Cortical Activation in the Primary Somatosensory Cortex: Healthy and Diagnosed Focal Hand Dystonia

Rebekah Schmidt
Department of Physical Medicine and Rehabilitation
University of Minnesota
Twin Cities, Minnesota 55455 USA

Faculty Advisor: Teresa Jacobson Kimberley, PhD, PT

Abstract

Current documentation on the pathophysiology of focal hand dystonia (FHD) is not conclusive regarding cortical activation. Most importantly, previous studies have not focused reports on the relative activation between hemispheres with stimulation of both hands. Purpose: to determine and compare the blood oxygen level dependent (BOLD) signal changes within primary somatosensory cortex (S1) during individual digit movement in subjects with FHD and healthy subjects. Methods: Eight healthy and five individuals diagnosed with FHD, all right hand dominant, participated in one session of functional magnetic resonance imaging (fMRI) while performing a specific finger tapping task. The BOLD response within the S1 was labeled as the region of interest and beta weights were exported for statistical analysis. Results: BOLD signal changes exhibited a significant hemisphere x hand x group interaction. Age was a significant covariate (p<0.001). Assessing BOLD signal changes for the right hemisphere, there was a group to hemisphere interaction (p<0.001). In post-hoc t-test comparison regarding contralateral hand control between groups there was a significant difference between groups (p<0.001). Conclusion: Limited studies have examined the ipsilateral and contralateral activation of both hands during individual digit movement in FHD. These results point to a somatosensory difference between healthy and individuals with dystonia. Specifically the results suggest a contralateral control difference within S1 cortical activation in the left hemisphere between healthy and diagnosed FHD.

Keywords: Focal Hand Dystonia, fMRI, Somatosensory Cortex

1. Introduction

Focal hand dystonia (FHD) is clinically characterized as a neurological disorder of involuntary muscle contractions in the hand or arm associated with performance of a specific task. This condition has a severe impact on an individual’s quality of life by inhibiting normal hand activity. The role of cortical activation in the pathophysiology of FHD is inconclusive. Some studies have shown increased activity in the primary sensorimotor areas while others document under-activation. Current evidence supports that it is likely that the central deficit involved in FHD lies within sensory-motor circuitry. Comparing the results of conflicting studies supports conception that the task and dystonic symptoms may impact results. Tasks that provoke the involuntary symptoms of dystonia are likely to display dystonic cortical activity while tasks that do not produce dystonic symptoms may then aim to provide findings of central brain differences compared to healthy controls. To evaluate dystonia in a dynamic state, functional magnetic resonance imaging (fMRI) is most commonly chosen to create a cortical activation map. The MRI signal is weighted by a ratio of oxygenated and deoxygenated blood, relating to regional cerebral blood flow and neural activity. This contrast is referred to as blood-oxygen-level dependence (BOLD) which allows for statistical comparison of cortical signal changes and the task design.

In order to develop an effective treatment and better understand the underlying pathophysiology, the cortical activity during motor tasks must be cohesively understood. Previous studies have not investigated the relative...
activation between hemispheres with movement of both hands. Limited studies of ipsilateral and contralateral control of affected and unaffected hands with FHD indicate a lack of knowledge addressing the relative difference between symptomatic and asymptomatic hand control. This study’s aim was to assess the BOLD response within the primary somatosensory cortex (S1) in each hemisphere using fMRI during motion of all digits in the absence of dystonic symptoms. The hypothesis was that there is a difference displayed by individuals with FHD in brain activity during hand movement specifically in S1 compared to healthy subjects.

2. Methodology

2.1. Subjects:

Thirteen total subjects were chosen to participate in the study. Control subjects consisted of eight neurologically healthy, right-hand dominant people (age mean ± SD 30.3 ± 5.59 y). Five subjects diagnosed with right hand dominant FHD (age mean ± SD 48.17 ± 9.41 y), not actively participating in rehabilitative treatments and had not received a botulism injection for at least six months. In accordance with the institutional review board of the University of Minnesota and the declaration of Helsinki, written informed consent was obtained from all participants.

2.2 Task:

Participants were given instructions to follow a visually-cued finger tapping sequences indicated by a picture of either a left or right hand with one finger colored green for each individual cue. The visual model was projected outside the scanner seen by the subject via a mirror placed within the scanner directly above the individual’s eyes. As the subject followed visual cues, single finger tapping was recorded during the entire sequence on a designated keyboard accessible to the subject. Cues were pseudo-random sequences in blocks of ten, each block consisted of a 3-second cue of each of the ten digits. Subjects were allowed to practice the task until the experimenter and subject both determined that no dystonic symptoms were present. Each total sequence was repeated at least twice for each subject. The first two sessions completed without problems were averaged and analyzed. During 1 scanning sequence, ten total blocks were presented.

2.3 MRI Processing:

Each participant completed one session of fMRI scanning while completing the task with the absence of dystonic symptoms anatomical and functional MRI for each subject were processed and standardized to Talairach space for analysis. Using BrainVoyager software (Brain Innovation, Maastricht, The Netherlands), manual tracing of the region of interest (ROI) was completed. The fMRI data used for ROI tracing consisted of thirty-six 2.0 mm slices for each subject. Each subject’s S1 anatomical location was identified in (Figure 1) voxel-specific tracing by an investigator blind to the co-registered eco-planar imaging data or group designation. Figure 2 illustrates the variance between subject’s S1 anatomical locations with color signifying each subject’s S1 ROI. Beta weight values for the identified ROI were averaged for each voxel and exported to Matlab 2009b (Mathworks, Inc., Natick, MA). Beta weight values are defined as a change in the intensity of activation. A positive beta-weight value resembles an increase in the intensity of activation and is referred to as ‘hyper-response’. A negative value is then a ‘hypo-response’

4.
2.4 Statistical Analysis:

Beta weights were exported from imaging software for analysis to SPSS Statistics 17.0 ©2010 SPSS Inc., an IBM Company, Chicago, IL. A one-way univariate general linear model analysis of variance (ANOVA) with a two-tailed a priori significance threshold of alpha = 0.05 was used in determination of difference between factors: group, hemisphere and hand. Within group 2-factor ANOVAs were conducted to evaluate variance in ipsilateral and contralateral activation for both hands. Post hoc testing for main effects was conducted as appropriate.

3. Results

Statistical tests revealed a significant main effect between group x hemisphere x hand. Age was a significant covariate, (F=141.3, p<0.001) and was thus added as covariable in subsequent analyses. Comparison between group x hemisphere activation during contralateral hand cueing revealed significant difference (F=414.9, p<0.001). When assessing BOLD signal changes for the left hemisphere, there was no group to hemisphere interaction (F=3.298, p=0.069) but there was in the right hemisphere (F=226.6, p<0.001). In post-hoc t-test comparison regarding contralateral hand control between groups there was a significant difference between groups (F=414.9, p<0.001). Group with FHD exhibited a contralateral left hemisphere hyper-response seen with dominant right hand movement (F=4.622, p=0.034), with no other differences between groups.
4. Discussion

Within subjects with dystonia, there was a significant finding in the left, contralateral hemisphere. Those individuals with FHD displayed a hyper-response during contralateral left hemisphere activation. Healthy subjects revealed no difference in the activation pattern for each hand between hemispheres. This finding supports similar fMRI studies that have concluded a hyperresponsiveness in the primary somatosensory cortex and primary motor cortex.

The lack of agreement across studies evaluating cortical activity within dystonia may be due to several reasons including: specified task, severity of dystonic symptoms, region of interest examined and imaging technique. Studies evaluating cortical activity within subjects with FHD have used several imaging techniques that complement each other by indicating abnormalities in S1, the basal ganglia thalamus and cerebellum. A similar study using voxel based morphology found decreases in the grey matter of the hand area, specifically in the left primary sensorimotor cortex, bilateral thalamus and cerebellum in patients with right hand specific dystonia. No other volumetric brain differences were found between controls and those with writer’s cramp. The implication of such physiological differences is not complete but further supports the conception that sensory abnormalities may be characteristic of dystonia. Multitracer approaches have supported the hypothesis that circuit deficits may be specifically located in cortico-striatal-pallido-thalamocortical and related cerebellar pathways. Positron emission tomography (PET) based investigations are also inconclusive as underactivity has been reported as well as dramatic overactivity in S1. A noteworthy study utilized PET concluding elevated sensorimotor activation patterns in both motor and exclusively audio-visual trails of subjects with dystonia. Maladaptive sensorimotor...
plasticity may be functionally correlated to such physiological abnormalities. Additional investigations are needed to explore this topic.

The designated tapping protocol included both hands lacking a rest period, resembling a bimanual task. This task was also designed to exclude dystonic symptoms, allowing an assessment of fundamental differences between healthy and subjects with dystonia. Additionally this design allowed an analysis of individuals with dystonia that may be characterized by various digits affected and levels of severity, incorporating interactions of both symptomatic and asymptomatic hemispheres. From the statistical evaluation of betaweight values, individuals with FHD display a heightened cortical response that may indicate supplementary neural resources are activated for processing. In contrast to our findings, some fMRI studies have reported decreased cortical responses when dystonic symptoms are not detected in individuals with writer’s cramp. Other fMRI studies provoking dystonic symptoms have supported the present findings by concluding contralateral overexcitation in S1.

Considerations to the study include the possibility that the specified task may have been accompanied by undetectable dystonic symptoms. In those with dystonia, abnormal EEG readings have been documented in the absence of dystonic symptoms while completing a finger tapping task. This is highly unlikely as the task was monitored by the participant and investigator to be symptom free. A limitation of the study was the absence of EMG data during task performance to control for movement outside the tapping procedure. Extraneous movement was monitored and the task repeated if detected.

The exaggerated cortical activity interpreted by the findings of this study is not fully understood. The observed contralateral hyper-response within S1 does however provide further evidence of a general sensory-motor circuit deficit. It is interesting to note that contralateral activation patterns of both asymptomatic and symptomatic hands produce a hyper-response seen in S1. This finding may signify that abnormalities characteristic to dystonia are not limited to the affected hemisphere or a specified muscle that produce dystonic symptoms. This study initiates the comparison of ipsilateral and contralateral control which may provide a more consistent evaluation of the neurologic irregularities observed in patients with FHD.

5. Conclusion

The findings of this study point to a somatosensory activation difference between healthy individuals and those with dystonia. Within subjects with FHD, results suggest a contralateral hyper-response within S1 activation during dominant right hand cueing. This could provide further evidence that there is a physiological difference, in addition to a cortical activity difference, between healthy and dystonic sensory processing.

6. Acknowledgments

The author wishes to express her appreciation to the University of Minnesota UROP program and the Minnesota Medical Foundation for providing the grants that funded this research. Special thanks to the Department of Physical Medicine, Kristen Pickett, PhD and to faculty advisor Teresa Jacobson Kimberley, PhD, PT for their training, assistance and encouragement.

7. References Cited

5. Kimberley TJ, Pickett KA. Differential activation in the primary motor cortex during individual digit movement.


