Healthy

Profile Plots

Appendix IV




```
SPLIT FILE OFF.
USE ALL.
COMPUTE filter_$=(trial = 2 ).
VARIABLE LABEL filter_$ 'trial = 2  (FILTER)'.
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.
UNIANOVA beta BY hand Hemisphere group
  /METHOD=SSTYPE(3)
  /INTERCEPT=INCLUDE
  /POSTHOC=hand(BTUKEY)
  /PLOT=PROFILE(Hemisphere*hand Hemisphere*hand*group)
  /CRITERIA=ALPHA(0.05)
  /DESIGN=hand Hemisphere group hand*Hemisphere hand*group Hemisphere*g
roup hand*Hemisphere*group.
```

Appendix IV

```
UNIANOVA beta BY hand Hemisphere group WITH age
  /METHOD=SSTYPE(3)
  /INTERCEPT=INCLUDE
  /PLOT=PROFILE(Hemisphere*hand*group)
  /CRITERIA=ALPHA(0.05)
  /DESIGN=age hand Hemisphere group hand*Hemisphere hand*group Hemisphe
re*group hand*Hemisphere*group.
```

Univariate Analysis of Variance

```
[DataSet1] G:\06252010_beta weights for final ana.sav
```

Between-Subjects Factors

		Value Label	N
hand	0	right	30225
	1	left	30225
Hemisphere	0	right	30130
	1	left	30320
group	0	Dystonia	23320
	1	Healthy	37130

Tests of Between-Subjects Effects

Dependent Variable:beta

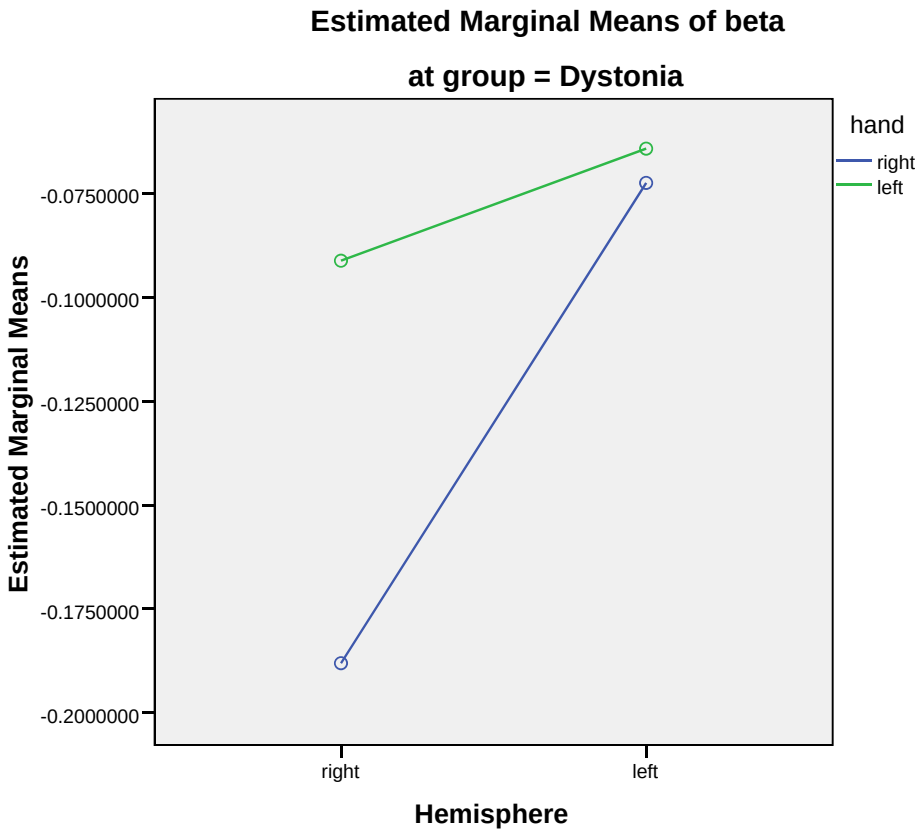
Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	195.725[a]	8	24.466	14.248	.000
Intercept	18.070	1	18.070	10.523	.001
age	129.648	1	129.648	75.501	.000
hand	11.840	1	11.840	6.895	.009
Hemisphere	16.452	1	16.452	9.581	.002
group	66.228	1	66.228	38.568	.000
hand * Hemisphere	19.089	1	19.089	11.116	.001
hand * group	8.132	1	8.132	4.736	.030
Hemisphere * group	20.050	1	20.050	11.676	.001
hand * Hemisphere * group	.875	1	.875	.509	.475
Error	103788.216	60441	1.717		
Total	105697.759	60450			
Corrected Total	103983.941	60449			

a. R Squared = .002 (Adjusted R Squared = .002)

Appendix IV

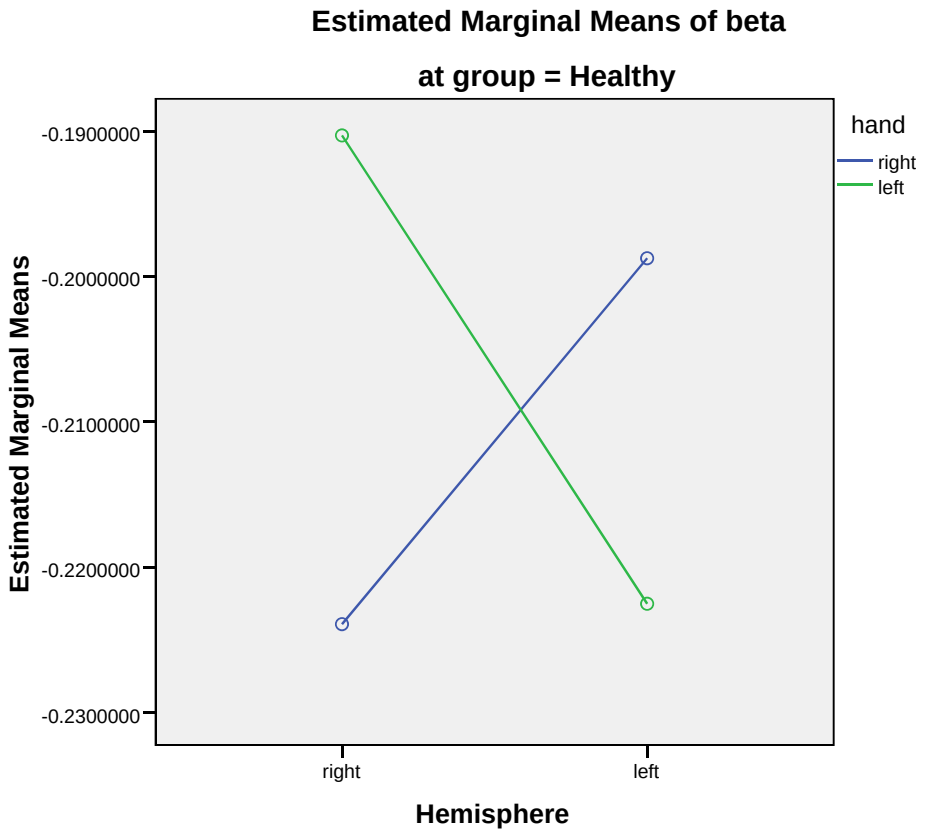
Profile Plots

Hemisphere * hand * group



Covariates appearing in the model are evaluated at the following values: age = 36.317

Appendix IV



Covariates appearing in the model are evaluated at the following values: age = 36.317

```
USE ALL.
COMPUTE filter_$=(trial = 2 ).
VARIABLE LABEL filter_$ 'trial = 2  (FILTER)'.
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.

SAVE OUTFILE='C:\Documents and Settings\tjk\My Documents\My Dropbox\Dis
sertation\06252010_beta '+
    'weights for final ana.sav'
  /COMPRESSED.
USE ALL.
COMPUTE filter_$=(trial = 2 ).
VARIABLE LABEL filter_$ 'trial = 2  (FILTER)'.
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
```

Appendix IV

```
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.
SPLIT FILE OFF.
UNIANOVA beta BY group Hemisphere hand WITH age
  /METHOD=SSTYPE(3)
  /INTERCEPT=INCLUDE
  /CRITERIA=ALPHA(0.05)
  /DESIGN=age group Hemisphere hand group*Hemisphere group*hand Hemisph
ere*hand group*Hemisphere*hand.
```

Univariate Analysis of Variance

```
[DataSet1] C:\Documents and Settings\tjk\My Documents\My Dropbox\Disser
tation\06252010_beta weights for final ana.sav
```

Between-Subjects Factors

		Value Label	N
group	0	Dystonia	23320
	1	Healthy	37130
Hemisphere	0	right	30130
	1	left	30320
hand	0	right	30225
	1	left	30225

Tests of Between-Subjects Effects

Dependent Variable:beta

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	195.725[a]	8	24.466	14.248	.000
Intercept	18.070	1	18.070	10.523	.001
age	129.648	1	129.648	75.501	.000
group	66.228	1	66.228	38.568	.000
Hemisphere	16.452	1	16.452	9.581	.002
hand	11.840	1	11.840	6.895	.009
group * Hemisphere	20.050	1	20.050	11.676	.001
group * hand	8.132	1	8.132	4.736	.030
Hemisphere * hand	19.089	1	19.089	11.116	.001

a. R Squared = .002 (Adjusted R Squared = .002)

Appendix IV

Tests of Between-Subjects Effects

Dependent Variable:beta

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
group * Hemisphere * hand	.875	1	.875	.509	.475
Error	103788.216	60441	1.717		
Total	105697.759	60450			
Corrected Total	103983.941	60449			

```
UNIANOVA beta BY group Hemisphere hand WITH age
  /METHOD=SSTYPE(3)
  /INTERCEPT=INCLUDE
  /PLOT=PROFILE(Hemisphere*hand*group)
  /CRITERIA=ALPHA(0.05)
  /DESIGN=age group Hemisphere hand group*Hemisphere group*hand Hemisph
ere*hand group*Hemisphere*hand.
```

Univariate Analysis of Variance

```
[DataSet1] C:\Documents and Settings\tjk\My Documents\My Dropbox\Disser
tation\06252010_beta weights for final ana.sav
```

Between-Subjects Factors

		Value Label	N
group	0	Dystonia	23320
	1	Healthy	37130
Hemisphere	0	right	30130
	1	left	30320
hand	0	right	30225
	1	left	30225

Tests of Between-Subjects Effects

Dependent Variable:beta

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	195.725[a]	8	24.466	14.248	.000
Intercept	18.070	1	18.070	10.523	.001
age	129.648	1	129.648	75.501	.000

a. R Squared = .002 (Adjusted R Squared = .002)

Appendix IV

Tests of Between-Subjects Effects

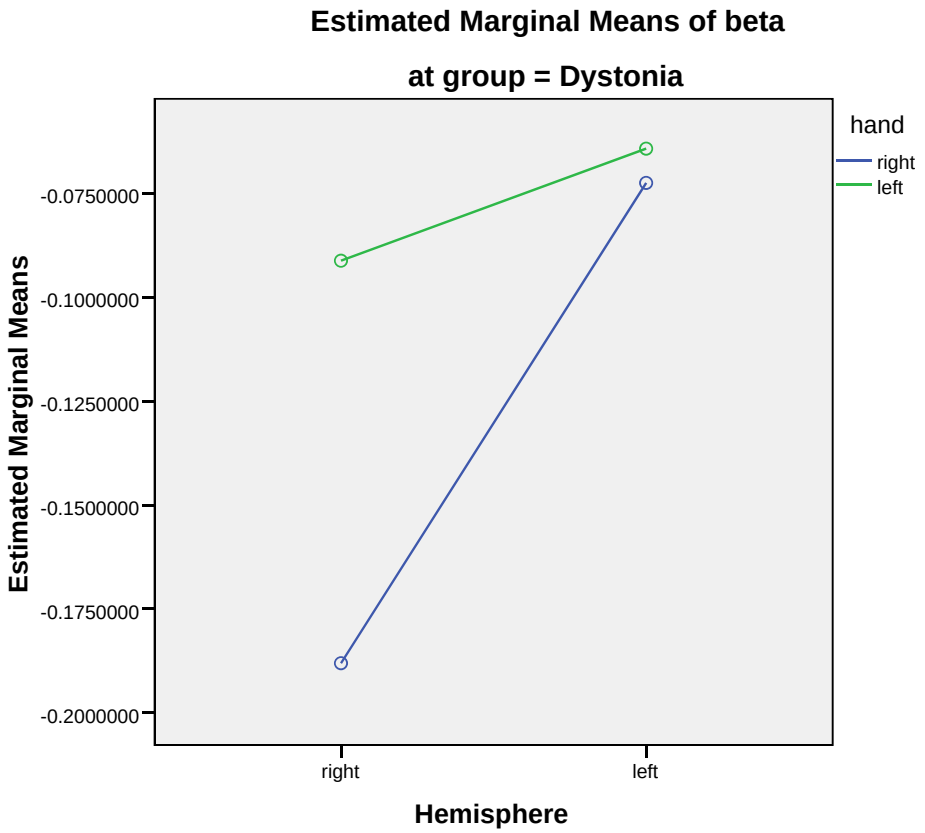
Dependent Variable:beta

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
group	66.228	1	66.228	38.568	.000
Hemisphere	16.452	1	16.452	9.581	.002
hand	11.840	1	11.840	6.895	.009
group * Hemisphere	20.050	1	20.050	11.676	.001
group * hand	8.132	1	8.132	4.736	.030
Hemisphere * hand	19.089	1	19.089	11.116	.001
group * Hemisphere * hand	.875	1	.875	.509	.475
Error	103788.216	60441	1.717		
Total	105697.759	60450			
Corrected Total	103983.941	60449			

Profile Plots

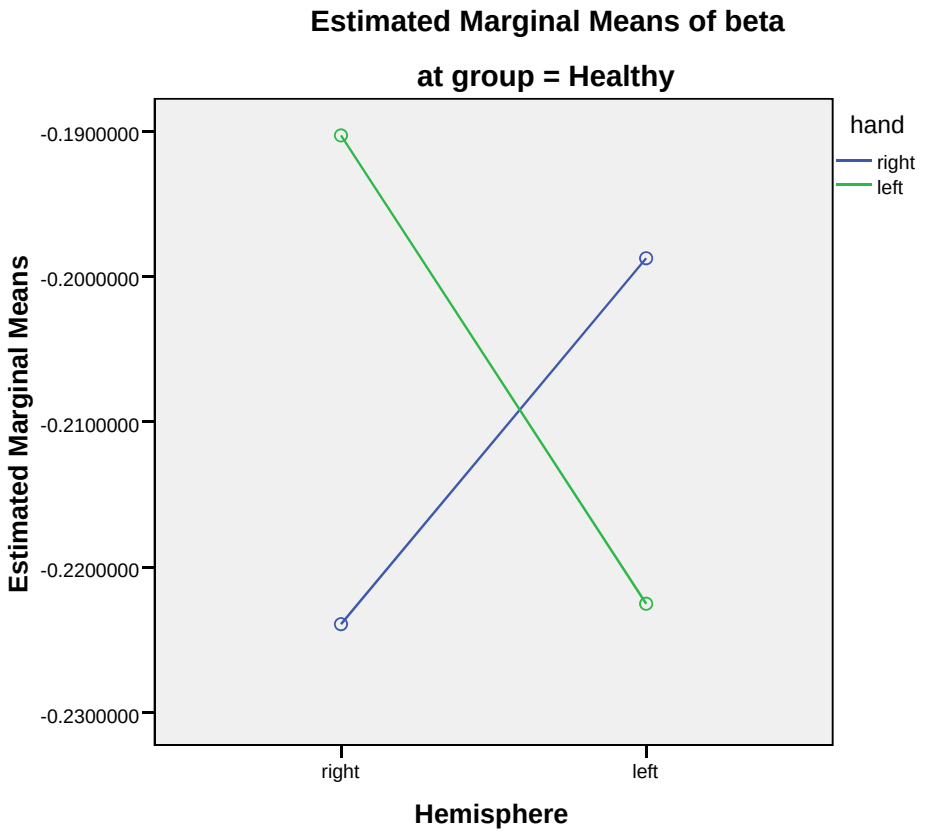
Hemisphere * hand * group

Appendix IV



Covariates appearing in the model are evaluated at the following values: age = 36.317

Appendix IV

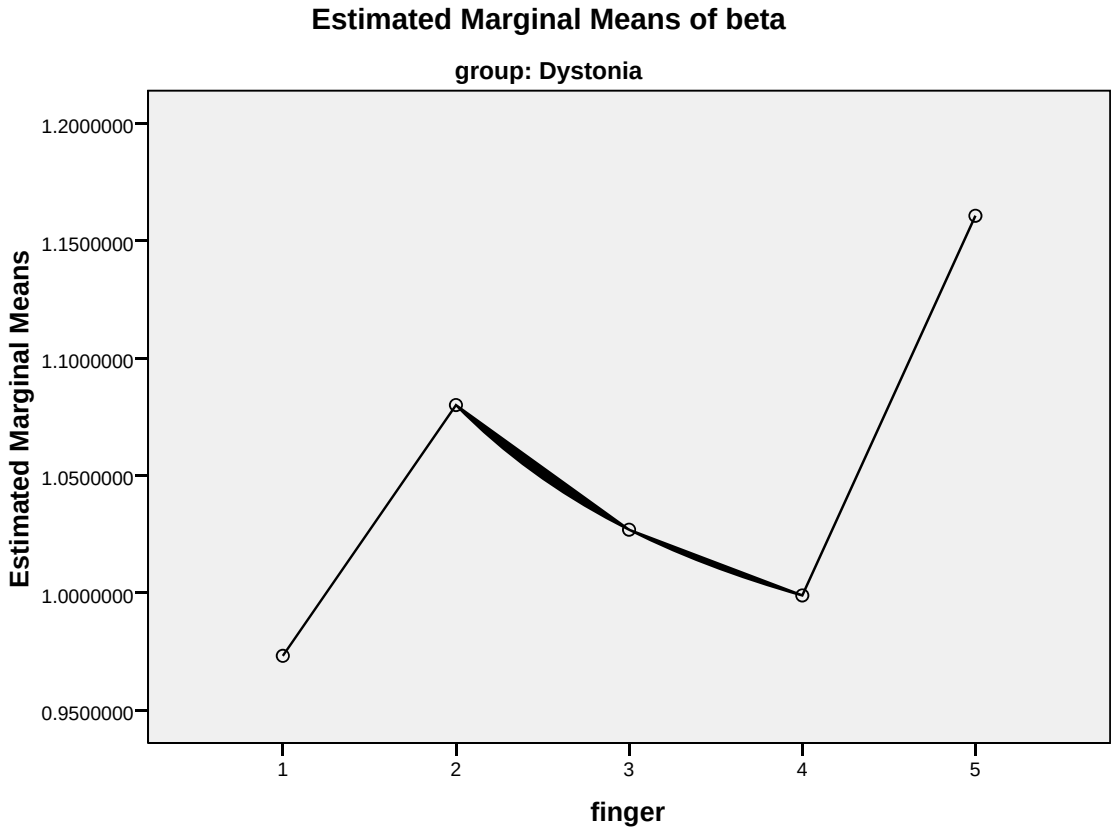


Covariates appearing in the model are evaluated at the following values: age = 36.317

Appendix V

SPSS output for individual finger analysis

Appendix V



Covariates appearing in the model are evaluated at the following values: age = 45.904

group = Healthy

Between-Subjects Factors[a]

		N
finger	1	837
	2	826
	3	820
	4	836
	5	873

a. group = Healthy

Appendix V

Tests of Between-Subjects Effects[b]

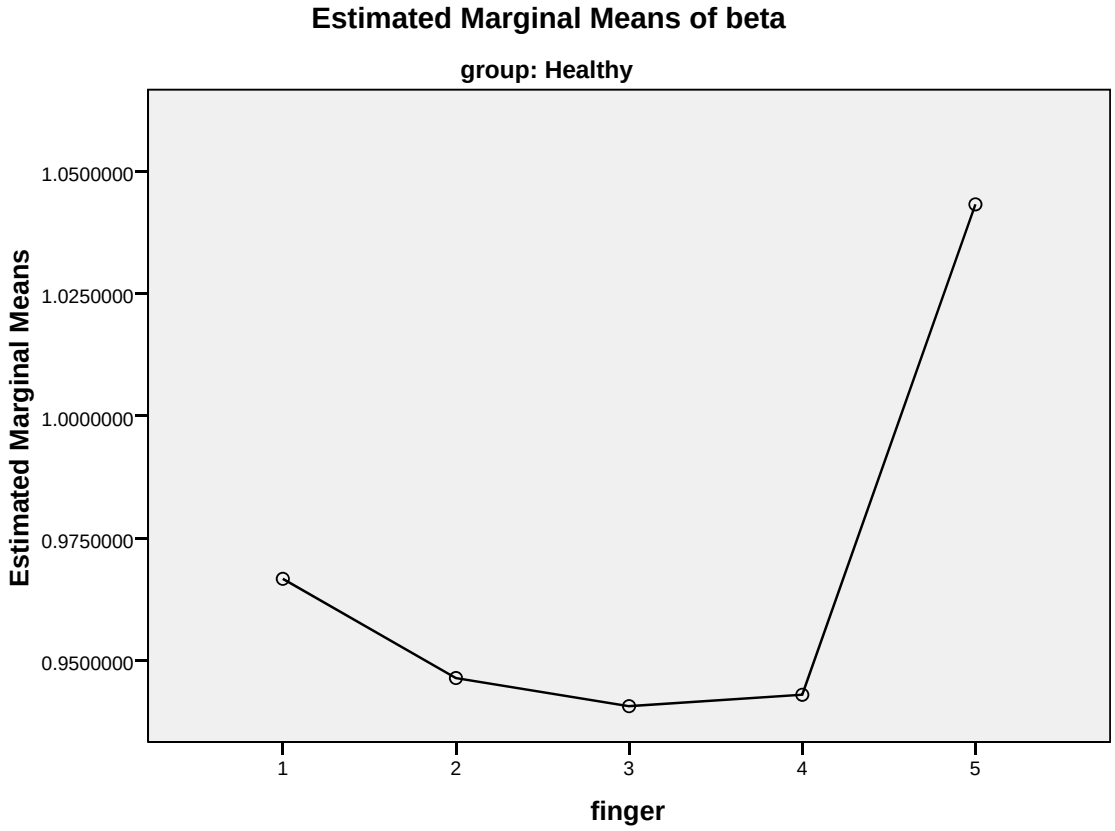
Dependent Variable:beta

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	6.862[a]	5	1.372	2.543	.026
Intercept	107.791	1	107.791	199.725	.000
age	.368	1	.368	.681	.409
finger	6.458	4	1.615	2.992	.018
Error	2259.170	4186	.540		
Total	6200.714	4192			
Corrected Total	2266.031	4191			

a. R Squared = .003 (Adjusted R Squared = .002)

b. group = Healthy

Profile Plots



Covariates appearing in the model are evaluated at the following values: age = 29.740

```
USE ALL.
COMPUTE filter_$=(trial = 2 & finger > 6  & beta > 0 & Hemisphere = 1).
VARIABLE LABEL filter_$ 'trial = 2 & finger > 6  & beta > 0 & Hemispher
e = 1 (FILTER)'.
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.
UNIANOVA beta BY finger WITH age
  /METHOD=SSTYPE(3)
  /INTERCEPT=INCLUDE
  /PLOT=PROFILE(finger)
  /CRITERIA=ALPHA(0.05)
  /DESIGN=age finger.
USE ALL.
COMPUTE filter_$=(trial = 2 & finger > 5  & beta > 0 & Hemisphere = 1).
VARIABLE LABEL filter_$ 'trial = 2 & finger > 5  & beta > 0 & Hemispher
e = 1 (FILTER)'.
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.
UNIANOVA beta BY finger WITH age
  /METHOD=SSTYPE(3)
  /INTERCEPT=INCLUDE
  /PLOT=PROFILE(finger)
  /CRITERIA=ALPHA(0.05)
  /DESIGN=age finger.
```

Univariate Analysis of Variance

[DataSet1] G:\06252010_beta weights for final ana.sav

group = Dystonia

Between-Subjects Factors[a]

		N
finger	6	558

a. group = Dystonia

Appendix V

Between-Subjects Factors[a]

		N
finger	7	517
	8	527
	9	492
	10	539

a. group = Dystonia

Tests of Between-Subjects Effects[b]

Dependent Variable:beta

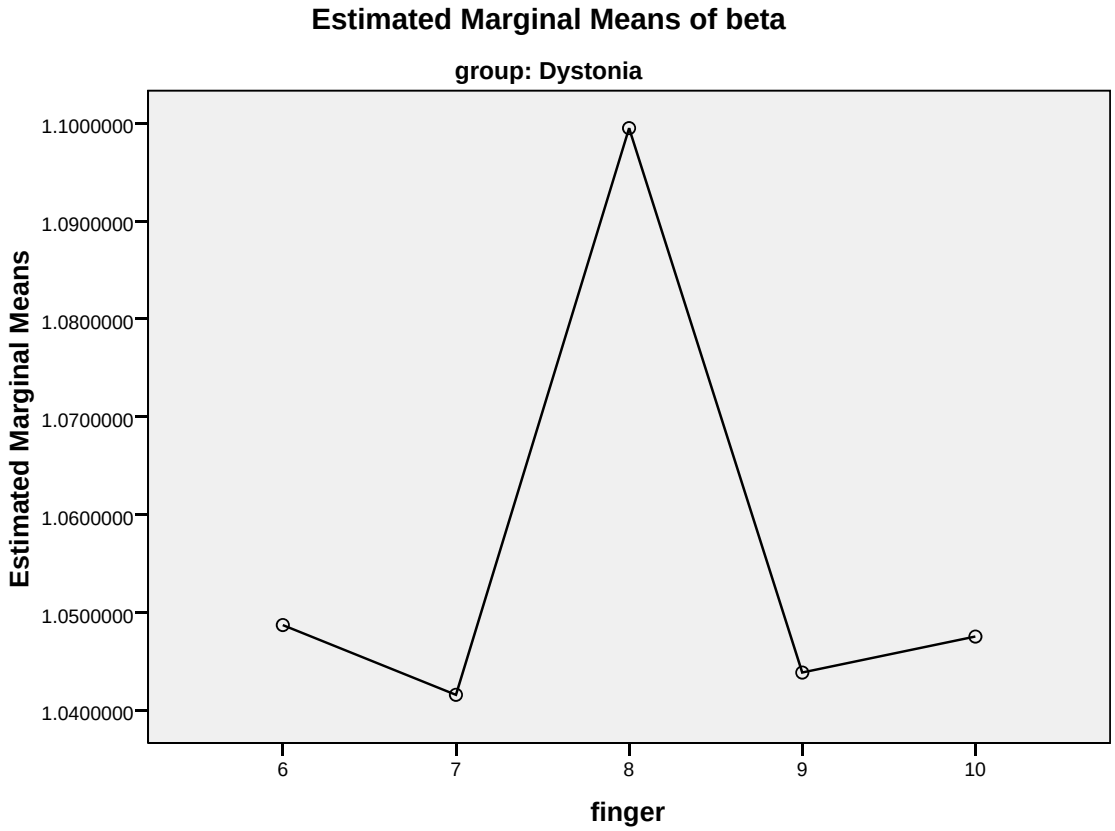
Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	1.337[a]	5	.267	.356	.878
Intercept	84.572	1	84.572	112.709	.000
age	.083	1	.083	.110	.740
finger	1.244	4	.311	.415	.798
Error	1971.177	2627	.750		
Total	4910.577	2633			
Corrected Total	1972.514	2632			

a. R Squared = .001 (Adjusted R Squared = -.001)

b. group = Dystonia

Profile Plots

Appendix V



Covariates appearing in the model are evaluated at the following values: age = 46.164

group = Healthy

Between-Subjects Factors[a]

		N
finger	6	842
	7	786
	8	868
	9	748
	10	777

a. group = Healthy

Appendix V

Tests of Between-Subjects Effects[b]

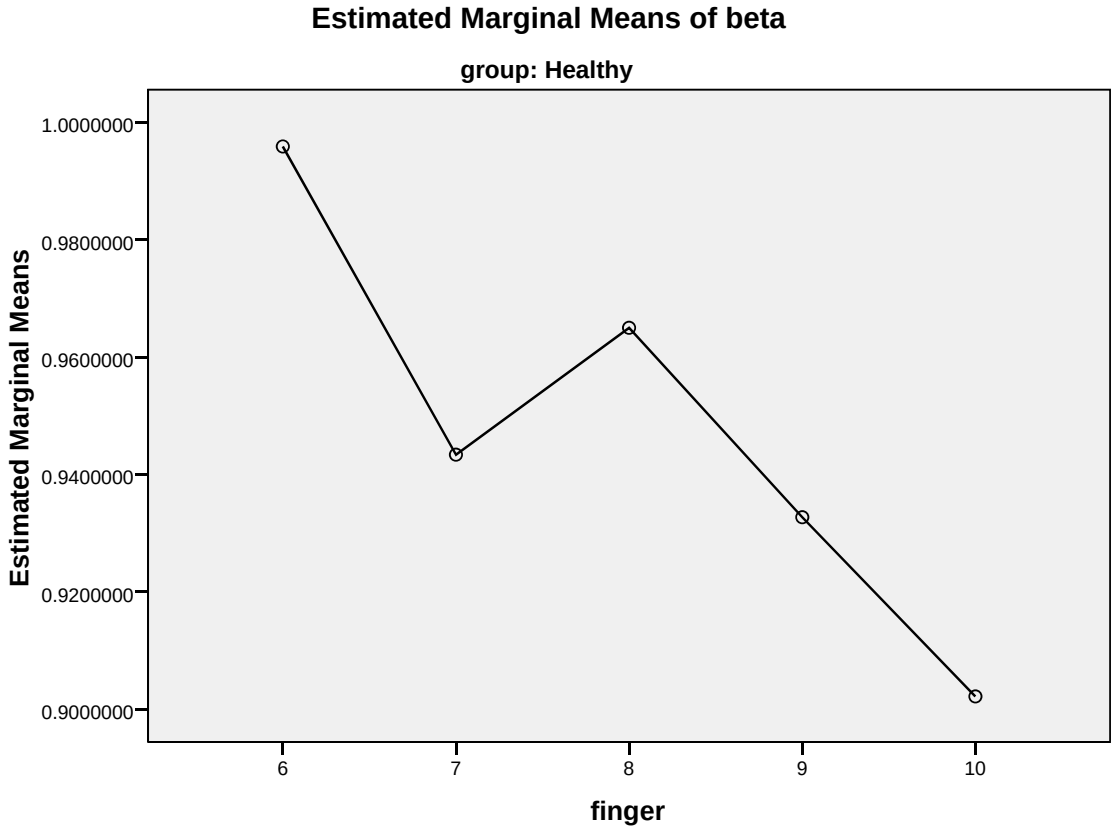
Dependent Variable:beta

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	7.381[a]	5	1.476	2.798	.016
Intercept	77.711	1	77.711	147.281	.000
age	3.593	1	3.593	6.809	.009
finger	3.993	4	.998	1.892	.109
Error	2118.460	4015	.528		
Total	5747.972	4021			
Corrected Total	2125.841	4020			

a. R Squared = .003 (Adjusted R Squared = .002)

b. group = Healthy

Profile Plots



Covariates appearing in the model are evaluated at the following values: age = 29.920

Appendix V

```
USE ALL.
COMPUTE filter_$=(trial = 2 & finger > 5  & beta > 0 & Hemisphere = 0).
VARIABLE LABEL filter_$ 'trial = 2 & finger > 5  & beta > 0 & Hemispher
e = 0 (FILTER)'.
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.
UNIANOVA beta BY finger WITH age
  /METHOD=SSTYPE(3)
  /INTERCEPT=INCLUDE
  /PLOT=PROFILE(finger)
  /CRITERIA=ALPHA(0.05)
  /DESIGN=age finger.
```

Univariate Analysis of Variance

```
[DataSet1] G:\06252010_beta weights for final ana.sav
```

group = Dystonia

Between-Subjects Factors[a]

		N
finger	6	474
	7	465
	8	508
	9	495
	10	474

a. group = Dystonia

Tests of Between-Subjects Effects[b]

Dependent Variable:beta

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	44.907[a]	5	8.981	13.877	.000
Intercept	208.349	1	208.349	321.906	.000
age	41.366	1	41.366	63.912	.000

a. R Squared = .028 (Adjusted R Squared = .026)

b. group = Dystonia

Appendix V

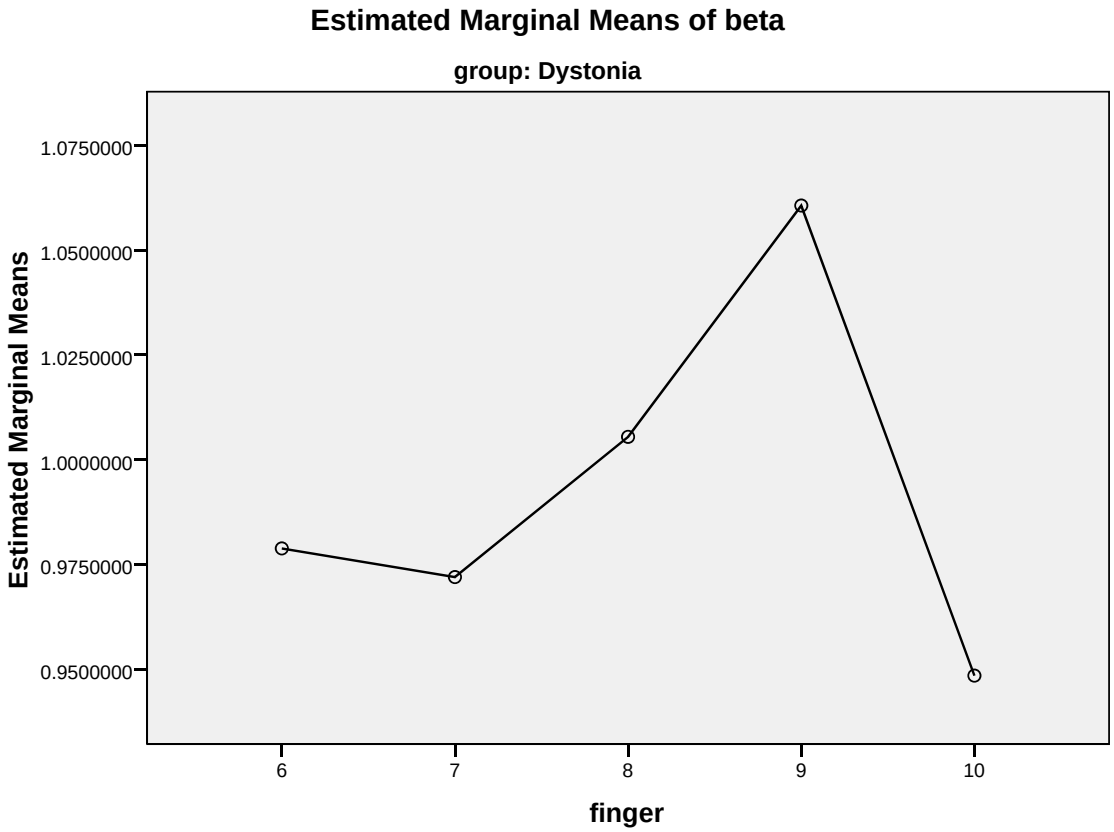
Tests of Between-Subjects Effects[b]

Dependent Variable:beta

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
finger	3.577	4	.894	1.382	.238
Error	1559.837	2410	.647		
Total	3991.592	2416			
Corrected Total	1604.744	2415			

b. group = Dystonia

Profile Plots



Covariates appearing in the model are evaluated at the following values: age = 45.710

group = Healthy

Appendix V

Between-Subjects Factors[a]

		N
finger	6	878
	7	795
	8	850
	9	804
	10	771

a. group = Healthy

Tests of Between-Subjects Effects[b]

Dependent Variable:beta

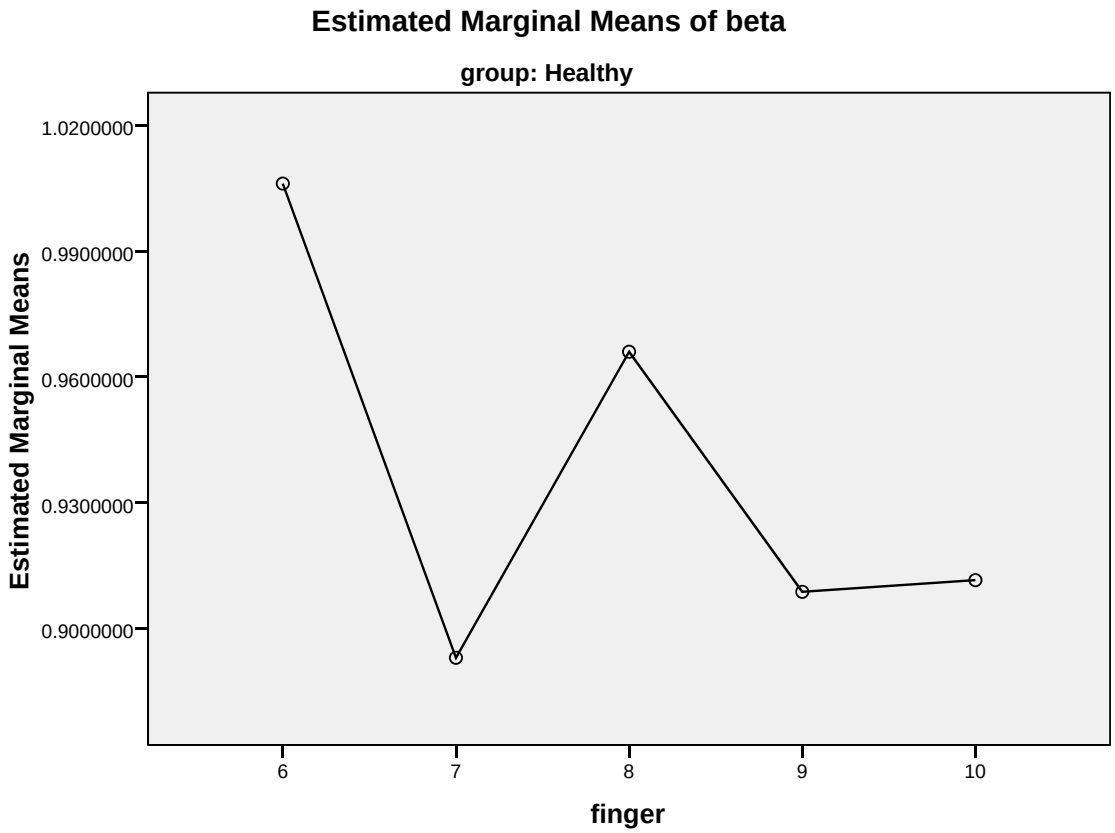
Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	8.853[a]	5	1.771	3.684	.002
Intercept	87.703	1	87.703	182.510	.000
age	1.626	1	1.626	3.383	.066
finger	7.550	4	1.887	3.928	.003
Error	1966.355	4092	.481		
Total	5588.213	4098			
Corrected Total	1975.207	4097			

a. R Squared = .004 (Adjusted R Squared = .003)

b. group = Healthy

Profile Plots

Appendix V



Covariates appearing in the model are evaluated at the following values: age = 29.619

```
USE ALL.
COMPUTE filter_$=(trial = 2 & finger < 6  & beta > 0 & Hemisphere = 1).
VARIABLE LABEL filter_$ 'trial = 2 & finger < 6  & beta > 0 & Hemispher
e = 1 (FILTER)'.
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.
UNIANOVA beta BY finger WITH age
  /METHOD=SSTYPE(3)
  /INTERCEPT=INCLUDE
  /PLOT=PROFILE(finger)
  /CRITERIA=ALPHA(0.05)
  /DESIGN=age finger.
```

Univariate Analysis of Variance

Appendix V

[DataSet1] G:\06252010_beta weights for final ana.sav

group = Dystonia

Between-Subjects Factors[a]

		N
finger	1	482
	2	548
	3	548
	4	520
	5	523

a. group = Dystonia

Tests of Between-Subjects Effects[b]

Dependent Variable:beta

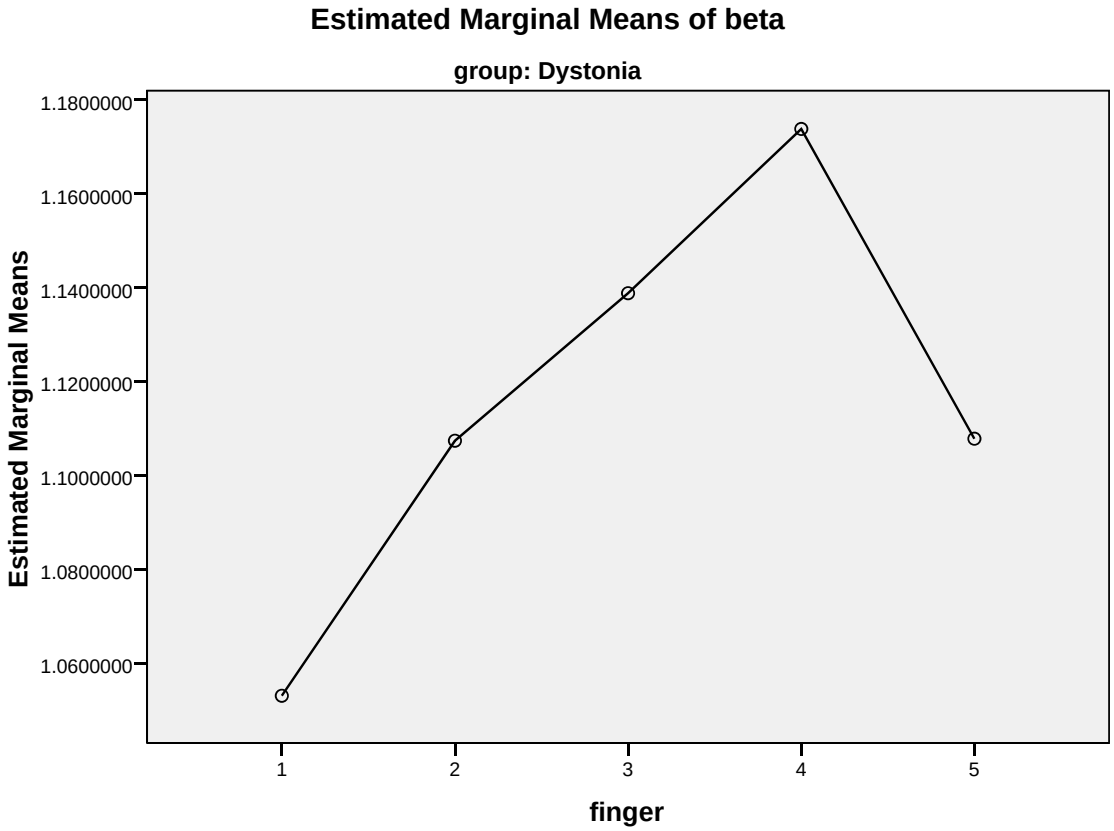
Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	6.480[a]	5	1.296	1.618	.152
Intercept	117.571	1	117.571	146.817	.000
age	2.504	1	2.504	3.126	.077
finger	3.999	4	1.000	1.248	.288
Error	2094.092	2615	.801		
Total	5372.277	2621			
Corrected Total	2100.572	2620			

a. R Squared = .003 (Adjusted R Squared = .001)

b. group = Dystonia

Profile Plots

Appendix V



Covariates appearing in the model are evaluated at the following values: age = 46.277

group = Healthy

Between-Subjects Factors[a]

		N
finger	1	783
	2	786
	3	845
	4	808
	5	790

a. group = Healthy

Appendix V

Tests of Between-Subjects Effects[b]

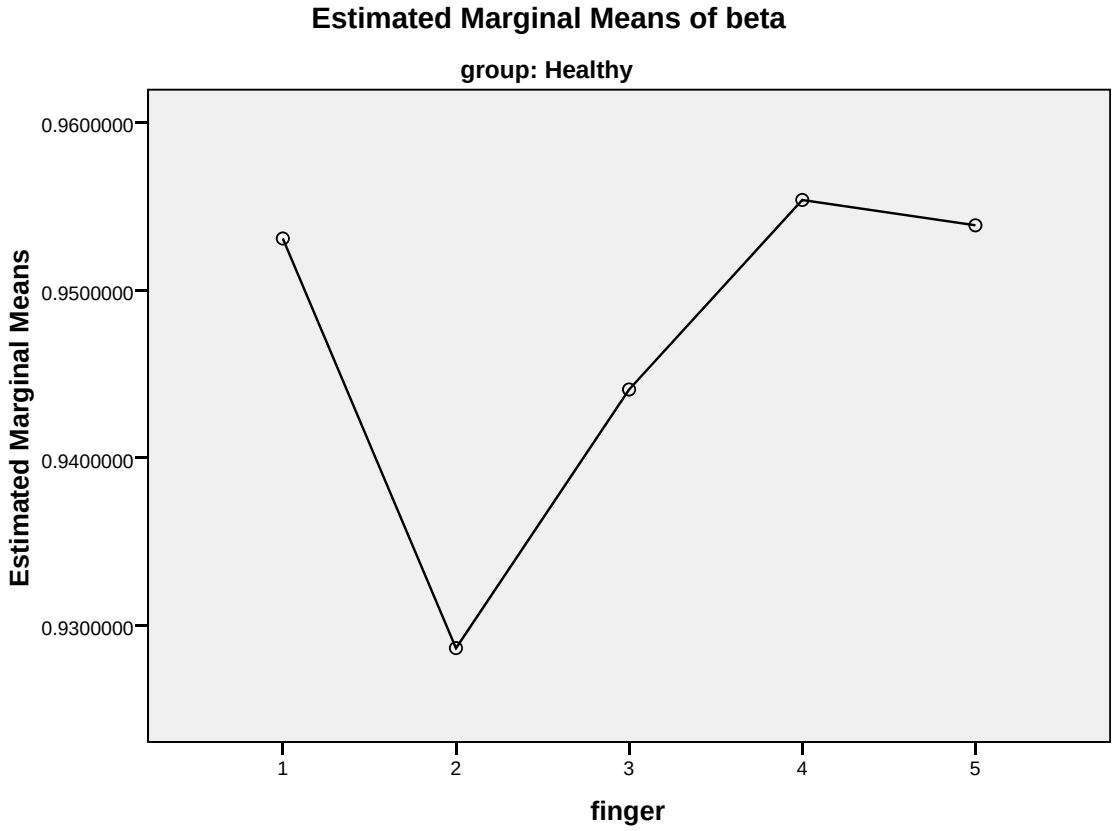
Dependent Variable:beta

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	2.898[a]	5	.580	1.119	.348
Intercept	86.823	1	86.823	167.649	.000
age	2.479	1	2.479	4.788	.029
finger	.394	4	.099	.190	.944
Error	2074.650	4006	.518		
Total	5675.630	4012			
Corrected Total	2077.548	4011			

a. R Squared = .001 (Adjusted R Squared = .000)

b. group = Healthy

Profile Plots



Covariates appearing in the model are evaluated at the following values: age = 29.840