Effects of Subthalamic Nucleus DBS on Haptic Perception and Sensorimotor Control in Parkinson's Disease

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Abstract

Parkinson's disease (PD) is a neurodegenerative disease that affects the basal ganglia-thalamocortical pathway resulting in a progressive decline in motor function. An established treatment for the motor symptoms of PD is deep brain stimulation (DBS) of the subthalamic nucleus (STN). Mounting evidence suggests that PD is also associated with somatosensory deficits, specifically a loss of kinaesthetic and haptic precision, yet the effect of STN-DBS on sensory processing is largely unknown. Thus, this study investigated whether STN-DBS affects somatosensory processing by systematically examining the precision of haptic perception of object size.

Without vision, 11 PD patients with implanted STN-DBS and 9 healthy controls haptically explored the heights of two successively presented three-dimensional blocks using a precision grip. In each trial, a 6cm reference block was judged against a comparison block (heights: 5.2-6.8 cm). Participants verbally indicated which block was taller (*perceptual* judgment). While still grasping the comparison block, they then matched its perceived size by opening the non-probing hand accordingly (*motor* judgment). Patients were tested during ON and OFF stimulation, following a 12-hour medication wash-out period. Based on their verbal responses haptic discrimination thresholds (DT) at the 75% correct response level and areas of uncertainty were derived. Based on the hand kinematic data collected by a motion capture system, a grip aperture error (difference between grip aperture and actual block height) was calculated.

The main results were: First, with their stimulators OFF, PD patients showed deficits in both perceptual and motor judgments compared to controls as measured by increased DT and aperture errors. When PD patients used their *more* affected hand to probe the block, DT was elevated by 233% (PD: 0.37 cm; controls: 0.11 cm) and mean aperture error increased by 97% (PD: 1.48 cm; controls: 0.75 cm). Second, DBS improved the precision of both *perceptual* and *motor* judgments. In the ON state, DT of the *more* affected hand decreased by 30% with respect to OFF state, while aperture error decreased by 15%. Third, probing with the motorically *more* affected hand resulted in less precise perceptual and motor judgments than probing with the *less* affected hand.

This study offers first evidence that STN-DBS improves haptic precision. Results of this study speak to the notion that deficits seen in PD are not simply motor based, but rather a function of deficits in proprioceptive processing. We conclude that DBS-related improvements in movement accuracy are not explained by improvements in motor function alone, but rather by improved somatosensory processing.

Table of Contents

List of Tables

List of Figures

Specific Aims

Haptic perception refers to one's ability to extract object features such as shape and texture by actively touching the object. Examining haptic function provides a window for investigating the benefits of STN-DBS for somatosensory processing because it relies on the integration of proprioceptive, tactile and pressure cues across time (Gibson, 1966).

Parkinson's disease (PD) is a neurodegenerative disease affecting the dopamine producing neurons within the basal ganglia-thalamocortical pathway that results in a progressive decline in motor function. Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an established treatment for PD that has shown to improve motor symptoms, allowing for a reduction in medication and thus reducing medication-induced dyskinesias (Krack et al., 1998; Limousin et al., 1998).

Along with the cardinal motor symptoms associated with PD, mounting evidence suggests deficits in perceptual information such as kinaesthetic (conscious perception of limb position and motion) and haptic sensory signals are also associated with PD (Konczak, Krawczewski, Tuite, & Maschke, 2007; Konczak, Li, Tuite, & Poizner, 2008; Li, Pickett, Nestrasil, Tuite, & Konczak, ; Maschke, Gomez, Tuite, & Konczak, 2003; Maschke, Tuite, Krawczewski, Pickett, & Konczak, 2006; Nolano et al., 2008; Zia, Cody, & O'Boyle, 2000). In PD the effect of STN-DBS on perceptual function in general and somatosensory-based perception in particular, is largely unknown. Only one study has investigated the effect STN-DBS has on kinaesthetic sensitivity (Maschke, Tuite, Pickett, Wachter, & Konczak, 2005) and no studies have looked at the effect STN-DBS has on haptic acuity (i.e., the ability to *discriminate* between two haptic stimuli). Therefore, this study considered the following general research questions: 1) What effect does PD have on haptic perception? 2) What is the effect of STN-DBS on haptic perception?

Specific Aims

1. To test the hypothesis that PD is associated with diminished haptic acuity. Specifically, I hypothesize that during stimulator OFF state, non-motor based

haptic size discrimination thresholds will be elevated in STN-DBS PD patients with respect to healthy controls.

2. To test the hypothesis that motor-based judgments of object size are impaired in PD. Specifically, I hypothesize that in the stimulator OFF state, differences between the physical size of the object being probed and the related hand aperture judgment (aperture error) will be greater in STN-DBS PD patients with respect to healthy controls.
3. To test the hypothesis that STN-DBS improves haptic acuity in PD. Specifically, I hypothesize that STN-DBS is associated with a reduction of haptic size discrimination thresholds when compared to stimulation OFF.
4. To test the hypothesis that STN-DBS improves the accuracy of hand aperture formation in PD. Specifically, I hypothesize that STN-DBS is associated with a reduced aperture error when compared to stimulation OFF.

Background and Significance

Vision and haptic exploration provide essential information about objects and their properties. This information is often integrated and subsequently used for many related sensorimotor activities such as reaching, grasping, and object manipulation. In this context, the term *sensory integration* is used to describe the combination of multiple streams of information to form one common percept (Stein, Meredith, & Wallace, 1993). Sensory integration is essential for perceiving ourselves and the external environment. Accurate voluntary movements then depend on *sensorimotor integration*, a mechanism by which sensory information is mapped on motor commands (Konczak et al., 2009). Amedi, Jacobson, Hendler, Malach, and Zohary (2002) argued that vision and haptic senses are the only two senses that can extract specific and precise geometric information about an object's shape. When vision becomes degraded, humans increasingly rely on haptic information for estimating object properties (Ernst & Banks, 2002). However, the process of integrating information from multiple modalities such as vision and haptics is adversely affected when excessive neural noise is present (i.e., diminished sensory information) and one or more sensory modalities become less accurate. This might be the case for patients with Parkinson's disease (PD), who have shown to become increasingly reliant on vision for controlling accurate movements due to deficits in proprioceptive information (Adamovich, Berkinblit, Hening, Sage, & Poizner, 2001; Schettino et al., 2006).

Relationship Between Haptic Perception and Motor Control

Increasing evidence documents that Parkinson's disease not only induces motor deficits, but also may lead to impaired kinaesthetic, tactile, and haptic function (Konczak et al., 2007; Konczak et al., 2008; Li et al., 2010; Maschke et al., 2003; Maschke et al., 2006; Nolano et al., 2008; Zia et al., 2000). Information from receptors in the muscles, tendons, and joint capsules provide information about muscle length and tension, contractile speed, and joint position, which is collectively termed proprioception (Konczak et al., 2009). With the understanding that these proprioceptive signals provide

the basis for both kinaesthetic and haptic sense, any noise introduced into these proprioceptive signals would also result in diminished kinaesthetic and haptic precision. In this sense, *precision* is a broad term that encompasses both *sensitivity* and *acuity* measurements. *Sensitivity* refers to the magnitude at which a stimulus can first be detected, or *detection threshold*. *Acuity* refers to the magnitude of the smallest perceivable difference between two detectable stimuli, or *discrimination threshold*.

The link between diminished proprioceptive processing and motor control in PD was highlighted by Adamovich et al. (2001) in a study where subjects had to point to a remembered target in complete darkness, or only with vision of the target, or only with vision of the finger tip. PD patients proved to be less accurate in tasks in which they had rely on proprioceptive information about their arm. In other words, they were less accurate during conditions in which they could not see their finger and had to rely strictly on proprioceptive processes to provide information about the location of their arm. *Accurate* motor commands depend on precise knowledge about the current state of the body (Wolpert, Ghahramani, & Jordan, 1995). Therefore, diminished proprioceptive information may lead to less precise movements. Thus, a diminished ability to process proprioceptive information will affect both kinaesthetic and haptic precision and ultimately those sensorimotor processes that use kinaesthetic and haptic signals.

On a neuronal level, Nagy, Eordegh, Paroczy, Markus, and Benedek (2006) showed that neurons of the basal ganglia respond to multimodal sensory afferents, specifically somatosensory afferents. At times, the response of these basal ganglia neurons was super-additive, indicating not only a multisensory response, but also being possible loci for multisensory integration (Calvert & Thesen, 2004). The notion of proprioceptive processing within the basal ganglia was underlined by Rodriguez-Oroz et al. (2001) showing that basal ganglia neurons, specifically in the subthalamic nucleus (STN), are responsive to both passive and active movements of the limb. Furthermore, Lewis and Byblow (2002) used transcranial magnetic stimulation (TMS) to investigate sensorimotor integration in PD during static and passive limb movement. They found an abnormal influence of afferent signals on corticomotor excitability in PD, which may have been

related to abnormal sensory input, or a defective sensory integration process, or a deficient motor response. A review by Abbruzzese and Berardelli (2003) contends that PD involves disturbances of proprioceptive regulation, possibly due to a mismatch between afferent signals and corollary discharge (i.e., predicted afferent signals), resulting in impaired sensory scaling. They conclude that abnormal central processing of sensory information in PD leads to changes in sensorimotor integration.

The Effect of STN-DBS on Haptic Perception and Sensorimotor Control

Deep brain stimulation (DBS) of the STN is known to alleviate certain cardinal motor symptoms associated with PD such as bradykinesia and rigidity. STN-DBS has become an increasingly common neurosurgical intervention for levodopa-responsive patients. Currently there are only a few studies that have quantified upper limb kinematics relative to STN-DBS (Agostino et al., 2008; Khandwala, Burack, Mink, Gdowski, & Gdowski, 2009) and only one study has quantified the effects of STN-DBS on perceptual sensitivity (Maschke et al., 2005). Agostino et al. (2008) had subjects move their hand along a zigzag vertical path marked with targets, stopping on each target before moving to the next. Results showed that DBS significantly improved movement time of a motor sequence as well as switching time from one sequential step to the next. Accuracy (i.e., whether sub-movements landed inside the target) decreased during the DBS-ON state. Khandwala et al. (2009) had two off-medication PD patients perform a button press task in both the DBS-ON and OFF state. Results showed that DBS-ON improved both reaction and movement times compared to DBS-OFF.

Relative to perceptual sensitivity, Maschke et al. (2005) examined the effect of STN-DBS on kinaesthesia in PD. Using a passive motion apparatus, a PD patient's arm was passively moved at a constant velocity with a displacement between 0.2°- 8°. Patients were then asked to judge if their arm moved toward or away from their body, or "could not tell". Results showed that PD patient's (DBS-OFF) arm had to move more than twice the angular displacement compared to controls before they could tell which direction their arm was being moved. However, kinaesthetic sensitivity improved in DBS-ON patients compared to DBS-OFF, although not to the level of controls. A study by (Devos

et al., 2003) evaluated an active movement task and showed improvements in a wrist flexion task during STN-DBS which they attributed to improved somatosensory processing. Given the relationship between proprioceptive processing and sensorimotor control and the results of the previously described studies, it seems plausible that DBS invoked improvements in perceptual precision may be the driving factor behind improvements in motor function.

Conclusion and Purpose

There is a growing body of evidence supporting the notion that motor symptoms seen in PD are a function of faulty central processing of somatosensory information (Konczak et al., 2007; Lewis & Byblow, 2002; Li et al., 2010). Furthermore, it is well known that STN-DBS alleviates the known motor deficits seen in PD. However, limited research on the effect of DBS on somatosensory processing in PD is available. Showing that DBS treatment has a positive effect on proprioceptive and haptic processing will provide further evidence that PD is not merely a motor disorder but rather a sensorimotor disorder. Therefore, the purpose of this study was to systematically investigate the effect of STN-DBS on haptic function in PD.

Methods

Subjects

PD patients. Eleven PD patients (mean ± SD, age: 58 ± 8.8 years) were recruited from the movement disorder outpatient clinic at the University of Minnesota as well as Park Nicollet's Struthers Parkinson's clinic. Patients were clinically diagnosed with idiopathic Parkinson's disease and had previously been implanted with a DBS electrode within the STN. All subjects were tested after an approximate 12-hour washout period from their routine anti-parkinsonian medication. Patients were tested for hand dominance utilizing the Edinburgh Handedness Inventory (Oldfield, 1971). All patients were assessed by a movement disorder specialist using the motor scale of the Unified Parkinson's disease rating scale (UPDRS-III, 18-31A) (Fahn, 1987) in both the DBS-OFF (mean ± SD, 41.44 ± 13.26) and DBS-ON state (mean ± SD, 26.91 ± 9.66) and the Hoehn and Yahr staging system (Hoehn & Yahr, 1967) (mean stage: DBS-OFF=2.25; DBS-ON=1.6). The UPDRS motor scale provides a standardized clinical rating of movement impairment, including resting and action tremor, rapid alternation of finger, hand, and foot movements, postural tone, postural stability, gait, and general body bradykinesia.

The *more* affected hand of the PD patients was indicated verbally by the patient and then confirmed using the UDPRS-III. Only one patient had a higher UPDRS score in their verbally indicated *less* affected hand (upper limb score = 8) compared to their verbally indicated *more* affected hand (upper limb score = 9). In this case the more affected hand was taken as the verbal indication of the patient. Patients were also assessed utilizing the MMSE (Folstein, Folstein, & McHugh, 1975), and Beck's Depression Inventory-II (Beck, Steer, Ball, & Ranieri, 1996) in order to screen for cognitive compromise. Exclusion criteria for PD patients were the following: 1) MMSE < 26, 2) Hoehn & Yahr stage V of disease, 3) Beck Depression score > 19, or 4) any diagnosis that included peripheral neuropathy, past severe head trauma, other central nervous system disorders affecting the brain, brainstem, or spinal cord (e.g., multiple sclerosis, dementia, depression, psychosis, spasticity), regular intake of benzodiazepines,

or orthopaedic disease interfering with arm movements. Further details of clinical characteristics and basic demographics of PD patients are listed in Table 1.

Table 1. Clinical characteristics and basic demographics of Parkinson's disease patients. Gender: M = male, F = female; Dominant hand: based on Edinburgh Handedness Inventory [range from 20 (right handed) to -20 (left handed)] (Oldfield, 1971); More affected hand: determined by patient self reporting and verified by UPDRS-III [questions 18-31A, range 0-4/question, 0-112 total possible score]. Disease duration: number of years since patient was diagnosed with PD; DBS duration: number of months the patient has been treated with deep brain stimulation (* indicates subjects with unilateral DBS); UPDRS: Unified Parkinson's disease rating scale (OFF: DBS-OFF, ON: DBS-ON)

N	Age	Gender	Dominant hand	More affected hand	Disease duration (years)	DBS duration (months)	UPDRS-III (OFF)	UPDRS-III (ON)
1	64	M	R	R	5	36	34	29
2	64	M	R	R	8	36	33	28
3	60	M	R	R	10	12*	33	22
4	49	M	R	R	13	108	46	39
5	47	F	R	L	13	60	31	17
6	53	M	R	L	8	12*	24	11
7	44	M	R	R	8	9*	45	28
8	62	M	R	R	6	48	70	43
9	73	M	R	R	20	72	45	23
10	63	M	R	R	14	3*	38	20
11	61	M	R	R	14	2	58	36

Control subjects. Nine healthy, age-matched subjects (59 ± 6.6 years) without a known history of neurological, musculoskeletal, or peripheral nerve disease served as a control group. Exclusion criteria for the control group were the following: 1) MMSE < 26; 2) Beck Depression > 19; or 3) any history of neurological, musculoskeletal, or peripheral nerve disease. Informed written consent was obtained from all subjects prior to participation. All subjects were tested for hand dominance utilizing the Edinburgh Handedness Inventory (Oldfield, 1971). The study was approved by the University of Minnesota institutional review board.

Experimental Set Up

Subjects were seated on a height-adjustable chair in front of the experimental apparatus with both hands resting on a specified start location (Figure 1A).

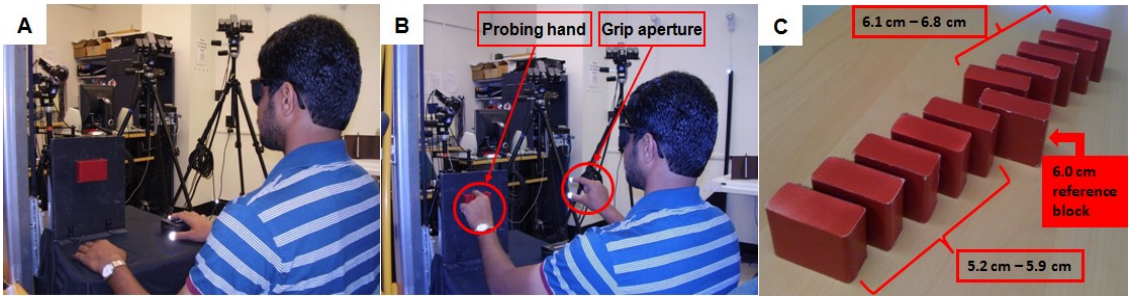

Figure 1. Experimental setup. **A)** Apparatus with a subject sitting in front of the apparatus with both hands resting in a specified start location. **B)** A subject haptically probing a wooden block with one hand and forming a grip aperture (motor judgment) with the other hand. The aperture was recorded via reflective markers on the index finger and thumb. **C)** Block sizes used in the testing paradigm. Comparison blocks: 5.2 cm–5.9 and 6.1 cm–6.8 cm. The reference block was 6.0 cm tall.

The experimental apparatus consisted of a vertically aligned rectangular wooden board to which the blocks were attached using velcro. The block was placed directly in front of the subject's hand for haptic exploring (probing). A series of 11 blocks was used as haptic stimuli. The block with the height of 6 cm served as the reference block and all other blocks were compared against the reference block. Heights of the comparison stimulus blocks were: 5.2, 5.4, 5.6, 5.8, 5.9, 6.1, 6.2, 6.4, 6.6 and 6.8 cm tall (Figure 1C). All blocks had the same width (9.25 cm) and depth (3.6 cm). Distance from the subject to the block was standardized at approximately 40 cm from their shoulder to the block. Reflective markers were placed on the tip of the thumb and index finger of the hand being used to form a grip aperture size judgment (motor judgment described below). Three-dimensional coordinates of both markers were recorded over the duration of the task using an optoelectronic motion capture camera system (Peak Performance Technologies, Inc., Centennial, CO) recorded at a sampling frequency of 120 Hz.

Procedure

Goggles occluded a subject's vision during data collection. Prior to testing, subjects completed 3 training trials that were not included in data analysis and then verbalized that they understood and were comfortable with the task.

The experiment consisted of a haptic *perception* task and a haptic perception-*motor* task. Within each trial, subjects first completed the *perceptual* judgment followed immediately by the *motor* judgment. During the *perceptual* task, subjects were presented with the *reference* block and asked to probe the height of that block for a period of 4 s using a precision grip. The block was removed and subjects were then presented with a *comparison* block to probe for a period of 4 s with the same hand as previous. The subject was then asked to give a size judgment, verbally answering the question "Which block was taller, the first block you probed or the second?" Next, while still grasping the (2^{nd}) comparison block, subjects performed the *perceptual-motor* task. With the non-probing hand they formed a hand aperture to match the perceived height of the currently grasped block (see Figure 2).

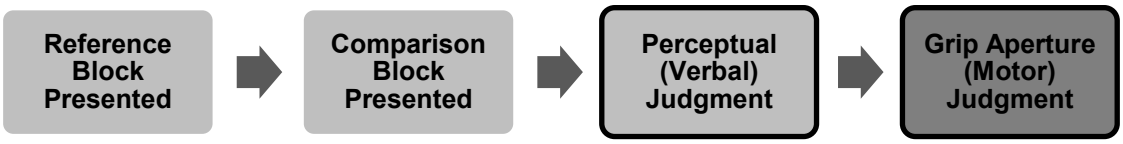

Figure 2. Flow chart of experimental procedure. Procedure included a verbally indicated haptic judgment of which block was taller, followed by a grip aperture that indicated the perceived size of the comparison block.

For the purpose of simplicity, the verbal judgment will be referred to as the *perceptual* judgment and the grip aperture formed to match the physical size of the comparison block will be referred to as the *motor* judgment throughout the remainder of this paper. All subjects completed both tasks with each hand.

Design

This study utilized a crossover design with all PD subjects completing the task in all conditions. PD subjects completed all trials using their *more affected* hand to probe the blocks and *less affected* hand to perform the motor judgment (30 perceptual judgments

and 30 motor judgments), or they probed with their *less* affected hand and used the *more* affected hand to perform the motor judgment (30 perceptual judgments and 10 motor judgments). In the latter condition a reduced amount of motor judgments were collected because the primary focus of the study was on the more affected hand and to reduce the amount of time patients were off medication and off stimulation. Control subjects completed all trials using their dominant or non-dominant hand to probe the blocks (30 perceptual judgments and 30 motor judgments per hand). This was done so control subjects could be dominant hand matched to PD patients since all 11 of the PD patients were right hand dominant, but 2 of them were more affected on the left side (see Table 1). For the remainder of this paper, we will refer to a specific task/trial by indicating the hand used to probe the block with the understanding that during the *motor* task the opposite hand is the hand used to complete the motor judgment (i.e., the grip aperture). For example, when referring to data relative to the *more* affected hand in PD, the *more* affected hand was used to probe the block and the *less* affected hand was used to perform the *motor* judgment.

The 10 comparison blocks were presented in random order. Subjects completed three perceptual judgments per block size and three motor judgments per block size (accept as indicated previously for PD subjects using their *less* affected hand) (see Table 2 for overview). The order in which the PD group (*more* affected vs. *less* affected) as well as the control group was tested (dominant vs. non-dominant hand) was randomized. All PD subjects were instructed to refrain from taking their anti-Parkinsonian medication approximately 12 hours prior to data collection. All PD subjects were tested during DBS "ON" and DBS "OFF" states. To reduce a possible order effect, each subject was randomly assigned as to whether they started first ON then OFF, or vice versa. The exact procedure for testing in both DBS states was as follows:

ON-OFF – Subjects reported to the data collection site with their stimulator ON and were evaluated using the UPDRS-III. After the subject completed all trials, their stimulator was turned OFF. After a period of no less than 20 minutes (Waldau, Clayton,

Gasperson, & Turner, 2011), the subject was again evaluated using the UPDRS-III. The subject then completed all judgment trials a second time.

OFF-ON – Subjects had their stimulator turned OFF no less than 20 minutes prior to data collection and were then evaluated using the UPDRS-III. After the subject completed all trials, their stimulator was turned ON. After a period of no less than 20 minutes (Waldau et al., 2011), subjects were evaluated using the UPDRS-III and then completed all judgment trials for the second time.

Table 2. Overview of test conditions and study design. PD patients completed all trials in the both the DBS-OFF and ON state. Patients only completed 10 motor judgment trials using their *less* affected hand to probe the block and *more* affected hand to complete the motor judgment. Order in which PD patients completed the trials (more affected hand vs. less affected hand; DBS-ON vs. DBS-OFF) was randomized. The order in which control subjects completed the trials (dominant vs. non-dominant hand) was randomized as well.

Parkinson's disease patients	DBS	Probing Hand	Trials
Perceptual Judgments	**ON**	More affected	30
		Less affected	30
	OFF	More affected	30
		Less affected	30
			Total = 120
Motor Judgments	**ON**	More affected	30
		Less affected	10
	OFF	More affected	30
		Less affected	10
			Total = 80
Age-matched healthy controls			
Perceptual Judgments		Dominant hand	30
		Non-dominant hand	30
			Total = 60
Motor Judgments		Dominant hand	30
		Non-dominant hand	30
			Total = 60

Measurements and Analysis

Perceptual judgments. Verbal responses of "Which block is taller?" were recorded. The percentage of correctly perceived as taller (PR) was computed for each comparison block size and pooled across all subjects for each condition. Based on the responses, a Boltzmann sigmoidal function of the following form was fitted to the data:

$$PR = \frac{C_i - C_f}{1 + e^{(x - x_0)/dx}} + C_f \qquad \text{Equation 1}$$

where PR is the percentage perceived as taller, C_i is the initial constant and C_f is the final constant to be estimated, e is Euler's number (2.7183), x is the presented comparison block size, x_0 is the center point of inflection, and dx is the rate of change, or in other words, the change in x corresponding to the most significant change in PR values. Based on the fitted function the discrimination threshold (DT) at the 75% correct response level was derived. For each DT a corresponding uncertainty area (UA), defined as the area between 25% and 75% perceived as taller, was computed. Since data were pooled across all subjects, differences in DT between conditions were determined by evaluating slopes of the fitted functions within the UA. A two-sample t-test was used to determine if the slopes were significantly different between conditions. Furthermore, percentage of total correct responses was calculated for each subject. A difference in means between conditions was analyzed using a one-way ANOVA.

Motor judgments . Three dimensional position coordinates for the tip of the index finger and thumb were recorded for a period of 5 s at 120 Hz. Using customized software routines based on Matlab Technical Programming Language (Matlab 7.0, The MathWorks, Inc., Natick, Massachusetts), finger position coordinates were used to calculate raw aperture size, i.e., the distance between the index finger and thumb, which correspond to the participant's judged height of a given block. The last 0.5s of the time series data for each trial was averaged and this mean raw aperture size value was used as the participant's judgment of block height.

Because reflective tape was wrapped around the tips of each subjects fingers and because the motion capture system records 3-dimensional position data relative to the center of each recorded maker, a *finger size correction* had to be made to take into account individual finger size. This was necessary to assure that recorded size judgments were based on the distance between the surface of the fingers and not the distance between the centers of each finger. Therefore, prior to data collection, subjects were asked to hold the 6 cm tall reference block in a static position using a precision grip (index finger and thumb) while their hand was recorded by the motion capture system for 5 s. This *finger size correction* term was defined as the absolute difference between hand aperture size and the physical height of the 6 cm block. The *finger size correction* term was then subtracted from the *raw aperture size* to determine *adjusted aperture size*:

adjusted aperture size = raw aperture size – finger size correction Equation 2

Adjusted aperture size was then used to determine the *aperture error. Aperture error* was computed as the difference between the adjusted aperture size and the actual height of the grasped comparison block:

aperture error = adjusted aperture size – actual block height Equation 3

This aperture error reflected how much a grip aperture (motor judgment) deviated from the actual height of the block being judged. Differences in mean aperture error between all conditions and all comparison block sizes was determined using a 5 (conditions) x 10 (comparison block sizes) repeated measure ANOVA. A level of $\alpha = 0.05$ was used for all statistical tests.

Link between perceptual and motor judgments. To examine the relationship between the two haptic precision measurements, a linear regression analysis was performed between DT and mean aperture error for each group/condition. A Pearson's product-moment correlation coefficient (r) was calculated by applying a linear fit using the following formula:

$$y = mx + b \qquad \text{Equation 4}$$

To examine the relationship between correct response rates and aperture errors, a set of confidence ellipses were applied to each group/condition which represented 95% confidence intervals of the group centroids. These ellipses graphically indicate the correlation between the two variables for each respective condition. A confidence ellipse was defined as:

Relationship between haptic acuity measures and clinical observations. To examine the relationship of both UPDRS-III scores and mean aperture error with duration of DBS treatment, a linear regression analysis was performed using a linear fit function based on Equation 4. Pearson's product-moment correlation coefficients for both relationships were then calculated based on the linear fit.

Results

Deficits Due to Parkinson's Disease

Perceptual judgments. In order to get a sense of the magnitude of deficits in haptic acuity seen in Parkinson's disease, discrimination thresholds were evaluated against the healthy control group. When PD patients used their *more* affected hand for probing, in the DBS-OFF state, their discrimination threshold was larger when compared to controls (DT for PD: 6.37cm; controls: 6.11cm). An analysis of slopes of the fitted functions showed the two groups were significantly different from each other (t_{18} = -35.23, p < 0.001). Figure 3A shows the respective fitted functions and 75% discrimination thresholds for the *more* and *less* affected hand of the PD patients and the control group.

To obtain a measure of overall error in the *perceptual* task, the total percentage of correct responses was also computed for each group. The mean correct response rate was significantly lower in the PD group compared to the control group (mean ± SE, PD: 77.0% ± 3.13; control: 85.9% ± 2.21; $F(1,18) = 5.01$, $p = 0.04$) (see Figure 3B).

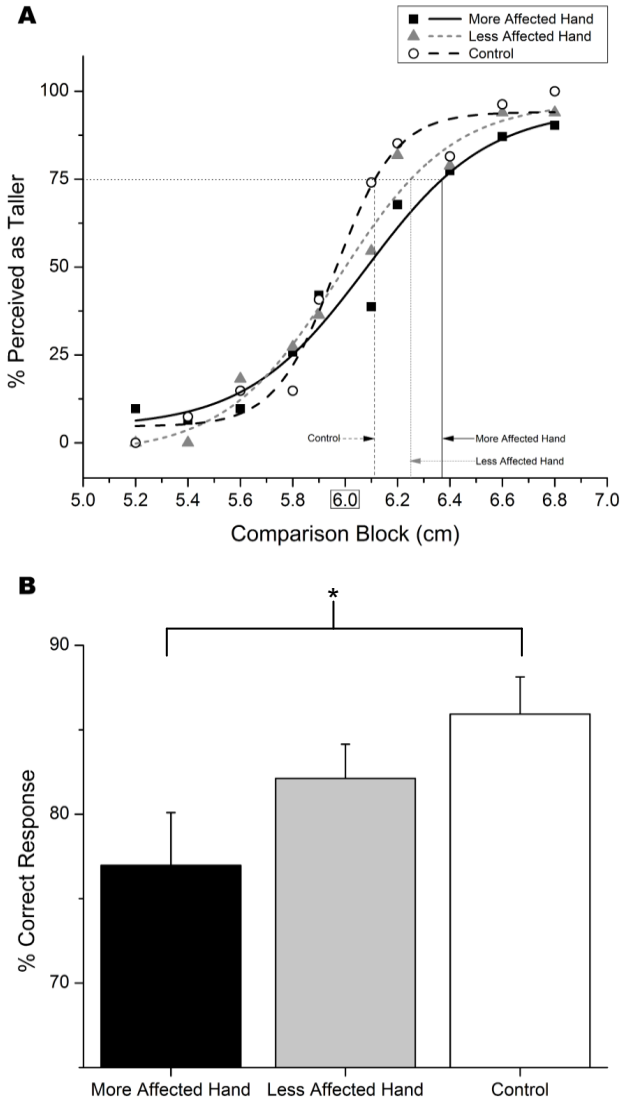

Figure 3. Perceptual judgment results for PD patient's *more* & *less* affected hand as well as the control group. **A)** Psychometric curvature functions for the control group as well as the PD group, in the DBS-OFF state using their *more* affected hand as well as their *less* affected hand to probe the comparison block. The fitted functions show the relationship between the comparison block size and the percent perceive as taller (than the 6cm reference block - boxed). The horizontal dashed line indicates 75% perceived as taller (75% correct response rate) and the respective vertical lines indicate the DT that corresponds to the 75% perceived as taller level. **B)** Mean percent of correct responses for the perceptual judgment task for the control group and the PD patients in the DBS-OFF state. (* indicates significant difference)

Motor judgments. In order to evaluate the effects of PD on accuracy of motor based judgments, aperture error was evaluated between PD patients using their *more* affected hand to probe the block in the OFF state and the control group. An analysis between comparison block sizes showed no differences in aperture errors ($p = 0.63$). Therefore, aperture error was collapsed across all block sizes giving each subject one mean aperture error for each condition. Data were either partially or completely lost in two of the subjects. One case was due to the subject not being able to complete the trials due to being uncomfortable and the other due to equipment errors, therefore, data of both subjects was excluded from analysis. Mean aperture error in PD patients showed to be significantly higher compared to the control group (mean ± SE, PD: 1.48cm ± 0.31; control: 0.75cm ± 0.11; $F_{1,16} = 4.83$, $p = 0.04$) (see Figure 4).

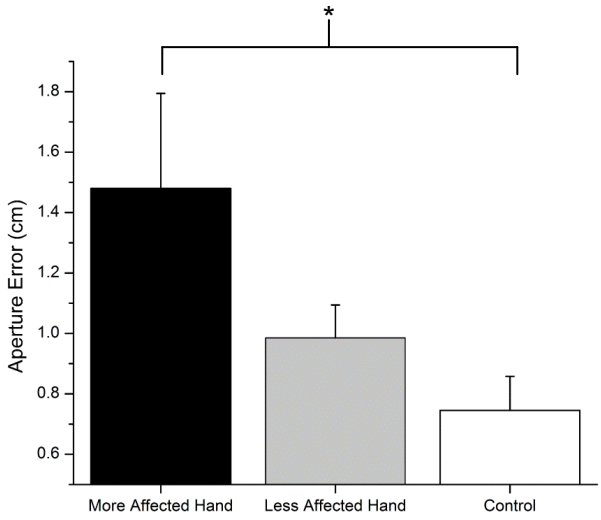

Figure 4. Motor judgment results for PD patient's *more* & *less* affected hand as well as the control group. Mean aperture error for the motor judgment task for the control group and the PD patients in the DBS-OFF state. Aperture error indicates the size deviation between the actual height of the block they are probing and their corresponding grip aperture intended to match the size of the block being probed. The bar graphs for the PD group are labeled according to the hand used for probing, which would then mean their other hand was used to perform the (grip aperture) motor judgment. (* indicates significant difference)

Effect of Deep Brain Stimulation on Haptic Sensing

Perceptual judgments. In order to evaluate the impact of DBS on haptic acuity, discrimination thresholds of PD patients in the DBS-OFF state were compared to being in the DBS-ON sate. STN-DBS had a positive effect on haptic perception in the *more* affected hand of PD subjects, lowering the DT of PD subjects in the DBS-ON state as well as increasing their overall percentage of correct responses compared to the DBS-OFF state. Specifically, while in the ON state, PD patients had a lower DT (DT = 6.26cm) compared to being in the OFF state (DT = 6.37cm). An analysis of slopes of the fitted functions showed the two groups were significantly different from each other (t_{18} = 17.62, $p < 0.001$). Figure 5A shows the respective fitted functions and discrimination thresholds for the ON and OFF state.

PD patients in the ON state produced a higher correct response rate (mean ± SE, 83.0% ± 2.22), compared to the OFF state (Figure 5B). However, the two conditions were not significantly different from each other ($p = 0.13$).

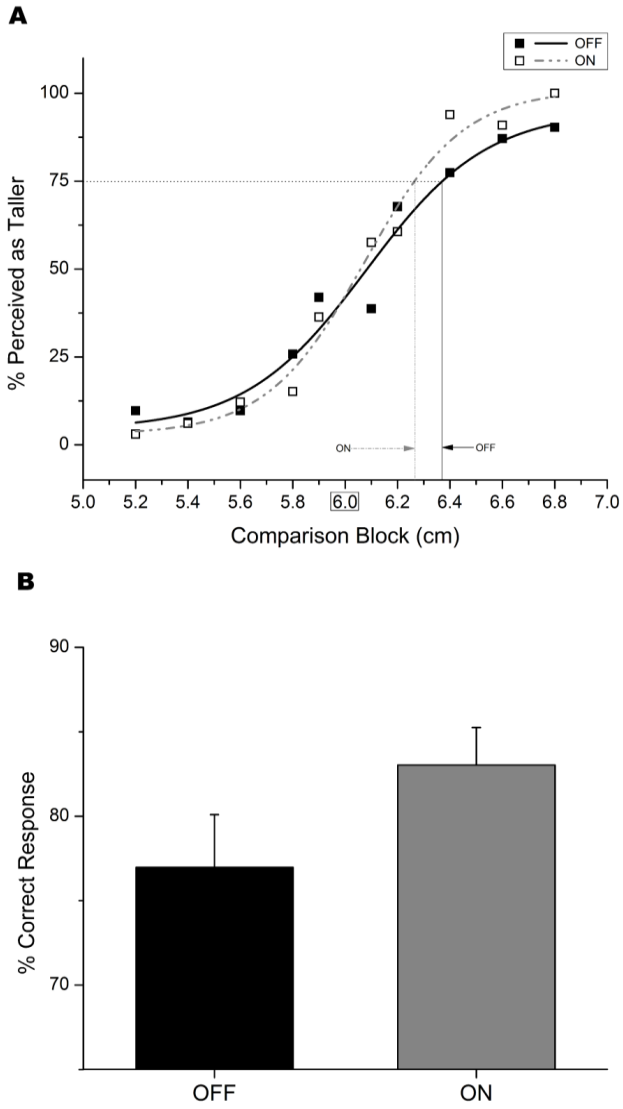

Figure 5. Perceptual judgment results for PD patients in the DBS-OFF vs. DBS-ON state. **A)** Psychometric curvature functions for the PD group, using their *more* affected hand to probe the block, in the DBS-OFF and ON state. The fitted functions show the relationship between the comparison block size and the percent perceive as taller (than the reference block). The 6cm reference block is indicated on the x-axis by a box around it. The horizontal dashed line indicates 75% perceived as taller (75% correct response rate) and the respective vertical lines indicate the DT that corresponds to the 75% perceived as taller level. **B)** Mean percent of correct responses for the perceptual judgment task for the PD patients in the DBS-OFF vs. ON state.

Motor judgments. In order to understand the impact of DBS on motor based judgments, aperture error was evaluated in PD patients when in both the DBS-OFF and ON states. PD patients (probing with the *more* affected hand) in the ON state demonstrated a decrease in aperture error compared to being in the OFF state (mean ± SE, ON: 1.25cm ± 0.17; 1.48cm ± 0.31) (see Figure 6). The difference was not statistically significant ($p = 0.54$).

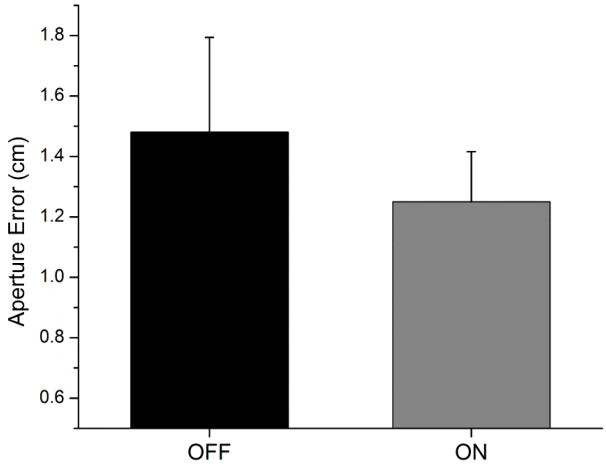

Figure 6. Motor judgment results for PD patients in the DBS-OFF vs. DBS-ON state. Mean aperture error for the motor judgment task for the PD patients, using their more affected hand, in the DBS-OFF vs. ON state. Aperture error indicates the size deviation between the actual height of the block they are probing and their corresponding grip aperture intended to match the size of the block using their other hand.

More vs. Less Affected Hand in PD

Perceptual judgments. In order to understand the effects of the progression of PD on haptic acuity, the *less* affected hand was also tested in PD patients. During the OFF state, when PD patients probed the block using their *less* affected hand, the corresponding DT was lower compared to probing with the *more* affected hand (DT for *less*: 6.25cm; *more*: 6.37cm. A comparison of slopes between the fitted functions showed a significant difference between the two conditions ($t_{18} = -9.47$, $p < 0.001$). Figure 3A shows fitted

curves and respective discrimination thresholds for the *less* affected and *more* affected hand (as well as the control group).

When evaluating total percentage of correct responses, probing with the *less* affected hand resulted in a higher mean correct response rate than probing with the *more* affected hand (mean ± SE, *less*: 82.3% ± 2.22; *more*: 77.0% ± 3.13) (see Figure 3B). This effect was not significantly different ($p = 0.19$).

Motor judgments. To evaluate the progression of PD as well as to provide insight into the influence of haptic acuity on motor based judgments, aperture errors were compared between the *more* and *less* affected hand. When PD patients probed the block with their *less* affected hand while in the OFF state, they demonstrated a decrease in mean aperture error when compared to probing t with their *more* affected hand. Specifically, probing with the *less* affected hand resulted in a lower mean aperture error compared to probing with the *more* affected hand (mean ± SE, *less*: 0.99cm ± 0.11; *more*: 1.48cm ± 0.31) (see Figure 4). These results, however, were not statistically significant ($p = 0.16$).

Link Between Perceptual and Motor Judgments

To provide further insight into the link between perceptual and motor judgments, correlations were analyzed between the data sets. We quantified the relationship between the discrimination threshold levels of each condition/group and mean group aperture errors. This resulted in a Pearson's product-moment correlation coefficient of $r = 0.96$ (Figure 7), which was significant ($p = 0.04$). Next, individual correct response rates were plotted against aperture errors. Confidence ellipses were applied to each condition/group and are shown in Figure 8.

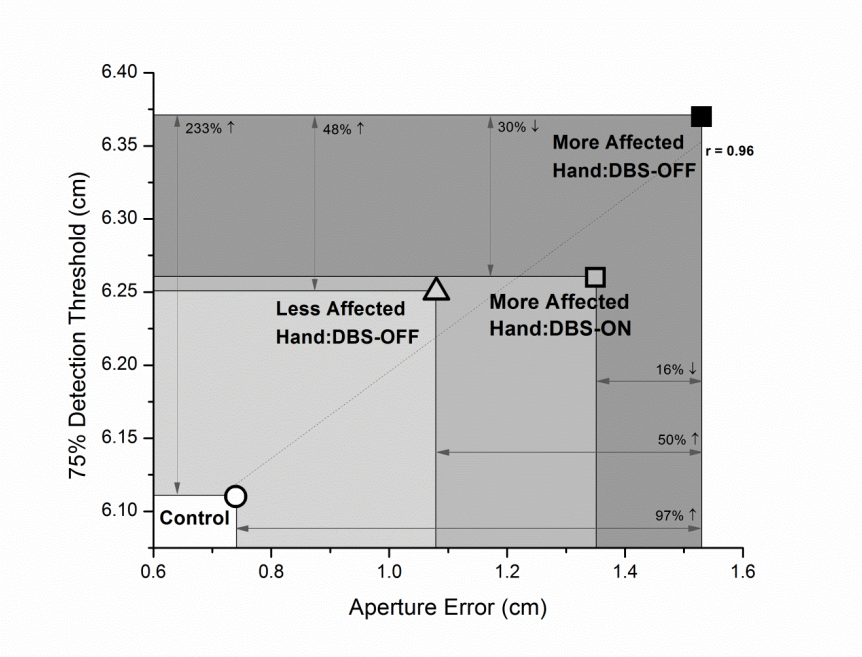

Figure 7. Discrimination Thresholds versus Aperture Error. Relationship between 75% DT and aperture error for all four group/conditions. Shaded areas highlight each group's relative relationship to each other. Arrows indicate percent difference between respective groups.

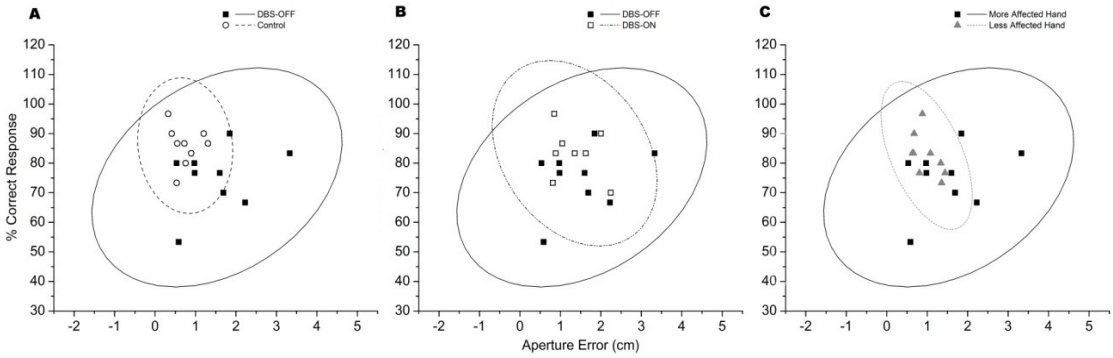

Figure 8. Correct response rate versus aperture error. Scatter plot showing relationship between correct response rate and aperture error for all individuals in each respective condition. Ellipsoidal curves represent 95% confidence intervals of the group centroids. A) Control group versus PD subjects in the DBS-OFF state using their *more* affected hand to probe the blocks. B) PD subjects in the DBS-OFF versus DBS-ON state using their more affected hand to probe. C) PD subjects in the DBS-OFF state using their *less* affected hand versus *more* affected hand to probe the block.

Relationship Between Haptic Acuity Measures and Clinical Observations

A set of regression analyses were performed to better understand how the measured aperture errors corresponded to clinical outcome measures. First, a linear regression analysis was performed between motor-UPDRS scores and aperture errors of the *more* affected hand, neither of which were statistically significant (DBS-OFF: r = 0.15, p = 0.69; DBS-ON: r = 0.31, p = 0.45). Second, the relationship between disease duration and motor-UPDRS scores were analyzed, showing neither to be statistically significant (DBS-OFF: r = -0.06, p = 0.85; DBS-ON: r = 0.16, p = 0.65).

Next, a set of regression analyses were performed to evaluate the effect of the duration of time that the patient has been treated with DBS. This was done to better understand both the long term affects of DBS and whether DBS maintains similar effects over time. The first analysis investigated the relationship between the duration of time since the DBS electrode was implanted and UPDRS-III scores (See Figure 9A). Results of the analysis yielded correlation coefficient values of r = 0.14 (DBS-OFF, p = 0.69) and r = 0.33 (DBS-ON, p = 0.33). The final analysis investigated the relationship between the duration of time since the DBS electrode was implanted and mean aperture error of the *more* affected hand in PD, in both DBS-OFF and ON states (See Figure 9B). Results of the analysis yielded correlation coefficient values of r = 0.94 (DBS-OFF, $p < 0.001$) and r = 0.51 (DBS-ON, p = 0.19).

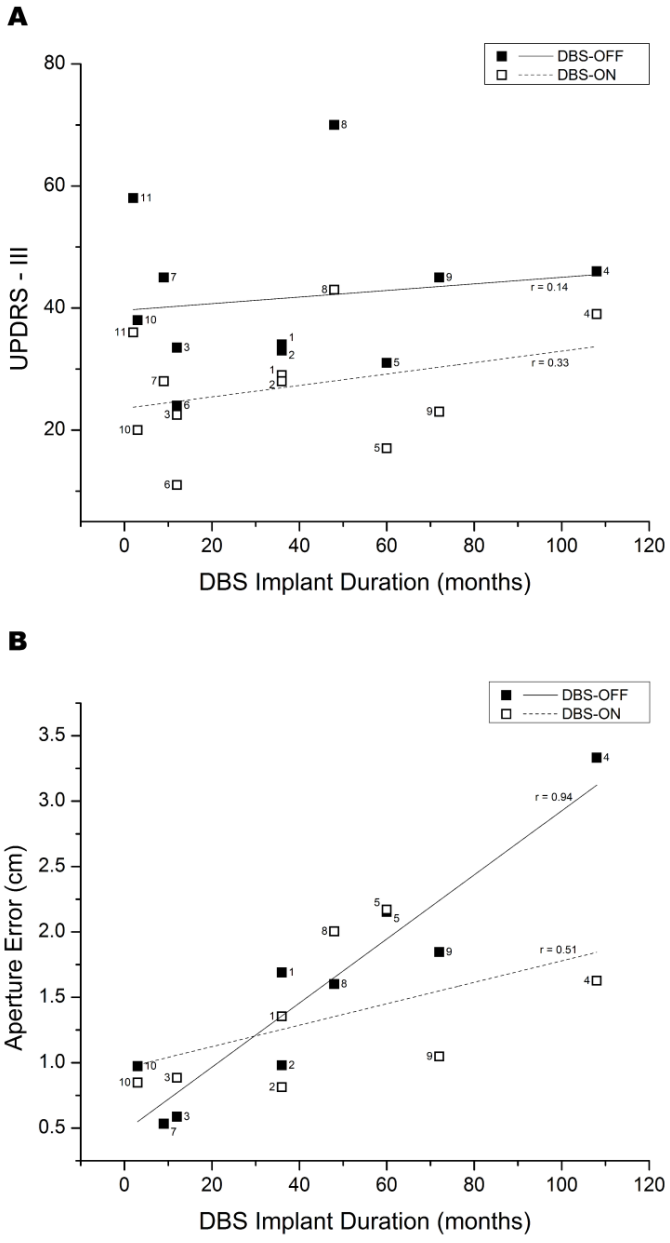

Figure 9. Relationship between duration since DBS implant and UPDRS, haptic precision. Linear fits are shown for both the DBS-OFF and ON states. Marker labels indicate patient number. **A)** Relationship between UPDRS-III scores of PD patients and number of months the patient has been implanted with the DBS electrode. UPDRS scores could range between 0-112. **B)** Relationship between aperture errors of PD subjects using their *more* affected hand to probe the block versus number of months the patient has been implanted with the DBS electrode.

Discussion

This study examined the effects of STN-DBS on haptic perception. Measures of haptic acuity were either based on "non-motor" verbal judgments reflecting the effect of DBS on perceptual processing, or they involved shaping the non-probing hand according to the perceived size. Thus, the second measure reflected perceptual and sensorimotor processing. The main findings of this study were as follows: First, it confirmed earlier reports (Konczak et al., 2008; Li et al., 2010) that PD leads to a reduction in haptic precision as documented by increased discrimination thresholds and an increase in aperture error. Second, STN-DBS improved haptic acuity when compared to the DBS-OFF state in our PD patient sample. STN-DBS also decreased aperture error during *motor* judgments. That is, the deviation between the actual height of the block being probed and their grip aperture judging the height of the block became smaller in the DBS-ON state when compared to the DBS-OFF state. Third, PD patients probing with their *less* affected hand resulted in more precise perceptual *and* motor judgments than probing with the *more* affected hand.

Haptic Precision is Reduced in PD

A main finding of this study was that haptic acuity was reduced in PD subjects. Compared to control subjects, PD subjects showed a 233% increase in discrimination threshold in the DBS-OFF state and a 10% decrease in mean correct response rate. These findings indicate that haptic precision is significantly compromised in PD. These findings corroborate the findings of previous studies that showed deficits in proprioceptive processing in PD. For example, a study by Maschke et al. (2005) evaluating detection thresholds for arm position sense showed a 177% decrease in kinaesthetic sensitivity when compared to a control group. Likewise, Li et al. (2010) and Konczak et al. (2008) reported elevated detection thresholds of PD subjects when judging the curvature of a virtual contour in comparison to controls. The results of the current study in conjunction with these previous reports of degraded kinaesthetic and haptic precision and other studies showing proprioceptive deficits in PD (O'Suilleabhain, Bullard, & Dewey, 2001;

Zia, Cody, & O'Boyle, 2003), may indicate a more generalized deficit in somatosensory processing.

With respect to the *motor* task, PD subjects showed a 97% increase in aperture error compared to the control group. In this task, subjects first relied on haptic *sensory* information to explore the size of the block with one hand and then *motorically* indicated the size of that block with the other hand. Active movements, such as those used to perform the motor judgment, rely on *sensorimotor* integration processes. Relative to the motor component of this task, it is thought that humans use previously stored motor commands to predict movements as well as predict the sensory feedback resulting from these movements (Holst, 1973). Copies of these motor commands are thought to be stored in the cerebellum and the predicted sensory feedback is derived from processes within the cerebro-cerebellar loop (Wolpert, Miall, & Kawato, 1998). This loop is thought be spared in PD (Maschke et al., 2003). Given this information, it would then seem plausible to hypothesize that motor deficits seen in PD are a function of altered somatosensory processing, independent of goal-orientated motor function. Results of this study show that deficits seen in the *perceptual* task are quite pronounced when compared with controls, but differences between PDs and controls are mildly reduced when judgments were made motorically. These results may show support for the presumed intact involvement of the cerebro-cerebellar loop and indicate evidence for altered sensory processing. Evidence for altered *sensorimotor* integration would be indicated by a relative difference between PD and controls in the *perceptual* judgments, followed by an even more pronounced relative difference between PDs and controls in the *motor* judgments, which we did not find. The slightly reduced but still significant differences between PD subjects and controls from the *perceptual* judgment to the *motor* judgment may shows support for the conclusions by Konczak et al. (2008) that intact information derived from active movements slightly masked proprioceptive deficits seen in PD but could not overcome these deficits in proprioceptive processing during the motor judgments.

Effects of STN-DBS on Haptic Acuity.

Currently there is minimal research as to the effects of DBS on somatosensory processing (Maschke et al., 2005). Our results indicate that STN-DBS has a positive effect on proprioceptive function. Relative to *perceptual* judgments STN-DBS resulted in a 30% decrease in DT compared to when in the DBS-OFF state. Likewise, STN-DBS also resulted in an 8% increase in correct response rate compared to the DBS-OFF state. These findings corroborate the findings of Maschke et al. (2005) who evaluated the degree of passive limb displacement required to detect arm movement. Results of that study showed a 20% decrease in threshold as a result of STN-DBS.

STN-DBS also had a positive effect on motor judgments. Relative to the *motor* task, STN-DBS resulted in a 15% decrease in mean aperture error. Two subjects did not show a decrease in aperture error in the DBS-ON state, however, the remaining subjects showed a 12-51% decrease in aperture error. In this case it is possible that significance was not reached due to a small sample size. It is also possible that significance was not reached like it was in the *perceptual* task due to the inclusion of a motor judgment task which involves an additional active movement. As stated previously, the seemingly intact cerebro-cerebellar loop may have masked some deficits in proprioceptive processing, resulting in no significance.

Although the exact therapeutic mechanism underlying the beneficial effect of STN-DBS is relatively unclear, there are a few hypotheses proposed to explain the relief of symptoms due to DBS: direct inhibition, indirect inhibition of pathological activity, increased regularity of globus pallidus interna and reduced miss-information, and resonance and carrier signal effect (Montgomery & Gale, 2008). Direct inhibition was initially a popular hypothesis given the similar effects seen between ablation and stimulation. However, this hypothesis is widely discounted since a large number of studies involving downstream structures have demonstrated changes consistent with increased activation of outputs from stimulated structures (Montgomery & Gale, 2008). Furthermore, McIntyre & Grill (1999) showed stimulation could hyperpolarize the cell body and dendrites and also excite an action potential at the axon initial segment, showing evidence for both an inhibitory and excitatory effect. One of the more intriguing

and increasingly popular hypotheses is in regard to the increased regularity of globus pallidus interna and reduced miss-information. This may indicate that stimulation of a structure is not exclusive to either inhibition or excitation, but rather to the enhanced regulation of the two processes. A study by Dorval, Kuncel, Birdno, Turner, and Grill (2010) also showed support for the notion that increased regularity within the basal ganglia leads to diminished motor symptoms associated with PD. The study by the Dorval et al. group showed that when patients with STN-DBS were stimulated with irregular DBS, bradykinesia symptoms were not alleviated. However, when stimulated with regular (130Hz) patterns, bradykinesia was alleviated. They concluded that eliminating irregular activity in the globus pallidus interna should reduce information processing errors within the thalamus and alleviate symptoms. This finding was also offered previously by Birdno & Grill (2008) who showed that regulating pathological patterns of activity, independent of firing rate, alleviated motor symptoms.

Since there is evidence that DBS has an effect more downstream than just locally on the stimulated structure (Montgomery & Gale, 2008), it is then important to consider the functional organization of the cortico-subthalamo-pallidal pathway. The STN, one of the main input structures of the basal ganglia, receives projections from multiple cortical motor areas, including the primary motor cortex, premotor cortex, supplementary motor area, and pre-supplementary motor cortex and these pathways are characterized by a predominant sensorimotor component (Romanelli, Bronte-Stewart, Heit, Schaal, & Esposito, 2004). Furthermore, movement related neurons have been identified within the STN, creating multiple somatotopic organizational maps that mirror the relative structures to which it is connected (Romanelli et al., 2004). Although functional organization relative to the movement specific neurons within the STN is not completely clear, one consistent finding in PD is evidence for excessive activity in the STN (Kopell, Rezai, Chang, & Vitek, 2006). This includes an increased amount of neurons responding to multiple movement stimulations and increased response to multiple sensory modalities, diminishing their anatomical specificity of response (Romanelli et al., 2004). Accepting the hypothesis from Dorval, Kuncel, Birdno, Turner, and Grill (2010) that

DBS relieves symptoms by minimizing pathologically disordered neuronal activity in the basal ganglia, it is possible that STN-DBS then re-establishes functional specificity of the STN. This subsequently improves processing of somatosensory information which is then used for sensorimotor processing and ultimately for motor function.

Viewing Parkinson's Disease as a Sensory Disorder

More versus less affected hand. To help shed some light on the effect PD has on proprioceptive processing, we also evaluated patient's less affected hand. Knowing the initial unilateral affect of PD, leading to a motorically *more* affected and *less* affected side, investigating the perceptual deficits of the *less* affected hand may provide further insight into how PD affects somatosensory function. PD patients revealed improvements in haptic acuity in both the *perceptual* and *motor* judgments when using their *less* affected hand to probe the blocks when compared to probing with their *more* affected hand. Using their *more* affected hand to probe the block resulted in a 48% increase in DT compared to using their *less* affected hand. This indicated that PD patients were haptically more sensitive when using their less affected hand, which we expected. These results also corroborate a previous study by Maschke et al. (2003), who showed a 40% reduction in DT when using the *less* affected arm compared to the *more* affected arm. Furthermore, when PD patients used their *more* affected hand to probe the blocks, they showed a 50% increase in mean aperture error when compared to probing with their *less* affected hand. Keeping in mind that subjects probe with one hand and motorically judge with the other, this means that PD patients were more accurate in making motor judgments with their *more* affected hand (i.e. the hand showing a greater motor impairment) and less accurate when using their *less* affected hand to perform the motor judgments. The emerging picture is that when proprioceptive information is relatively precise, motor judgments are more accurate. This result may provide evidence that PD does not directly affect motor capabilities but rather somatosensory processing, which leads to compromised motor function.

Perceptual versus motor judgments. To highlight the relationship between perceptual acuity and the subsequent motor judgment, grouped data of both judgments were plotted

against each other (Figure 7). This relationship shows the relative effect PD has on haptic perceptual acuity and how DBS can alleviate these deficits, albeit not to the level of controls. The figure also shows the relationship between haptic perceptual acuity (DT) and motor judgments (aperture error) despite the clinically defined motor function of each hand, indicating that the accuracy of the motor judgments correlated to haptic acuity with little influence by the clinically defined motor deficits. This means that probing with the *less* affected resulted in a more precise haptic sense and this was also seen in the motor judgments despite using the motorically *more* affected hand for motor judgments. This indicates that sensory processing relative to the less affected hand is less diminished compared to the *more* affected hand and thus produces more precise judgments. DBS then improves sensory processing, resulting in more precise judgments compared to the DBS-OFF state. Figure 8 then shows the relationship between the haptic acuity measures of correct response rate and aperture error for all subjects. The ellipsoid curves within each graph provide insight into the variability of individual subjects between each condition/group. The graph indicates the relatively high variability among PD patients probing with their *more* affected hand in the OFF state. Variability then decreases in the DBS-ON state compared to the OFF state. Furthermore, variability decreases further when subjects probe with their *less* affected hand. These findings may corroborate the hypothesis of Dorval et al. (2010) in that the high variability seen in haptic perceptual judgments may be a function of irregular neuronal firing patterns. The regulation of firing patterns due to DBS may then improve somatosensory processing, which then reduces the variability of proprioceptive-based judgments.

Haptic acuity measures versus clinical outcomes. The current gold standard of clinically rating deficits in PD is the UPDRS and more specifically, rating motor function, the UPDRS-III. Results of this study showed no significant correlations between UPDRS-III scores and haptic acuity in neither the *perceptual* task nor the *motor* task. This may be due to the coarseness of the UPDRS scale. A further analysis of clinical outcomes revealed some interesting correlations. Figure 9A shows the correlation between the number of months since the patient was implanted with the DBS electrode

and UPDRS-III scores. Although a linear regression analysis reveals a slight increase in UPDRS-III scores as DBS implant duration increases, the correlation is low. Figure 9B shows the correlation between the number of months since the patient was implanted with the DBS electrode and aperture error. This correlation showed to be relatively strong, particularly in the DBS-OFF state, with aperture errors increasing as implant duration increases. Interestingly, aperture errors correlated poorly with both disease duration and age. Any notion of long term effects of DBS treatment is speculative and needs further investigation as previous literature on the effects of chronic DBS is limited and inconclusive (Castrioto et al., 2011; Vitek, 2012). Aside from the possible effects of chronic DBS, when comparing the two relationships to each other (Figure 9A & 9B), it is clear that the stronger correlation lies in the relationship between aperture error and DBS implant duration. Given the UPDRS is purely a measure of motor function whereas aperture error is based on sensory information, this may suggest that the assessment of proprioceptive function provides an alternative, and possibly more precise representation of the severity of the disease state. Of course, this can in part be argued against since aperture error did not correlate strongly with disease duration. However, validated UPDRS scores also show a poor correlation with disease duration. Even so, the relationship between disease duration and disease state can vary greatly between patients. Importantly, what can be taken from figure 9B is the effect that DBS has on haptic function. In the DBS-OFF state aperture errors show a strongly correlated increase as DBS implant duration increases. However, DBS was able to alleviate this affect by reducing aperture errors. This highlights the favorable effect of DBS on haptic function and presents further evidence for the notion that DBS provides a beneficial effect on proprioceptive processing.

Alternative Conclusions

Haptic deficits in PD. One possible explanation for differences in thresholds for PD patients has been the effects of dopamine replacement therapy. Previous studies have shown mixed results as to the effects of dopamine replacement therapy on perceptual sensitivity (Li et al., 2010; O'Suilleabhain et al., 2001). However, in our study we

attempted to control for this factor by having patients refrain from taking any Parkinsonian related medication within 12 hours of participation in the study. Another factor that may influence deficits in PD thresholds is cognitive dysfunction. A series of examinations were given to all PD subjects in an attempt to exclude those showing significant cognitive dysfunction. Results of the examinations showed no pronounced decline in any of the subjects. Likewise, working memory has been shown to decline in PD. Although this cannot be completely ruled out as a confounding factor, the duration of time between probing the reference block and probing the comparison block (~ 1s) would seemingly not be a duration that would cause significant compromise.

A final possible influencing factor may lie within the transfer of perceptual information from one hand to the other during the motor judgment. The noise introduced during the perceptual judgment, and subsequent sensorimotor task, due to inter-hemispheric transfer may have had a significant influence on data outcomes. We attempted to control for this between the control group and PD subjects by dominant hand matching control subjects to the PD subjects. This means that nine of the eleven PD subjects were motorically *more* affected on their dominant hand and two subjects were *more* affected in their non-dominant hand. To control for this in group comparisons, the control group data included two age-matched control subjects using their non-dominant hand to complete the paradigm. Furthermore, the transfer of somatosensory information has shown to be primarily transferred via the posterior corpus collosum, which has been shown to be intact on PD patients (Boelmans et al., 2010). However, portions of the anterior corpus collosum have been shown to be diminished in PD patients, which involve connections to the premotor cortex (Gattellaro et al., 2009). So this diminished functional connectivity cannot be completely discounted but differences seen in this study are unlikely due to this since similar differences have been shown in studies involving unilateral perceptual judgments where no interhemispheric transfer of information was required.

Effects of STN-DBS. One influencing factor could be the order in which PD subjects completed the paradigm. We attempted to control for an order affect by randomizing the

order in which the tasks were completed (first DBS-OFF then DBS-ON; ON then OFF). The time period to turn from DBS-ON to DBS-OFF, or vice versa, may also influence data. We also attempted to control for duration between changes in state. A waiting period of 20 minutes (minimum) was required as the waiting time between turning the DBS device ON or OFF which was validated by Waldau et al (2011) as a sufficient amount of time to cause a change in state. Subjects were also asked to verbally indicate whether they felt ON or OFF, depending on the state change.

STN-DBS is also most certainly influenced by the location of the implanted electrode as well as the stimulation parameters which include: number of contacts used, voltage, rate of stimulation, and pulse width. Although recognized as major influencing factors, the impact of each parameter on neurophysiological function is not well understood and the heterogeneity among patients relative to these parameters makes it difficult to control for and is beyond the scope of this study.

Conclusions

This study provides insight into deficits in haptic perceptual processing in PD. This study also quantified, for the first time, that STN-DBS improves the processing of somatosensory signals used for haptic perception and sensorimotor control. Treatment of STN-DBS substantially improved haptic acuity which was also reflected in improved motor judgments. These data provide promising results that improving somatosensory and especially proprioceptive processing in PD may be beneficial for improving upper limb motor function. Although the exact physiological basis underlying the effects STN-DBS has on motor function is not yet clear, results of this study add to evidence that the basal ganglia, specifically the STN, is central to proprioceptive and sensorimotor processing. In this sense, the enhanced motor function due to STN-DBS seen in PD may, in fact, be a result of restoring proprioceptive and somatosensory processing.

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