Hypophonia in Parkinson Disease: Neural correlates of Voice treatment with LSVT revealed by PET

Mario Liotti1, Lorraine Ramig2,3, Deanie Vogel5,7, Pamela New5, Chris Cook4, Peter Fox, M.D.4,5,6

Department of Psychology, University of Aberdeen, Scotland, U. K.1

m.liotti@abdn.ac.uk

The Department of Speech, Language and Hearing Science, University of Colorado at Boulder2

ramig@spot.colorado.edu

The Wilbur James Gould Voice Center, Denver3

The Research Imaging Center4, and the Departments of Medicine (Neurology)5 and Radiology6, University of Texas Health Science Center at San Antonio

newp@uthscsa.edu, cookc@uthscsa.edu, fox@uthscsa.edu

The Department of Speech Communication Disorders, Our Lady of the Lake University, San Antonio7.

voged@lake.ollusa.edu

ABSTRACT

This study investigated the neural correlates of hypophonia in individuals with Idiopathic Parkinson’s disease (IPD) before and after the Lee Silverman Voice Treatment (LSVT), using 15O-H2O Positron Emission Tomography (PET). Regional cerebral blood flow (rCBF) changes associated with overt speech-motor tasks relative to the resting state were measured in the IPD subjects before and after therapy, and in a group of healthy controls. Before LSVT, patients had strong speech-related activations in motor and premotor cortex, supplementary motor cortex and inferior lateral premotor cortex which were significantly reduced post-LSVT. In addition, significant right-sided activations were present in anterior insular cortex, caudate head, putamen, and dorsolateral prefrontal cortex following LSVT. Finally, the LSVT-induced neural changes were not present with transient experimenter-cued increases of loudness in LSVT-untreated patients. This treatment-dependant functional reorganization suggests a shift from an abnormally effortful to a more automatic implementation of speech-motor actions.

1. INTRODUCTION

The prevalence of disordered communication is particularly high in the one and one-half million individuals with Idiopathic Parkinson disease (IPD); however, only 3-4% receives speech treatment [1]. Optimal pharmacological or neurosurgical treatments for rigidity, tremor and akinesia do not appear to significantly affect measures of speech and voice function [2]. In contrast, clinical efficacy has been demonstrated for voice therapy (Lee Silverman Voice Treatment or LSVT [3-4]), and changes in acoustic [5], aerodynamic [6] and articulatory [7] measures associated with the treatment have been documented. In addition, LSVT appears to improve facial expression and posture, suggesting a more generalized multisystem influence on communication [8]. The widespread effects of LSVT strongly implicate a central origin for the neural mechanisms associated with voice improvement. However, to date, the central mechanisms of LSVT are basically unknown. No functional imaging studies have been carried out using speech-motor tasks in individuals with IPD, or have investigated the neural correlates of hypophonia.

The aims of the present study were two-fold. The first goal was to identify neural correlates of LSVT-induced voice improvement, which may suggest putative central mechanisms of LSVT. The second goal was to test whether experimenter-cued transient increases in loudness in untreated individuals with IPD would mimic the effects of LVST, or whether the latter reflect plastic changes due to functional reorganization of speech-motor networks developing over the course of the LSVT.

2. METHODS

2.1. Subjects

The experimental group included five patients (four men, one woman, all right-handed) with diagnosis of IPD and marked speech and voice disorder. Mean age was 61±4 years. Symptom severity was mild to moderate (Hoehn and Yahr scores 2 and 3). Mean onset of the illness was 5.6±2.6 years. They were all on levodopa medication. Patients had no history of past or present additional neurological or psychiatric disease. LSVT was administered according to the usual schedule [3-4] by a language pathologist trained and certified in LSVT. The
control group included five right-handed healthy volunteers (2 men, 3 women). Mean age was 58.6±14 years. They had no history of current or past neurological or psychiatric disease, or substance abuse.

2.2. Imaging methods

PET measurements of cerebral blood flow were carried out using a bolus $^{15}$O-water technique. Each IPD patient was studied in two sessions: before voice treatment (LSVT), and immediately after LSVT. In the pre-LSVT session, patients were imaged during the following tasks: Paragraph Reading- Habitual voice level; Paragraph Reading -experimenter-cued Loud voice level; Sustained Phonation (ilai) - experimenter-cued Loud voice level; and Eyes Closed Rest (two repetitions each). In the post-LSVT session, there were 3 tasks: Paragraph Reading, Sustained Phonation (both at spontaneous voice level) and Eyes Closed Rest (two repetitions each). Control subjects were imaged in a single session, in the Paragraph Reading task, and at Rest (two repetitions each).

Paragraph Reading Task (“rainbow passage”). In the first session (pre-LSVT), patients were scanned while reading at a Habitual voice level (2 repetitions), and again after instructions to “read as loud as possible” (2 repetitions). In the second session (post-LSVT) no instructions concerning loudness were provided. Anatomical magnetic resonance imaging (MRI) scan was also acquired for each for the purposes of spatial transformation of the PET data, region-of-interest analysis and parametric image display.

2.3. PET Data Analysis

For each subject and session, voxel-by-voxel pair-wise contrasts were performed to identify regional changes present during Overt Paragraph Reading relative to Eyes Closed Rest (IPD patients and Controls) and Sustained Phonation relative to Eyes Closed Rest (IPD patients only). Locations of focal maxima and minima exceeding a z-score of 2.9 (p<0.01, two-tailed) are reported here.

3. RESULTS

3.1. Behavior

Voice data acquired in the scanner were not suitable for analysis due to technical artifacts in three patients. Data acquired outside the PET suite, immediately before and after LSVT showed that post-LSVT loudness was significantly higher during sustained phonation (68.2±5.2 vs. 85.6±1.7 dB, F(1,4)=33.4, p<.005). Paragraph Reading (64.±8.4 vs. 75.8±8.5 dB, F(1,4)=12.5, p=.02) and spontaneous conversation (66.8±3.7 vs. 71.6±4, F(1,4)=31.1, p=.005).

3.2. PET results

3.2.1. IPD Group

Sustained Phonation Task. Pre-LSVT- Significant activations were present in primary motor and premotor cortical regions, including supplementary motor area (SMA), the motor-mouth primary representation (M1), stronger on the right, and bilateral inferior lateral premotor cortex (ILPm), the left anterior insula, bilateral auditory association cortex (BA 21 and 22), cerebellar vermis, and left posterior lateral cerebellum. Post-LSVT- In contrast, there were no significant activations in motor and premotor cortex post-treatment. Phonation-related activations were localized in bilateral anterior insular cortex (much greater on the right), dorsolateral Prefrontal cortex BA9 (much greater on the right), right putamen, right caudate nucleus, and left thalamus.

Paragraph Reading Task. Pre-LSVT. There were robust activations in supplementary motor cortex (SMA), left primary motor cortex (M1-mouth) and lateral cerebellum (both sides). Effect of loudness- Activations in premotor/motor cortex and cerebellum were very similar independent of the voice level, habitual or loud, without significant differences. Post-LSVT- Cortical motor/premotor regions were much less activated, and none reached significance threshold. Activations in the cerebellum included a cluster in lateral cerebellum, present also pre-LSVT, and several more medial sites in the vermis which were not activated pre-LSVT.

3.2.2. Control Group

Paragraph Reading Task. The only effect outside visual cortex (reading) to exceed significance threshold was an rCBF increase in left posterior cerebellum. Sub-threshold clusters of activation were present in bilateral superior premotor cortex and left lateral cerebellum. Importantly, no hint of significant activation was present in supplementary motor cortex (SMA) at any level of statistical threshold.

4. DISCUSSION

The functional brain correlates of successful LSVT were decreases in activation in cortical motor/premotor regions during phonation and reading, and increases in activity in right anterior insula, right basal ganglia, and right prefrontal cortex elicited by the sustained phonation task.

In the pre-treatment session of the IPD patients, robust activations were observed in the supplementary motor area (SMA), in the M1-mouth region, and a lesser extent in inferior lateral premotor cortex (ILPm), during both speech-motor tasks. Post-LSVT, all motor-premotor activations were markedly reduced and non-significant, in spite of increased loudness. In the control group (Overt Paragraph Reading vs. Rest), sub-threshold activations were present bilaterally in superior-lateral motor premotor cortex (M1-region). Importantly, no significant activation was observed in the SMA region at any statistical threshold. Based on these combined findings, we interpret the motor-premotor regional effects in the IPD group pre-LSVT as pre-treatment abnormalities, normalizing after voice treatment.

It has been proposed that in individuals with IPD motor cortical areas are recruited to perform sequential finger movements, as the result of increasing corticortical activity to compensate for striatal dysfunction [9]. Similarly, we propose that hypophonic individuals with IPD recruit more strongly motor/premotor regions during speech-motor tasks.

Fragmented speech-motor output due to basal ganglia dysfunction may entail the need for repetitive re-initiation of vocalization activity in SMA. In alternative, SMA overactivity may be a compensatory mechanism to override impaired basal ganglia motor function during speech-motor activities [9].

Right Basal Ganglia. Following voice treatment, significant activity was found in right putamen and caudate...
nucleus in the Sustained Phonation task. Increased signal in the basal ganglia is important in a disease whose primary pathology is in the basal ganglia. Electrophysiological evidence in monkeys [10], and PET data in healthy humans [11], suggest a role of the basal ganglia in the re-scaling of velocity, strength and force in limb-motor tasks. It is suggested that such role may extend to speech-motor function. Sustained phonation may depend on the ability of continuously re-scaling speech/motor output (loudness) based on incoming sensory information (auditory and somatosensory). It is hypothesized that LSVT, with its emphasis on increased awareness of loudness, may yield a normalization of activity in the right putamen/pallidus region.

**Anterior Insula.** The largest and most significant regional effect following LSVT was an activation in right anterior insular cortex during the Sustained Phonation task. In the monkey, the insular cortex connects reciprocally to premotor regions [12], and its role in humans as crucial speech-motor structure is becoming increasingly apparent by both functional imaging studies [13] and lesion-behavior correlation studies [14]. Activation in right anterior insula is also consistent with a crucial role of this structure in the representation of expressive prosodic aspects of speech, including emotional and non-emotional prosody [15] and singing [16]. Anatomy and connectivity studies in the monkey show that in the insula exteroceptive/motor and interoceptive/autonomic signals converge to produce a global representation of body state [12]. Because of its role as convergence zone of widespread signals, the right anterior insula activation following LSVT may help explain its multisystem effects, including enhanced facial expression and emotional expressive prosody [8].

**Right DLPFC cortex.** Another finding of this study is the increased activity in right DLPFC post-LSVT. Several PET studies have shown relative right DLPFC hypoactivation in individuals with IPD during limb-motor tasks [9], reversed by treatment with right pallidotomy [17] or subthalamic stimulation [18]. DLPFC receives projections from the basal ganglia and related thalamic nuclei. The defective signal in right DLPFC cortex may be explained by degeneration of mesofrontal dopaminergic afferents, or by a functional deafferentation of the prefrontal cortex from its basal ganglia-thalamic inputs [9]. The activation of the head of the caudate and the right DLPFC may be interpreted as the normalization of a pre-treatment abnormality, or the recruitment of an alternative fronto-striatal loop able to affect pallidal output [9].

6. REFERENCES


