Preliminary Voice and Speech Analysis Following Fetal Dopamine Transplants in 5 Individuals With Parkinson Disease

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A surgical procedure involving transplantation of fetal dopamine cells into the striatum of persons with advanced Parkinson disease (PD) has recently been performed in an attempt to alleviate Parkinsonian and drug-dose related symptoms (e.g., the "on-off" phenomena). Improvements in limb motor and neurological function, as well as less severe and shorter on-off episodes have been reported following fetal cell transplant (FCT) surgery. Acoustic, electroglottographic, and perceptual measures were analyzed pre- and post-surgery to determine if phonatory and articulatory function were affected by this relatively new form of treatment. In addition, speech and motor exam measures were compared to determine if similar directional changes across motor systems were apparent. Findings suggest that FCT surgery did not systematically influence voice and speech production. Also, it appears that FCT surgery may differentially affect phonatory, articulatory, and limb motor systems. Findings are discussed relative to these differential effects.

KEY WORDS: fetal cell transplant, Parkinson disease, acoustic, voice, speech

The discovery that Parkinson disease (PD) is caused by a nigrostriatal dopamine deficiency has led to fairly successful management of this disease with L-dopa. However, problems, such as drug resistance and drug-dose related fluctuations, occur in some individuals after prolonged, continuous use (Barbeau, 1974; Marsden & Parkes, 1976). For this reason, neural transplantation of fetal dopamine tissue in PD has been pursued. The underlying principle of this procedure is that neural transplantation may replenish the dopamine deficiency by stimulating a steady and sustained release of this neurotransmitter or its precursors directly into the brain (Stein & Glasier, 1995).

Initial fetal cell transplantation (FCT) trials in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine induced Parkinsonian animal models suggested that transplanted dopaminergic neurons can survive and produce improved motor and neurologic function (Bakay et al., 1987; Redmond et al., 1986; Sladek et al., 1987). Subsequent clinical trials of human FCT surgery have proved beneficial for some individuals with PD. Improved simple and complex movements of the extremities, as measured by standardized rating scales and timed tests of motor performance, have been observed (Freed et al. 1992; Freed et al., 1990; Lindvall et al., 1989; Widner et al., 1992). Less severe and shorter on-off episodes

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and reduced drug doses are other positive findings that have been reported following mesencephalic fetal cell transplantation to the striatum (Freed et al., 1992; Lindvall et al., 1989), with some improvements lasting up to 3 years (Lindvall et al., 1994). Physiologic evidence obtained from positron emission tomography scans tends to support these behavioral observations. Progressive increases in 6-L-[¹⁸F] fluorodopa uptake have been found in transplant areas (Freed et al., 1992; Lindvall et al., 1990; Peschanski et al., 1994; Sawle et al., 1992; Spencer et al., 1992), suggesting restoration of dopamine synthesis or transmission. In addition, examination of neural tissue from FCT recipients post-mortem shows grafted dopaminergic neurons do indeed reinnervate the striatum (Kordower et al., 1995). Although these cumulative findings are encouraging and indicate positive effects, many questions concerning the underlying mechanism of change and the long-term and overall effects of the surgery remain unanswered.

One such question relates to the effect of this surgical procedure on speech and voice production. Numerous studies have shown that both phonatory and articulatory disorders are prevalent in PD (Darley, Aronson, & Brown, 1969; Logemann, Fisher, Boshes, & Blonsky, 1978). Descriptors associated with the voice and speech of individuals with PD include hoarseness, reduced vocal loudness, and pitch variability and imprecise articulation (Aronson, 1990). The effect of neurosurgical and neuropharmocological treatment on the voice and speech characteristics of individuals with PD requires further investigation, but there is evidence to suggest that these treatments differentially affect voice, speech, and limb motor systems. Persons who undergo ablation or electrical stimulation of thalamic nuclei usually experience amelioration of tremor and rigidity, but may develop speech symptoms similar to dysarthria (Cooper, 1961; Petrovici, 1980;). As mentioned, L-dopa can alleviate symptoms in the limbs, but similar effects on respiratory and phonatory systems have not been observed (Daniels, Oates, Phyland, Feiglin, & Hughes, 1996; Larson, Ramig, & Scherer, 1994; Solomon & Hixon, 1993). Despite these reports of differential effects, there are neuroanatomical and physiological reasons to believe similar outcomes may occur across phonatory, articulatory, and limb motor systems following FCT surgery.

These reasons are best considered in relation to the function and structure of the cortical-basal ganglionic motor circuit. Simply, this circuit originates in premotor, supplementary, and primary motor cortices. These areas send output via direct and indirect pathways to the putamen, internal, and external portions of the globus pallidus and substantia nigra, which in turn have projections back to cortical motor areas through specific thalamic nuclei. Within this circuit, a balanced release of inhibitory and excitatory neurotransmitters is critical for normal motor control (Goetz, DeLong, Penn, & Bakay, 1993). When an imbalance occurs, neuropathologies such as PD develop, which affect both limb and speech motor control.

Another feature of this circuit is that different phases of movement processing are represented in separate "parallel" channels that are distributed across several neural structures. For example, neural activity related to movement preparation in the limbs has been observed not only in cortical motor areas, but also in the striatum and globus pallidus (Alexander, DeLong, & Crutcher, 1992). Although it remains unknown if a similar type of processing for speech production occurs, it is noteworthy that certain structures within this circuit, such as the supplementary motor area and thalamic nuclei, have an integral role in speech motor control. For example, neural activity has been recorded in the supplementary motor area prior to voluntary speech movements (Deecke, Kornhuber, Lang, Lang, & Schreiber, 1985) and speech impairments have been observed following stimulation of this area (Van Buren & Fedio, 1976). Finally, a well-defined somatotopic representation for the legs, arms, and face has been identified throughout the cortical-basal ganglionic circuit (Alexander et al., 1992). Given that the speech mechanism is represented at all neural levels of this circuit, that structures within this circuit are critically involved in speech production, and that both speech and limb movements are affected by the neurotransmitter imbalance, it seems plausible that FCT surgery would affect the function of all motor systems inherent to this circuit similarly. In other words, it seems reasonable to assume that FCT surgery would not selectively influence one motor system-that is, legs-over another-that is, face—within this primary motor feedback system.

This idea is consistent with the motor control theory that suggests limb and speech movements are governed by the same organizational processes (Kelso, Tuller, & Harris, 1983). Evidence in support of this theory showed that when simultaneous cyclical finger movements and a string of syllables with varying stress patterns were produced, the finger movements conformed to the stress pattern. Specifically, longer finger movements accompanied the production of stressed syllables and shorter finger movements accompanied the production of unstressed syllables (Kelso & Holt, 1980). It was suggested that this "coupling" between systems reduces task complexity (degrees of freedom) by establishing predictable relations across systems so that the system can function as a total, stable coordinative structure (Kelso et al., 1983; Kelso & Tuller, 1984). Although the neuroanatomical correlates underlying this theory are unknown, it seems possible that the limb and facial areas within the cortical-basal ganglionic loop may be involved in

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coordinating interrelated movement patterns across systems. In light of these considerations, it was hypothesized that FCT would produce similar effects across phonatory, articulatory, and limb motor systems. Specifically, improvements across all motor systems were expected following FCT surgery.

Acoustic measures of phonation and articulation, as well as electroglottographic (EGG) and perceptual measures were investigated to determine the effect of FCT surgery on speech and voice production in 5 individuals with PD. These measures assess different aspects of speech and voice that are frequently impaired in PD and some of the measures indirectly provide information about laryngeal and articulatory movements. A second purpose of this study was to determine if directional changes in voice and speech paralleled documented changes for overall movement, gait, and posture. This question was addressed by comparing results of voice, speech, and motor exam measures. Clearly, these findings may be important for the clinical management of persons with PD as well as provide additional information on the neuromotor substrates of speech and voice.

Methods Participants

Four males and one female were studied. They were between 46 and 68 years of age at the time of the surgery. Two of the participants (P4 and P5) were part of a subject pool presented by Freed et al. (1992). Each participant received bilateral putamen implants of mesencephalic fetal dopamine tissue and no surgical complications were reported (refer to Freed et al., 1992, for specific surgical procedure). Four participants were diagnosed with idiopathic PD and one was diagnosed with parkinsonism. Years post-disease onset ranged between 9 and 18 years. Pre-surgery speech severity was judged as mild for 4 of the participants and as mild to moderate for 1 of the participants. Speech severity ratings were based on individual self-ratings from the NTID speech intelligibility scale (Johnson, 1975) and listener perceptual ratings that were performed in the present study. Participant characteristics are summarized in Table 1.

Measurements

The measures that were used to assess the influence of FCT surgery on phonation and articulation included the phonatory variables of jitter (JIT), shimmer (SHIM), semitone standard deviation of the voice fundamental frequency (STSD) and EGGW-25, the speech acoustic variables of vowel duration (VD), glide extent

 Table 1. Participant characteristics.

Participant	Age	Gender	Diagnosis	YPO	SDR	
P1	46	м	IPD	12	Mild-Mod.	
P2	50	М	IPD	9	Mild	
P3	68	М	IPD	11	Mild	
P4*	66	М	Park	9	Mild	
P5*	64	F	IPD	18	Mild	

Note: IPD = Idiopathic Parkinson disease; Park = Parkinsonism; YPO = years post-onset; SDR = speech disorder rating; * = P4 corresponds to P7 and P5 corresponds to P4 in Freed et al. (1992) study.

(GE), voice onset time (VOT) and spirantization (SPIR), and the listener perceptual variables of speech intelligibility (SI), articulatory precision (AP), and voice quality (VQ).

Phonatory variables measure phonatory stability (JIT and SHIM) and laryngeal abductory and adductory movements (EGGW-25) (Scherer, Vail, & Rockwell, 1993) during sustained phonation and voice fundamental frequency variability (STSD) in reading, whereas articulatory acoustic variables provide information about vocal tract movement dynamics (VD and GE) and constriction (SPIR) as well as oral-laryngeal coordination (VOT) (Abramson, 1977; Klatt, 1975). Finally, listener ratings provide information on perceptual voice and speech characteristics. By comparing these measures before and after FCT surgery, a wide range of communication output was assessed, including subtle phonatory perturbations, vocal fold and vocal tract movements, and speech intelligibility in connected speech.

Data Collection

Acoustic and electroglottographic (EGG) recordings were obtained 3 consecutive days before surgery and at either 6 and 12 months or 3 and 12 months after surgery. Multiple pre-surgical trials were obtained to account for variability related to maximum performance tasks and to the performance of individuals with PD (Kent, Kent, & Rosenbek, 1987; King, Ramig, Lemke, & Horii, 1994). Recordings were obtained across drug cycle fluctuations both pre- and post-surgery. Inspection of voice and speech measures during "on" and "off" states did not reveal systematic changes related to drug state. All pre- and post-surgical voice and speech data were collected by the same examiner and although the examiner was not blinded to the participants' surgical status, care was taken to provide consistent instructions and feedback at each recording session.

At each pre- and post-session, six maximum sustained /a/ phonations and the "Rainbow Passage" were recorded, and at two of the three pre-sessions and all of the post-surgery sessions the sentences "Buy Bobby a puppy" and "The potato stew is in the pot" (Weismer, 1984) were recorded. These speech tasks are often used to obtain the phonatory and articulatory acoustic measures of interest.

The maximum sustained /a/ phonations were elicited by having each individual take a deep breath and say /a/ for as long as he or she could at a comfortable pitch and loudness level. The "Rainbow Passage" (Fairbanks, 1960) and sentences (Weismer, 1984) were read at a comfortable rate and loudness level. The above protocol was performed for all individuals except P5. For this person, the EGG signal and sentences (Weismer, 1984) were not recorded; therefore, information about vocal fold abductory/adductory and vocal tract movement dynamics is not available.

Each recording occurred in an IAC sound-treated booth with the participant seated comfortably in a dental chair. Acoustic signals were recorded by a headmount microphone placed 8 cm away from the participant's mouth. EGG signals were obtained by placing and securing the electrodes of a Synchrovoice Research Electroglottograph on either side of the thyroid cartilage. The microphone signal was amplified (ATI-100 preamplifier) and both microphone and EGG signals were visually monitored on an oscilloscope (Tek-2245A) and recorded to a Panasonic SV-3700 2-channel DAT recorder.

Each participant was also evaluated using the Motor Examination (ME) subscale of the Unified Parkinson Disease Rating Scale (UPDRS) (Fahn & Elton, 1987). This evaluation was performed by a neurologist through an interview process at one of the pre- and all of the post-surgery sessions. Since these ratings were a component of the Freed et al. (1992) study, the experimental design differed and multiple pre-surgical ratings were not performed. Also, at the time of the ratings, the neurologist was not blinded to the participant's surgical status.

The ME subscale of the UPDRS assesses activities that include but are not limited to facial expressiveness, hand and finger movements, leg agility, body bradykinesia and hypokinesia, rigidity, action and rest tremor, and postural and gait control. Fourteen activities comprise this subscale and each activity is rated on a scale of 0 to 4, where 0 indicates normalcy and 4 indicates severe impairment. Also, each activity, except for one, is rated bilaterally. Thus, the best total score for the ME subscale is 0 (no impairment) and the worst is 108 (severe impairment). Interrater concordance is statistically significant for each individual item on the ME subscale and for all items as a group (0.902) (Fahn & Elton, 1987).

Data Analysis Phonatory Measures: Acoustic and Electroglottographic Analysis

The maximum sustained /a/ phonations were lowpass filtered at 10 kHz and digitized (sampling rate of 20 kHz) and the measures, jitter, shimmer (with linear trend removed), and EGGW-25, were obtained. For jitter and shimmer, 2 s segments from the temporal midpoint of each vowel were analyzed with the computer software GLIMPES (Glottal Imaging by Processing External Signals; Titze, 1984). This software uses a minimum peak identification method to differentiate adjacent cycles and allows for online verification of valid cycle demarcation by displaying a cycle-to-cycle overlay for each segment.

If severe phonatory instability was present, as indicated by aperiodicity, subharmonics, or chaos in the acoustic waveform, the demarcation process resulted in erroneous jitter and shimmer values. When this occurred, jitter and shimmer analysis was performed on the 2 s segment that immediately followed the instability. This standard segment selection approach resulted in pre- and post-surgical means for jitter and shimmer that were based on three to five segments per individual.

To calculate EGGW-25, in-house software averaged six consecutive EGG cycles from the temporal midpoint of each vowel for each pre- and post-surgery token. The means of four tokens were then averaged for each preand post-surgical session. EGGW-25 is defined as the width of the EGG signal at 25% of the amplitude of the wave divided by the period (Scherer et al., 1993). It is highly correlated with other measures of glottal adduction, such as the abduction quotient and frame-by-frame videoendoscopic analysis of vocal process adduction (Scherer et al., 1993).

The first paragraph of the "Rainbow Passage" was anti-alias filtered at 2.5 kHz, digitized (sampling rate of 5 kHz), and analyzed with CSpeech (Milenkovic, 1987) to obtain semitone standard deviation (STSD) of the voice fundamental frequency.

Articulatory Measures: Acoustic Analysis

To measure articulatory acoustic variables, sentence productions of "Buy Bobby a puppy" and "The potato stew is in the pot" were low-pass filtered (8 kHz), digitized (sampling rate 20 kHz), and simultaneously displayed as wide-band spectra (bandwidth = 300 Hz; frequency range of 0-10 kHz) and waveforms using CSpeech (Milenkovic, 1987).

Vowel duration (VD) and glide extent (GE) were obtained for the diphthong /ai/ in "Buy." VD was measured from the first to last visible glottal pulse in the first and second formants of the vocalic nucleus. GE was defined as the amount of frequency change along the glide segment of a diphthong (Gay, 1978). Once the vocalic nucleus was defined, the midpoints of the second formant frequency were manually traced and corresponding time-by-frequency values were automatically calculated and stored in a data file. GE was measured by inspecting the stored time-by-frequency values and determining the difference in frequency between glide onset and offset. Glide onset was identified as the first point in which the frequency exhibited a consistent increase, whereas glide offset was identified as the point in time where the frequency of the second formant showed a consistent decrease or remained unchanged.

GE, instead of transition extent, was used to indirectly measure vocal tract movement dynamics because acoustic analysis of PD single word and sentence productions has revealed multiple instances of "stairstepping" transitional trajectories. This means a portion of the trajectory did not meet the 20 Hz/20 ms criterion of transitional extent (Weismer, Martin, Kent, & Kent, 1992), but nevertheless continued to show an increase in frequency (Johnson, 1993; Johnson & Ramig, 1995). GE, therefore, seemed to provide a more accurate indicator of articulatory dynamics for vocalic productions in PD.

Spirantization (SPIR), defined as the duration of aperiodic noise, was measured during two stop gap intervals (Weismer, 1984), between "a" and "puppy" and "po" and "tato." A stop gap interval corresponds to the time between the offset of glottal pulsing in the first and second formants of the vocalic nucleus and the articulatory closure for a stop voiceless consonant, which is manifested as a stop burst (Weismer, 1984). Cursors were positioned at the onset (offset of glottal pulsing for the vocalic nuclei) and offset (onset of the stop burst) of each stop gap interval. When multiple stop bursts were observed, the first stop burst was used to define the offset of the stop gap interval.

Voice onset time (VOT) was measured in the stressed position of two words, between "p_uppy" and "pot_ato." Cursors were positioned at the onset of the stop burst and at the onset of glottal pulsing in the first and second formants of the subsequent vowel. Again, the onset of the first stop burst defined the beginning of VOT when multiple stop bursts were present. The means for articulatory acoustic measures were based on four productions of the word "Buy" and "puppy" and three productions of the word "potato" for each data collection session.

Listener Perceptual Ratings

Listener perceptual ratings were made in an IAC sound-treated booth by two speech-language pathologists with 5–7 years of clinical experience. The listeners

were aware of participants' neurological diagnosis, but were blind to their surgical status. A master tape recording of randomized pre- and post-surgery productions of the "Rainbow Passage" was played from a Panasonic SV-3700 2-channel DAT recorder over a loudspeaker. The listeners remained a constant distance from the loudspeaker and did not adjust loudness levels during the rating session. The average signal presentation level was 65 dB SPL (SD = 3.4) at 50 cm.

The speech samples were rated for overall speech intelligibility, articulatory precision, and voice quality using computerized visual analog rating scales (Kempster, 1984; Kreiman, Gerratt, Kempster, Ehrmann, & Berke, 1993). Each perceptual attribute was represented by an undifferentiated vertical line that was 100 mm in length. The end points of each line were labeled to indicate the extreme of the perceptual attribute, for example, normal voice quality to severely disordered voice quality. For each passage, three lines, one for each perceptual variable, were displayed simultaneously and the listeners placed a mark on each line with a mousecontrolled cursor that represented the extent to which they perceived the perceptual characteristic to be present (Kreiman et al., 1993). The mark on the perceptual scale was automatically converted to a numerical value and stored to a data file for subsequent pre- to post-surgery comparisons.

Measurement Reliability

To evaluate reliability for articulatory acoustic temporal measures and listener perceptual ratings, the average absolute difference within and between raters was calculated. Reliability findings are displayed in Table 2. Intra- and interrater differences for 10% of the articulatory acoustic temporal measures were between 4-8 ms. The average absolute differences for intrarater listener perceptual ratings were between 1–13 mm. Interrater differences for the listener perceptual ratings were between 13-27 mm. Because intra- and interrater reliabilities were low for the listener perceptual rating of voice quality (see Table 2), this variable was excluded from further analysis. Reliability for phonatory acoustic and EGG measures was not performed because standard segmentation (Ramig & Dromey, 1996; Ramig, Scherer, Klasner, Titze, & Horii, 1990; Ramig, Scherer, Titze, & Ringel, 1988) and automated analysis procedures (Titze, 1984) were used to obtain these measures.

Statistical Design

To determine if differences existed in the voice and speech measures as a function of FCT surgery, comparisons of each individual's pre- to post-surgical means were made. Comparison of this statistic was considered most

	Articulatory acoustic measures				Listener perceptual ratings			
	VD (ms) (range)	VOT (ms) (range)	SPIR (ms) (range)		AP (mm) (range)	SI (mm) (range)	VQ (mm) (range)	
Intrarater	8 ms (1–12)	6 ms (0–13)	4 ms (0–14)	Intrarater1	4 mm (1–7)	3 mm (2–6)	13 mm (0–23)	
Interrater	7 (0–12)	5 (0–16)	4 (0–14)	Intrarater2	2 (1–3)	1 (0–3)	6 (1–18)	
				Interrater	13 (7–30)	15 (0–28)	27 (0–43)	

Table 2. Average absolute differences for measurement reliability.

Note: VD = vowel duration; VOT = voice onset time (average for both word positions); SPIR = spirantization (average for both stop gap intervals); AP = articulatory precision; SI = speech intelligibility; VQ = voice quality.

appropriate to describe potential changes because of the small and heterogeneous subject sample and the irreversible nature of the surgical procedure (Kratochwill & Levin, 1992). Differences in pre- to post-surgery means were considered remarkable only if the post-surgical mean exceeded the pre-surgical mean by ± 1 standard deviation (*SD*). Although this criterion was arbitrarily chosen, it seemed acceptable for the following reasons. First, ± 1 *SD* defines a meaningful amount of difference and is comparable to the statistical measurement of a large effect size (Cohen, 1988). Second, ± 1 *SD* defines the normal variability that is observed in normal aged subjects for some of the phonatory and articulatory acoustic measures that were investigated (Ramig & Ringel, 1983; Weismer, 1984).

Standard deviations were calculated for each measure, except the ME score, from all pre-surgical observations. A *SD* could not be calculated for the ME measure because only one score was obtained pre-surgery (see Methods). Therefore, only consistent directional changes that occurred as a function of the surgery were considered remarkable for this measure. When reviewing the results, it is important to realize that for some measures, negative directional changes signify improved function. Specifically, a decrease rather than an increase in jitter, shimmer, spirantization, voice onset time, and the motor exam score indicate improved function.

Results Phonatory Measures

Phonatory stability measures were variable pre-to post-surgery and showed only two notable changes. One was a decrease in P5's jitter (Figure 1a) by 2.5 SDs at 6 months post-surgery and by 1.5 SDs at 12 months postsurgery. The second was a decrease in P2's shimmer (Figure 1b) at 6 months post-surgery by 2 *SD*s. EGGW-25 values (Figure 1c) were not remarkably different between the pre- and post-surgery sessions for any of the participants and fell within a range of .43–.75. STSD (Figure 1d) decreased from pre- to both post-surgery sessions for P2 and P3. It increased slightly at 3 months post for P4, then returned to baseline levels at 12 months post-surgery.

Articulatory Acoustic Measures

Notable changes in /ai/ duration (Figure 2a) were observed for P1 and P4. P1's vowel duration increased at 6-months post-surgery by 1 SD and at 12-months postsurgery by 2 SDs, whereas P4's durations were bidirectional, decreasing by 1.5 SDs at 6 months, then increasing by 6.5 SDs 12 months after FCT surgery. The slight pre- to post-surgery changes observed in glide extent (Figure 2b) across participants were unremarkable, with the exception of P4's values. Glide extent values for P4 decreased by 1.5 SDs at 6 months, then increased by slightly more than 1 SD at 12 months post-surgery.

Figures 3a and 3b show the results for spirantization of word initial /p/ ("a_puppy") and word medial /t/ ("po_tato"). Spirantization of /p/ tended to increase preto post-surgery for all participants. This increase was most notable for P3 and P4 at the 12-month post-surgery session. Although there was a tendency for spirantization of /t/ values to increase, with the exception of P2's values, which decreased pre- to post-surgery, there was only one remarkable change. This was for P1 whose values for spirantization of /t/ increased by approximately 3 *SD*s from the pre- to 12-month post-surgical session. Directional changes for VOT of /p/ (Figure 3c) and /t/ (Figure 3d) were observed for some participants. However, none of the pre- to post-surgery changes for VOT exceeded ± 1 *SD*.

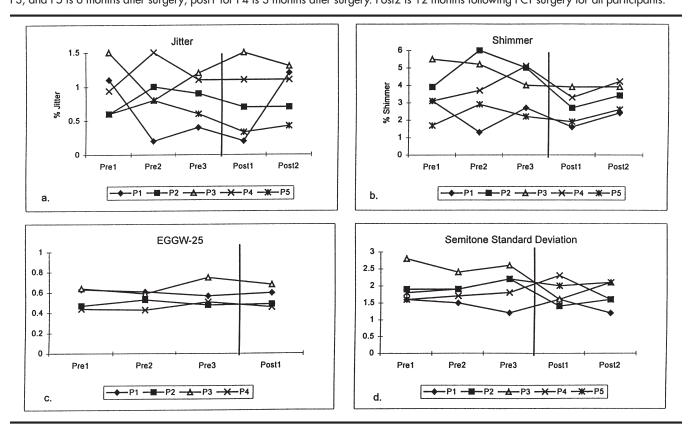
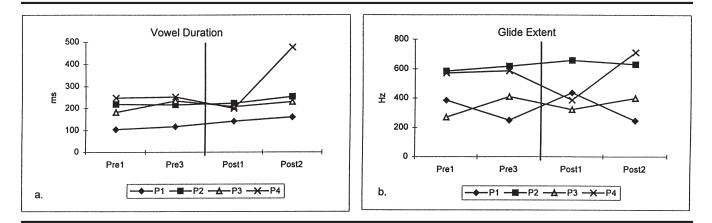


Figure 2. Results for the speech acoustic variables of (a) vowel duration and (b) glide extent for each participant and pre- and post-surgery recording session. The solid vertical line divides the pre- and post-surgery data points. Post1 for P1, P2, P3, and P5 is 6 months after surgery; post1 for P4 is 3 months after surgery. Post2 is 12 months following FCT surgery for all participants.



Listener Perceptual Ratings

Since interrater reliability was good for speech intelligibility and articulatory precision, perceptual ratings from both listeners were combined and the pre- to post-averages were compared. Pre-surgery listener ratings for these two perceptual variables were not remarkably different from ratings after FCT-surgery. Findings for these variables were also similar in that the majority of the ratings occurred at the upper end of the visual analog scale, indicating minimal impairment of speech intelligibility and articulatory precision. Since the results for these two listener perceptual variables were comparable, only findings for speech intelligibility are displayed in Figure 4a.

Figure 3. Results for (a) spirantization of word initial /p/ ("a_puppy"), (b) spirantization of word medial /t/ ("po_tato"), (c) voice onset time of word initial /p/, and (d) word medial /t/, for each participant and pre- and post-surgery recording date. The solid vertical line divides the pre- and post-surgery data points. Post1 for P1, P2, P3, and P5 is 6 months after surgery; post1 for P4 is 3 months after surgery. Post2 is 12 months following FCT surgery for all participants.

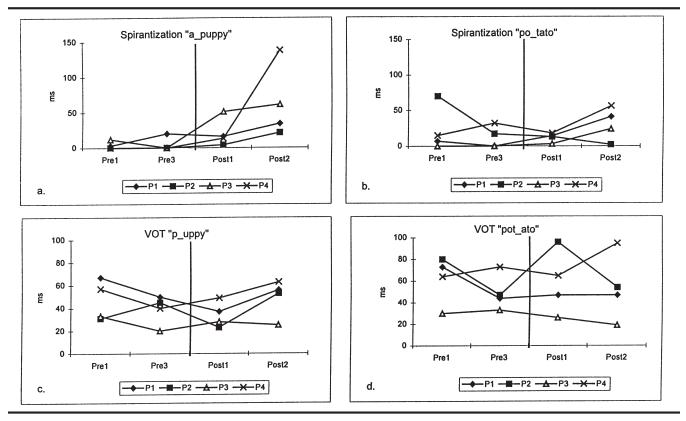
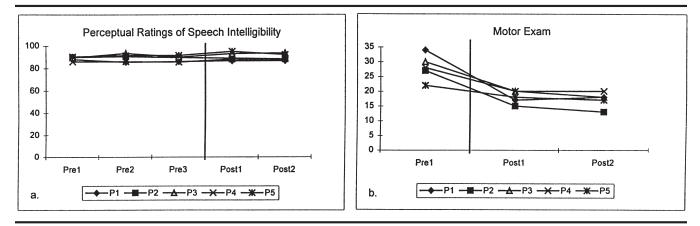


Figure 4. Results for the (a) listener perceptual ratings of speech intelligibility and for the (b) neurologist's rating of the motor exam subscale of the United Parkinson Disease Rating Scale for each participant and pre- and post-surgery recording session. The solid vertical line divides the pre- and post-surgery data points. Post1 for P1, P2, P3, and P5 is 6 months after surgery; post1 for P4 is 3 months after surgery. Post2 is 12 months following FCT surgery for all participants.



Motor Exam Ratings

Motor exam scores (Figure 4b) showed a marked decrease from pre- to both post-surgical sessions. This directional change toward more normal gait and limb agility was apparent for all individuals (Freed et al., 1992).

Summary of Findings

A summary of pre- to post-surgical findings for each participant and measure is shown in Table 3. To simplify interpretation of the summary, directional changes that indicate an improvement are shown by a plus sign,

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whereas directional changes that signify a decline in function are shown by a minus sign. This classification is independent of directional changes in the raw data. For example, jitter decreased for P5 at both post-surgical sessions. These decreases are represented by plus signs because a decrease in jitter signifies improvement.

Discussion

The purposes of this preliminary study were to determine if FCT surgery influenced speech and voice production and if these motor systems were influenced similarly to overall movement, gait, and posture. Although ME scores indicated FCT surgery did improve overall motor performance, findings for voice and speech measures indicated that FCT surgery did not systematically influence phonation or articulation in these 5 individuals.

No changes or only slight changes were observed in measures reflective of phonatory stability. EGGW-25 data suggested laryngeal adduction remained relatively constant independent of the surgical procedure. Fundamental frequency variability, as measured by STSD, improved, became worse, or stayed the same after FCT surgery. Because of this inconsistency, it is difficult to say if possible control parameters of voice fundamental frequency variability, such as laryngeal muscle or respiratory related activity, were affected by the surgical procedure.

Similar inconsistencies were observed pre- to postsurgery for the speech acoustic measures of VD and GE, again making it difficult to determine if improvements in vocal tract range of movement (Gay, 1978; Weismer et al., 1992) occurred as a result of the surgical treatment. Spirantization values for /p/ and in some instances for /t/ tended to increase following FCT surgery, suggesting there was increased supraglottal "leaking" in the "silent" vowel-to-consonant interval. However, the magnitude of these changes rarely exceeded the range associated with normal variability (Weismer, 1984). The changes observed in VOT may also be attributed to normal variability and suggest that efficiency of oral-laryngeal coordination and voice rise time were not influenced by FCT surgery. In general, phonatory and articulatory measures were variable and did not show consistent, remarkable changes across individuals pre- to post-FCT surgery.

It is possible that direct physiologic measures, such as laryngeal electromyography, may have detected changes. This seems unlikely though, given that the measures investigated here assessed a range of speech behaviors, from subtle cycle-to-cycle phonatory perturbations to perceptual characteristics of speech production, and consistent changes were not observed as a function of the surgery. Another explanation for these findings may be related to the severity of speech and voice involvement exhibited by these individuals presurgery. Their speech was only mildly or mild-to-moderately impaired. Notable differences in speech and voice measures may be observed as a function of FCT surgery if the PD participants that are studied demonstrate more severe speech impairments.

The most consistent finding was that all individuals showed improved ME scores from pre- to 3, 6, and 12 months post-surgery. Although direct comparisons in the ME score and voice and speech measures are not possible because of the difference in the resolution of the measures, that is, gross, behavioral (ME score) versus fine, quantitative (VOT, SPIR) measures, it is remarkable that positive changes in the ME score were

Table 3. Summary of directional changes for voice, speech, and motor exam measures pre- to post-FCT surgery.

	P1		P2		P3		P4		P5	
	6 mo	12 mo	6 mo	12 mo	6 mo	12 mo	3 mo	12 mo	6 mo	12 mo
JIT	0	0	0	0	0	0	0	0	+	+
SHIM	0	0	+	0	0	0	0	0	0	0
EGGW-25	0	0	0	0	0	0	0	0	NA	NA
STSD	0	0	-	-	-	-	+	0	0	0
VD	+	+	0	0	0	0	-	+	NA	NA
GE	0	0	0	0	0	0	-	+	NA	NA
SPIR /p/t/	0/0	0 / -	0/0	0/0	0/0	-/0	0/0	-/0	NA	NA
VOT /p/t/	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	NA	NA
SI	0	0	0	0	0	0	0	0	0	0
ME	+	+	+	+	+	+	+	+	+	+

Note: + = improvement; - = decline; 0 = no change; NA = data not available. JIT = jitter; SHIM = shimmer; STSD = semitone standard deviation; VD = vowel duration; GE = glide extent; SPIR /p/t/ = spirantization for word initial /p/ and medial /t/; VOT /p/t/ = voice onset time for word initial /p/ and medial /t/; SI = listener perceptual ratings of speech intelligibility; ME = motor exam score from United Parkinson Disease Rating Scale.

consistently observed following surgery and that similar trends were not apparent for any of the voice or speech measures. Even the listener perceptual ratings, which are probably most comparable to the ME score, in that both are qualitative, did not reveal discernible pre- to post-surgical differences.

It is possible that the ME findings were influenced by examiner bias. However, marked improvements in quantitative motor performance tests, such as arm movement velocities, and scores of standardized clinical tests, such as the UPDRS, have been observed by other investigators after FCT surgery (Lindvall et al., 1990; Widner et al., 1992). Given that the present findings are consistent with previously reported results, it seems likely that the motoric changes reported here occurred as a result of the surgical procedure rather than examiner bias.

Differences related to neural innervation, organization, and origin between limb and speech motor systems exist. Corticospinal fibers provide primarily unilateral innervation to spinal nuclei for limb movements, whereas corticobulbar fibers provide bilateral innervation to cranial nuclei for laryngeal and supralaryngeal movements. Limb skeletal muscles tend toward an agonist-antagonist organization, whereby efficient, coordinated movements are accomplished via reciprocal inhibition (Kandel & Schwartz, 1985). Such well-defined agonist-antagonist muscle relations are not as apparent in the speech mechanism. For example, orofacial muscles may act as synergists or antagonists depending on the desired movement (Dubner, Sessle, & Story, 1978). Also, coactivation rather than reciprocal muscle activation has been observed during normal speech production (Moore, Smith, & Ringel, 1988). Differences such as these may explain why FCT surgery seems to have a greater effect on limb versus speech motor symptoms.

Another notable difference between limb and speech systems relates to movement complexity. It has been shown that as limb movement complexity increases, movement control decreases in persons with PD (Phillips, Muller, & Stelmach, 1989; Stelmach, 1991). It may be that the physiologic changes associated with FCT surgery are sufficient to modify the dynamics of simple limb movements, but insufficient to modify complex movements associated with speech production.

Finally, the differential effect may be related to voluntary effort. After FCT surgery, participants may devote more effort toward modifying their most disabling feature, that is, gross motor movements. This increased effort combined with potential neurochemical changes in the brain may explain the obvious changes that occurred post-surgery in overall motor performance. Since speech was only slightly impaired before surgery, it may be that only minimal effort was directed toward improving speech clarity. Thus, the differential effects observed across neuromotor systems after FCT surgery may be the result of physiologic or behavioral factors or a combination of the two.

Although these preliminary data do not indicate that FCT surgery influenced speech production in these individuals, further investigations are warranted. First, FCT techniques are continually developing and factors such as the best age, placement, and volume of fetal tissue have yet to be determined. Second, continued investigations that use direct physiologic measures and study larger sample sizes as well as individuals with comparable speech and limb impairments may provide additional information about the effect of FCT surgery on voice and speech function. Finally, studies of this nature may help clarify the role of neurotransmitters in speech production as well as answer the question of why differential motor effects are observed as a function of treatment type in Parkinson disease.

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References

- Abramson, A. S. (1977). Laryngeal timing in consonant distinctions. *Phonetica*, 34, 295–303.
- Alexander, G. E., DeLong, M. R., & Crutcher, M. D. (1992). Do cortical and basal ganglionic motor areas use "motor programs" to control movement? *Behavioral and Brain Sciences*, *15*, 656–665.
- Aronson, A. E. (1990). *Clinical voice disorders*. New York: Thieme-Stratton.
- Bakay, R. A. E., Barrow, D. L., Fiandaca, M. S., Iuvone, P. M., Schiff, A., & Collins, P. C. (1987). Biochemical and behavioral correction of MPTP parkinson-like syndrome by fetal cell transplantation. *Annals New York Academy of Science*, 495, 641–657.
- **Barbeau, A.** (1974). The clinical physiology of side effects in long-term L-dopa therapy. *Advances in Neurology*, *5*, 347–365.
- **Cohen, J.** (1988). Statistical power analysis for the behavioral sciences (2nd ed.). Hillsdale, NJ: Lawrence Erlbaum Associates.
- **Cooper, I. S.** (1961). *Parkinsonism: Its medical and surgical therapy*. Springfield, IL: Charles Thomas.
- Daniels, N., Oates, J., Phyland, D., Feiglin, A., & Hughes, A. J. (1996). Vocal characteristics and response to levadopa in PD. *Movement Disorders*, 11 (Suppl 1), 117.
- Darley, F., Aronson, A., & Brown, J. (1969). Differential diagnostic patterns of dysarthria. *Journal of Speech and Hearing Research*, 12, 246–269.
- Deecke, L., Kornhuber, H. H., Lang, W., & Schreiber, H. (1985). Timing function of the frontal cortex in sequential motor and learning tasks. *Human Neurobiology*, 4(3), 143–154.

Journal of Speech, Language, and Hearing Research

Dubner, R., Sessle, B. J., & Storey, A. T. (1978). *The neural basis of oral and facial function*. New York: Plenum.

- Fahn, S., & Elton, R. L. (1987). Members of the UPDRS development committee. Unified Parkinson's Disease Rating Scale. In S. Fahn, C. D. Marsden, D. B. Calne, & M. Goldstein (Eds.), *Recent developments in Parkinson's disease* (Vol. 2, pp. 153–64). Florham Park, NJ: Macmillan Healthcare Information.
- **Fairbanks, G.** (1960). *Voice and articulation drill book*. New York: Harper and Brothers.
- Freed, C. R., Breeze, R. E., Rosenberg, N. L., Schneck, S. A., Kreik, E., Qi, J. X., Lone, T., Zhang, Y. B., Snyder, J. A., Wells, T. H., Ramig, L. O., Thompson, L., Mazziotta, J. C., Huang, S. C., Grafton, S. T., Brooks, D., Sawle, G., Schroter, G., & Ansari, A. A. (1992). Survival of implanted fetal dopamine cells and neurologic improvement 12 to 46 months after transplantation for Parkinson's disease. New England Journal of Medicine, 327 (22), 1549–1555.
- Freed, C. R., Breeze., R. E., Rosenberg, N. L., Schneck, S. A., Wells, T. H., Barrett, J. N., Grafton, S. T., Huang, S. C., Eidelberg, D., & Rottenberg, D. A. (1990). Transplantation of human fetal dopamine cells for Parkinson's disease. Archives of Neurology, 47 (5), 505–512.
- Gay, T. (1978). Effect of speaking rate on vowel formant movements. *Journal of the Acoustical Society of America*, 63 (1), 223–230.
- Goetz, C. G., DeLong, M. R., Penn, R. D., & Bakay, R. A.
 E. (1993). Neurosurgical horizons in Parkinson's disease. *Neurology*, 43, 1–7.
- Johnson, A. B. (1993). The effect of intensive voice therapy on vowel duration and slope of second formant transitions in patients with Parkinson disease. Unpublished master's thesis. University of Colorado, Boulder.
- Johnson, A. B., & Ramig, L. O. (1995). Formant trajectory and segmental characteristics of males with Parkinson disease. NCVS Status and Progress Report, 8, 113–130.
- Johnson, D. D. (1975). Communication characteristics of NTID student. *Journal of Academic Rehabilitative Audiology*, 8(1/2), 17–32.
- Kandel, E. R., & Schwartz, J. H. (1985). Principles of neural science (2nd ed.). New York: Elsevier.
- Kelso, J. A. S., & Holt, K. G. (1980). Exploring a vibratory systems account of human movement production. *Journal* of *Neurophysiology*, 43, 1183–1196.
- Kelso, J. A. S., & Tuller, B. (1984). Converging evidence in support of common dynamical principles for speech and movement coordination. *American Journal of Physiology: Regulatory, Integrative and Comparative Physiology, 246*, 928–935.
- Kelso, J. A. S., Tuller, B., & Harris, K. S. (1983). A "dynamic" pattern perspective on the control and coordination of movement. In P. F. MacNeilage (Ed.), *The production of speech* (pp. 137–173). New York: Springer-Verlag.
- **Kempster, G. B.** (1984). A multidimensional analysis of vocal quality in two dysphonic groups. Unpublished doctoral dissertation, Northwestern University, Evanston, IL.
- Kent, R. D., Kent, J. F., & Rosenbek, J. C. (1987). Maximum performance tests of speech production. *Journal of Speech and Hearing Disorders*, 52, 367–387.

- King, J. B., Ramig, L. O., Lemke, J. H., & Horii, Y. (1994). Variability in acoustic and perceptual parameters of phonation in patients with Parkinson's disease. *Journal* of Medical Speech-Language Pathology, 2, 29–42.
- Klatt, D. H. (1975). Voice onset time, frication and aspiration in word initial consonant clusters. *Journal of Speech* and Hearing Research, 18, 686–706.
- Kordower, J. H., Freeman, T. B., Snow, B. J., Vingerhoets, F. J., Mufson, E. J., & Sanberg, P. R. (1995). Neuropathological evidence of graft survival and striatal reinnervation after the transplantation of fetal mesencephalic tissue. New England Journal of Medicine, 332 (17), 118–24.
- Kratochwill, T., & Levin, J. R. (1992). Single-case research design and analysis: New directions for psychology and education. Hillsdale, NJ: Lawrence Erlbaum Associates.
- Kreiman, J., Gerratt, B. R., Kempster, G. B., Ehrmann, A., & Berke, G. S. (1993). Perceptual evaluation of voice quality: Review, tutorial, and a framework for future research. *Journal of Speech and Hearing Research*, 35, 512–520.
- Larson, K. K., Ramig, L. O., & Scherer, R. S. (1994). Acoustic and glottographic voice analysis during drugrelated fluctuations in Parkinson disease. *Journal of Medical Speech-Language Pathology*, 2 (3), 228–239.
- Lindvall, O., Brundin, P., Widner, H., Rehncrona, S., Gustavi, B., Frackwiak, R., Leenders, K. L., Sawle, G., Rothwell, J. C., Marsden, C. D., & Bjorklund, A. (1990). Grafts of fetal dopamine neurons survive and improve motor function in Parkinson's disease. *Science*, 247, 574–577.
- Lindvall, O., Rehncrona, S., Brudin, P., Gustavii, B., Astedt, B., Widner, H., Lindholm, T., Bjorklund, A., Leenders, K. L., Rothwell, J. C., Frackowiak, R., Marsden, C. D., Johrels, B., Steg, G., Feedman, R., Hoffer, B. J., Seiger, A., Bugdeman, M., Stromberg, I., & Olson, L. (1989). Human fetal dopamine neurons grafted into the striatum in two patients with severe Parkinson's disease. A detailed account of methodology and a 6-month follow-up. Archives of Neurology, 46(6), 615–631.
- Lindvall, O., Sawle, G., Widner, H., Rothewell, J. C., Bjorklund, A., Brooks, D., Brundin, P., Frackowiak, R., Marsden, C. D., & Odin, P. (1994). Evidence of longterm survival and function of dopaminergic grafts in progressive Parkinson's disease. *Annals of Neurology*, 35 (2), 172–180.
- Logemann, J., Fisher, H., Boshes, B., & Blonsky, E. (1978). Frequency and co-occurrence of vocal tract dysfunctions in the speech of a large sample of Parkinson patients. *Journal of Speech and Hearing Disorders*, 43, 47–57.
- Marsden, C. D., & Parkes, J. D. (1976). "On-off" effects in patients with Parkinson's disease on chronic levadopa therapy. *Lancet*, 1, 292–296.
- Milenkovic, P. (1987). Least mean square measures of voice perturbation. Journal of Speech and Hearing Research, 30, 529–538.
- Moore, C. A., Smith, A., & Ringel, R. L. (1988). Taskspecific organization of activity in human jaw muscles. *Journal of Speech and Hearing Research*, *31*, 670–80.

Peschanski, M., Defer, G., N'Guyen, J. P., Ricolfi, F., Monfort, J. C., Remy, P., Geny, C., Samson, Y., Hantraye, R., Jeny, R., Gaston, A., Keravel, Y., Degos, J. D., & Cesaro, P. (1994). Bilateral motor improvement and alteration of L-dopa effect in two patients with Parkinson's disease following intrastriatal transplantation of foetal ventral mesencephalon. *Brain*, 117, 487–499.

Petrovici, J. N. (1980). Speech disturbances following stereotaxic surgery in ventrolateral thalamus. *Neurosurgical Review*, 3(3), 189–195.

Phillips, J. G., Mueller, F., & Stelmach, G. E. (1989). Movement disorders and the neural basis of motor control. In S. Wallace (Ed.), *Perspectives on the coordination of movement* (pp. 367–417). Amsterdam: North Holland.

Ramig, L. O., & Dromey, C. (1996). Aerodynamic mechanisms underlying treatment-related changes in vocal intensity in patients with Parkinson disease. *Journal of Speech and Hearing Research*, 39, 798–807.

Ramig, L. O., & Ringel, R. (1983). Effects of physiologic aging on selected acoustic characteristics of voice. *Journal* of Speech and Hearing Research, 26, 22–30.

Ramig, L. O., Scherer, R. C., Titze, I. R., & Horii, Y. (1990). Acoustic analysis of voice in amyotrophic lateral sclerosis: A longitudinal case study. *Journal of Speech and Hearing Disorders*, 55, 2–14.

Ramig, L. O., Scherer, R. C., Titze, I. R., & Ringel, S. P. (1988). Acoustic analysis of voices of patients with neurologic disease: Rationale and preliminary data. *Annals of Otology, Rhinology and Laryngology*, 97, 164–172.

Redmond, D. E., Sladek, J. R., Roth, R. H., Collier, T. J., Elsworth, J. D., Deutch, A. Y., & Haber, S. (1986). Fetal neuronal grafts in monkeys given methylphenyltetrahydropyridine. *Lancet*, 1, 1125–1127.

Sawle, G. V., Bloomfield, P. M., Bjorklund, A., Brooks, D. J., Brundlin, P., Leenders, K. L., Lindvall, O., Marsden, C. D., Rehncrona, S., Widner, H., & Frackwiak, R. S. J. (1992). Transplantation of fetal dopamine neurons in Parkinson's disease: PET [18F]6-Lfluorodopa studies in two patients with putaminal implants. Annals of Neurology, 31, 166–173.

Scherer, R., Vail, V., & Guo, C. G. (1995). Required number of tokens to determine representative voice perturbation values. *Journal of Speech and Hearing Research*, 38, 1260–1269.

Scherer, R., Vail, V., & Rockwell, B. (1993). Examination of the laryngeal adduction measure EGGW. NCVS Status and Progress Report, 5, 73–82.

Sladek, J. R., Collier, T. J., Haber, S. N., Deutch, A. Y., Elsworth, J. D., Roth, R. H., & Redmond, E. (1987). Reversal of Parkinsonism by fetal cell transplants in primate brain. *Annals New York Academy of Science, 495*, 641–657.

Solomon, N. P., & Hixon, T. J. (1993). Speech breathing in Parkinson's disease. Journal of Speech and Hearing Research, 36, 294–310.

Spencer, D. D., Robbins, R. J., Naftolin, F., Phil, D., Marek, K. L., Vollmer, T., Leranth, C., Roth, R. H., Price, L. H., Gjedde, A., Bunney, B. S., Sass, K. J., Elsworth, J. D., Kier, L., Makuck, R., Hoffer, P. B., & Redmond, D. E. (1992). Unilateral transplantation of human fetal mesencephalic tissue into the caudate nucleus of patients with Parkinson's disease. New England Journal of Medicine, 327 (22), 1541–1548.

Stein, D. G., & Glasier, M. M. (1995). Some practical and theoretical issues concerning fetal brain tissue grafts as therapy for brain dysfunctions. *Behavioral and Brain Sciences*, 18, 36–45.

Stelmach, G. E. (1991). Basal ganglia impairment and force control. In J. Requin & G. E. Stelmach (Eds.), *Tutorials in motor neuroscience* (pp. 137–148). Netherlands: Kluwer Academic Publishers.

Titze, I. (1984). Parameterization of the glottal area, glottal flow and vocal fold contact area. *Journal of the Acoustical Society of America*, 75, 570–580.

Van Buren, J. M. & Fedio, P. (1976). Functional representation on the medial aspect of the frontal lobes in man. *Journal of Neurosurgery*, 44 (3), 275–289.

Weismer, G. (1984). Acoustic descriptions of dysarthric speech: Perceptual correlates and physiological inferences. In J.C. Rosenbek (Ed.), *Current view of dysarthria: Nature, assessment and treatment* (pp. 293–314). New York: Thieme Stratton.

Weismer, G., Martin, R., Kent, R.D., & Kent, J.F. (1992). Formant trajectory characteristics of males with amyotrophic lateral sclerosis. *Journal of the Acoustical Society* of America, 91, 1085–1098.

Widner, H., Tetrud, J., Rehncrona, S., Snow, B.,
Brudin, P., Gustavii, B., Bjorklund, A., Lindvall, O.,
& Langston, J. W. (1992). Bilateral fetal mesencephalic grafting in two patients with parkinsonism induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). New England Journal of Medicine, 327, 22, 1556–1563.

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