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Impairments of Speech Fluency in Lewy Body Spectrum Disorder

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Abstract

Few studies have examined connected speech in demented and non-demented patients with Parkinson's disease (PD). We assessed the speech production of 35 patients with Lewy body spectrum disorder (LBSD), including non-demented PD patients, patients with PD dementia (PDD), and patients with dementia with Lewy bodies (DLB), in a semi-structured narrative speech sample in order to characterize impairments of speech fluency and to determine the factors contributing to reduced speech fluency in these patients. Both demented and non-demented PD patients exhibited reduced speech fluency, characterized by reduced overall speech rate and long pauses between sentences. Reduced speech rate in LBSD correlated with measures of between-utterance pauses, executive functioning, and grammatical comprehension. Regression analyses related non-fluent speech, grammatical difficulty, and executive difficulty to atrophy in frontal brain regions. These findings indicate that multiple factors contribute to slowed speech in LBSD, and this is mediated in part by disease in frontal brain regions.

Keywords

Parkinson's disease; speech; language; fluency; dementia with Lewy bodies

INTRODUCTION

Language production in PD is generally considered to be spared the ravages of neurodegenerative disease (Bayles, 1990), although the articulation of speech may be compromised due to disruption of the motor speech apparatus. However, PD is known to affect cognition, in addition to causing the hallmark symptoms of a motor disorder. Cognitive deficits in mild PD may include impaired memory, executive dysfunction, and visuospatial deficits (Bosboom, Stoffers, & Wolters, 2004; Brown & Marsden, 1990; Levin, Tomer, & Rey, 1992). One hypothesized mechanism of cognitive difficulty implicates dopamine depletion in the substantia nigra. This causes impaired functioning of the basal ganglia, an area that may mediate cognitive functioning through its rich connections with frontal cortex. This may also lead to impaired frontal lobe functioning more directly through

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compromised projections from the ventral tegmental portion of the substantia nigra to regions of the frontal lobe. A second hypothesized mechanism involves cholinergic dysfunction resulting from degeneration of the ascending cholinergic systems, producing a decrease in cholinergic innervation of the cerebral cortex and cell loss in the basal nucleus of Meynert. This appears to disrupt attention or effortful control processing, indirectly affecting memory and learning (Dubois, Pilon, Lhermitte, & Agid, 1990; Emre, 2003a, 2003b).

A progressive reduction in cognitive functioning in a proportion of PD patients eventually reaches the status of dementia (PDD). This is estimated to occur in about 20% of PD patients early in the disease process (Brown & Marsden, 1984; Ebmeier et al., 1991; Grossman, 1999; Mayeux et al., 1988), with estimates ranging from 11% to 36% (Giladi et al., 2000; Girotti et al., 1988; Lees, 1985; Parashos, Johnson, Erickson-Davis, & Wielinski, 2009). Up to 80% of patients with PD may eventually develop PDD as the disease progresses (Aarsland, Andersen, Larsen, & Lolk, 2003; Buter et al., 2008; Hely, Reid, Adena, Halliday, & Morris, 2008). Dementia in PD is associated with a proliferation of Lewy bodies in the cerebral cortex. This histopathologic picture is identical to that seen in dementia with Lewy bodies (DLB), a condition that is said to differ clinically from PDD in that there is a later onset of a motor disorder in DLB compared to PDD (McKeith et al., 2005). Thus there exists a spectrum of cognitive disorders associated with extrapyramidal features, unified by the presence of Lewy bodies, varying in the relative onset of motor and cognitive features, and including PD patients potentially converting to clear dementia. We refer to this family of conditions as Lewy body spectrum disorder (LBSD). It includes nondemented patients (PD), cognitively impaired patients with a relatively early onset motor disorder (PDD), and demented patients with minimal or late onset motor disorder (DLB). We acknowledge that this view of PD, PDD, and DLB as a spectrum of cognitive disorders is not universally accepted. Other researchers have identified both similarities and differences in the cognitive consequences of these diseases (Aarsland et al., 2003; Downes et al., 1998). In general, however, both the cognitive and brain atrophy differences that have been found among the groups are interpretable as quantitative differences in degree of change, rather than qualitative differences in the nature of these conditions (Double et al., 1996; Harrington et al., 1994). The shared features of proliferation of Lewy bodies in cerebral cortex and a qualitatively similar range of cognitive deficits are the grounds for our regarding these conditions as a spectrum of disorders.

The speech of LBSD patients is thought to be slowed (Volkman, Hefter, Lange, & Freund, 1992). It has been assumed that slowed speech is due to the motor feature of LBSD, with abnormal pauses at sentence boundaries (Illes, 1989) and impaired prosody, with occasional rushes of speech (Sachin et al., 2008). However, there is evidence that cognitive deficits in PD can affect language as well (Bastiaanse & Leenders, 2009; Colman et al., 2009; Grossman, 1999; Hochstadt, 2009; Pereira et al., 2009), and others have reported somewhat reduced syntactic complexity in speech production (Cummings, Darkins, Mendez, Hill, & Benson, 1988; Murray & Lenz, 2001). Most studies of language in LBSD are limited to nondemented patients, although there are exceptions (Parashos et al., 2009; Piatt, Fields, Paolo, Koller, & Troster, 1999).

In the present study, we examined the linguistic, cognitive, and motor features of non-aphasic patients with LBSD in order to identify factors contributing to their reduced fluency in connected speech. We elicited a semi-structured speech sample by asking subjects to narrate a wordless children's picture story, and we examined several possible sources of impairment that might contribute to LBSD patients' reduced fluency. One potential source of nonfluent speech may be the patients' motor disorder. For example, articulatory difficulty may slow the patients' speech. A second source may be related to the reduced initiation commonly seen in the motor examination of LBSD patients, and this may produce pauses in

the speech stream that reduce fluency. Another source of nonfluent speech may be the executive deficit in these patients. This may interfere with the planning and organization needed to produce fluent speech. Finally, there may be linguistic deficits that interfere with fluent speech production, such as difficulty with lexical retrieval or an impairment of the mechanism for constructing a syntactically well-formed sentence. We predicted that patients with DLB and PDD would exhibit slowed speech relative to non-demented PD patients. We also predicted that several factors would contribute to their slowed speech, including motor, executive, and linguistic impairments seen in LBSD.

We related impairments of speech fluency in LBSD to their neuroanatomic underpinnings using volumetric MRI. Consistent with the hypothesized basis for cognitive difficulty in LBSD, volumetric MRI studies have shown frontal gray matter loss in PD, although there may also be extension to temporal, occipital, and parietal cortical areas in DLB/PDD (Burton, McKeith, Burn, Williams, & O'Brien, 2004; Whitwell et al., 2007). Voxel-based diffusion tensor imaging has shown white matter abnormalities in multiple brain regions including the frontal lobes (Lee et al., 2010). Functional imaging has shown disturbance of frontostriatal metabolism in these disorders (Lewis, Dove, Robbins, Barker, & Owen, 2003; Lozza et al., 2004; Sawamoto et al., 2008). We predicted that there would be widespread cortical atrophy in LBSD and that reduced fluency in these patients would be related to prefrontal disease.

METHODS

Subjects

We studied 35 non-aphasic patients with LBSD, diagnosed in the Cognitive Neurology or Movement Disorders clinics of the Department of Neurology at the University of Pennsylvania by experienced neurologists (RG, AS, MG) according to published criteria (Hughes, Daniel, Kilford, & Lees, 1992; McKeith et al., 2005; McKeith et al., 1996; McKeith, O'Brien, & Ballard, 1999). The non-demented group consisted of 21 patients with PD. Eight patients were diagnosed with DLB and 6 had a diagnosis of PDD, making a group of 14 patients who exhibited evidence of dementia (DLB/PDD). In determining the diagnosis, the convention recommended by the Third Report of the DLB Consortium (McKeith et al., 2005) was followed: a diagnosis of PDD was made when motor symptoms preceded the onset of dementia by at least one year, and a diagnosis of DLB was made when dementia preceded the development of motor symptoms by at least one year. Features of DLB recognized in the Third Report of the DLB Consortium (McKeith et al., 2005), such as fluctuating cognition, variations in attention and alertness, and visual hallucinations, were mild and did not interfere with performance at the time of testing.

Patients were assigned to DLB, PDD or PD subgroups using a consensus evaluation based on published criteria that entailed two independent raters reviewing a semi-structured neurologic history, a complete neurologic exam, and a detailed mental status exam. In addition to clinical criteria, patients were classified as having dementia if (1) the Mini-Mental State Exam (MMSE) score was less than or equal to 24, or (2) if the MMSE was greater than 24 but the patient performed in the demented range on the Mattis Dementia Rating Scale (DRS-2; age-adjusted score less than or equal to 5) (Folstein, Folstein, & McHugh, 1975; Lucas et al., 1998; Mattis, Jurica, & Leitten, 2001). This latter criterion was implemented for patients judged clinically to be demented who had a predominantly dysexecutive syndrome that was not detected by the MMSE, an instrument that is relatively insensitive to executive deficits. The UPDRS Part I, item 4, Motivation/Initiative, was also recorded to assess the effect of initiation on patients' performance. The score for this item ranges from 0 to 4, where 0 is normal motivation and initiative; 1 is less assertive than usual;

2 is loss of initiative or disinterest in elective activities; 3 is loss of initiative or disinterest in routine activities; and 4 is withdrawn, with complete loss of motivation.

Demographic and clinical characteristics are summarized in Table 1. Because LBSD is a spectrum disorder, means are presented for the combined subgroups and also for each patient subgroup separately. Clinical features include dopaminergic medication use, cholinesterase inhibitor medication use, Unified Parkinson's Disease Rating Scale (UPDRS) motor assessment (Fahn, Elton, & UPDRS Program Members, 1987), and Hoehn & Yahr stage (Hoehn & Yahr, 1967). Dopaminergic medication use is expressed as levodopa equivalents. In accordance with Hobson, et al. (2002), the following dosages of medication are taken as equivalent: 100 mg levodopa; 130 mg controlled-release levodopa; 70 mg levodopa in conjunction with catechol-O-methyl transferase (COMT) inhibitor; 1 mg pergolide; 1 mg pramipexole; 5 mg ropinirole. Other PD medications (e.g., anticholinergics and monoamine oxidase inhibitors) were not included in the determination of levodopa equivalent dose. Exclusionary criteria included other causes of dementia, such as metabolic, endocrine, vascular, structural, nutritional, and infectious etiologies and primary psychiatric disorders. The DLB/PDD patients were mildly impaired according to the Mini Mental State Exam (MMSE) (Folstein et al., 1975). One-way ANOVAs indicated that control, PD, and DLB/PDD subject groups were matched for age and education. Disease duration and UPDRS motor disorder did not differ significantly across LBSD subgroups. Sixteen age- and education-matched healthy seniors were evaluated on the experimental task as control subjects. All subjects completed an informed consent procedure in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the University of Pennsylvania.

Materials

The subjects' task was to tell the story of the wordless children's picture book, *Frog, Where Are You* (Mayer, 1969). An outline of the story is given elsewhere (Ash et al., 2006). Briefly, the story begins with a boy and his dog admiring a frog that they keep in a large jar as they prepare to go to bed for the night. The frog escapes, and the following morning, the boy and his dog find that the window is open and the frog is gone. The story illustrates the adventures of the boy and his dog as they search for the frog in the forest behind their house. Ultimately, they find their frog with a lady frog and a brood of baby frogs. The book's sequence of 24 drawings elicited an extended speech sample with a known target that was comparable in content across subjects and gave patients an opportunity to demonstrate the breadth of their language production capability. We elected to study speech production in this manner to elicit a narrative without taxing the memory resources of the speakers and to eliminate the interruptions of turn-taking that occur in free conversation. We used a longer story rather than the description of a single picture in order to elicit a reasonably lengthy speech sample that was representative of the patient's speech and language abilities. We used a relatively unknown story rather than a fairy tale to avoid the intrusion of previously learned material.

Procedure

Each subject was asked to look through the book to become familiar with the story. When ready, the subject was asked to start at the beginning and narrate the story as if telling it to a child. Due to the nature of the protocol, there was no influence of the examiner on the time taken by the subjects to tell the story. Seventeen narrations were recorded on a Macintosh Powerbook G3 laptop computer using the Macintosh external microphone (part #590-0670) and the computer program SoundEdit 16, v. 2, with 16-bit recording at a sampling frequency of 44.1 kHz. Twenty-six were recorded on a Dell Inspiron 2200 PC using the signal processing software Praat (Boersma & Weenink, 1992–2005) with 16-bit recording at a

sampling rate of 22.05 kHz, using a Radio Shack omnidirectional lavalier electret condenser microphone. Eight were recorded on a Marantz PMD 670 digital recorder with 16-bit recording at a sampling frequency of 32 kHz, using a Sennheiser MKE2 omnidirectional lavalier condenser microphone.

The recordings of the narratives were transcribed in detail by trained transcribers using the signal processing software Praat. The transcription conventions used to capture the irregularities in patients' speech are defined elsewhere (Ash et al., 2006). The narratives were coded from the transcripts by trained judges, referring to the original speech files as needed. All coding was checked by a linguist (SA) with expertise in grammatical, phonetic, and phonological analysis.

Speech analysis

The overall quality of the subjects' speech was assessed by general measures of output (Table 2). These included the total number of complete words spoken; the number of words per minute (WPM); and pauses within the stream of speech. Pauses of two seconds or longer were recorded. This threshold was selected as a conservative estimate of the duration of an abnormally long pause. In a study of pausing within sentences and clauses in the spontaneous speech of healthy speakers, Goldman-Eisler (1972) reported that 35% of sentences were separated from each other by less than .75 sec, 50% were separated by more than one second, and 15% were separated by more than two seconds. In the present study, the total duration of pauses of at least two seconds was calculated and expressed as a percentage of the total duration of the narrative.

As a measure of competence in lexical retrieval, we measured the percentage of open class (content) words in the speech sample. Also, the proportion of utterances that were grammatically well formed was assessed. An utterance was defined as an independent clause and all clauses or phrases dependent on it (Hunt, 1965). Thus a series of independent clauses conjoined by *and* was counted as the number of utterances equal to the number of independent clauses. An incomplete sentence was also counted as an utterance if it stood alone in the flow of speech. A well-formed utterance was one that was complete, with a subject and predicate, and free of grammatical errors, whether or not it was appropriate to the story. In addition, the proportion of utterances with complex structures was calculated. Complex structures included dependent clauses and phrasal adjuncts, defined elsewhere (Ash et al., 2009). A third measure of grammaticality was the proportion of nouns that were produced with a determiner when a determiner was required. These three measures of grammaticality were closely correlated with each other, so a single measure of grammatical structure for each utterance was calculated by summing the three proportions, yielding a measure of grammatical production with a range of 0 to 3.

A measure of articulatory performance was calculated based on four considerations. First, phonetic and phonemic errors were counted (Ash et al., 2010), and the frequency of such errors per 100 words in the speech sample was calculated. Second, the frequency of incomplete words (false starts) per 100 words was calculated. Third, the number of editing breaks and hesitation markers (filled pauses) per 100 words was calculated. Fourth, the number of dysfluent words per 100 total words was calculated. Dysfluent words were those that were replaced or repeated by self-correction in the stream of speech. An example of an utterance containing dysfluent words is given in (1), where the dysfluent words are shown in italics. The sentence was spoken by a 74-year-old man with PDD, with an MMSE of 23 and a disease duration of 8 years.

- (1) Ah, *little-* little Joe, was uh playing *with his ... two ... th-* sss- with his three friends, two dogs and a frog, in his uh bedroom, which was a four-poster.

The four measures of articulatory performance were added together to derive an overall measure of speech production (articulation) errors per 100 words.

Neuropsychological evaluation

The patients underwent neuropsychological testing within an average of 79 ($\pm$ 64) days of the date of narrative recording. Comparisons were made to performance on these tests using a panel of 25 healthy seniors matched for age and education.

We assessed subjects on tests of memory, executive functioning, and semantics. Episodic memory was tested by delayed free recall of a list of orally presented words (maximum score = 10). Executive functioning was assessed by letter-guided word-naming fluency (FAS, the averaged total number of non-repeated words in 1 minute for each letter), a test of mental search capability; category naming fluency for animals (total number of non-repeated animal names in 1 minute), a test of the mental planning needed to search a semantic field; reverse digit span (total number of digits correctly repeated in reverse order), a test of working memory; time taken to complete Trails B (up to 180 sec), a test of planning and mental flexibility; and time taken to complete an 80-item color-word Stroop interference test (up to 180 sec), a test of inhibitory control. Semantics was tested by an abbreviated form of the Boston Naming Test (% correct), and by the Pyramids and Palm Trees test averaged for presentation by words and pictures (maximum score = 52), a test of object associative knowledge. Comprehension of syntax was tested by probing the subject's ability to identify the agent or patient in sentences with active or passive voice, subject- and object-relative clauses, and right-branched vs. center-embedded clauses (maximum score = 48).

Statistical considerations

Levene's test of homogeneity of variance indicated that some measures of language and neuropsychological test scores did not meet the requirement of homogeneity of variance for parametric statistical tests. Therefore we used nonparametric tests to assess the differences between and within subject groups. Comparisons between subject groups were calculated by the Mann-Whitney U statistic, and correlations were calculated using Spearman's rho.

Imaging methods

Eleven LBSD patients, including 7 patients with PD and 4 patients with DLB/PDD, had a volumetric brain MRI scan within one year of the narrative task. These 11 patients did not differ statistically from the larger set of 35 LBSD patients on any neuropsychological or language measures. (See Appendix, Table A1).

Ten patients had MRI scans acquired using a GE 1.5T scanner with 1.2-mm slice thickness and a 144×256 matrix. For one patient and 45 age-matched controls, images were collected using a SIEMENS Trio 3.0T scanner with 1-mm slice thickness and a 195×256 matrix. Images from both scanners were deformed into a standard local template space with a 1-mm^3 resolution using PipeDream (<https://sourceforge.net/projects/neuropipedream/>) and Advanced Normalization Tools (ANTS, <http://www.picsl.upenn.edu/ANTS/>). These tools have been validated as stable and reliable for performing multivariate normalization (Avants, Epstein, Grossman, & Gee, 2008; Klein et al., 2009). Both PipeDream and ANTS mapped T1 structural MRI images to an optimal template space, using diffeomorphic and symmetric registration methods (Avants & Gee, 2004; Avants et al., 2010). The registered images were segmented into gray matter probability maps using template-based priors and then registered to MNI-template space for statistical comparisons. Gray matter probability images were smoothed in SPM5 (<http://www.fil.ion.ucl.ac.uk/spm/software/spm5>) using a 4-mm full-width half-maximum Gaussian kernel to minimize individual gyral variations.

In SPM5, a two-sample t-test covarying for scanner contrasted gray matter probability between patients with LBSD and healthy controls to identify regions of significant cortical atrophy. For this atrophy analysis, an explicit mask was defined by generating a mean gray matter image from the healthy controls in order to limit the analysis to voxel-wise comparisons within gray matter. We used a $p < .02$ (uncorrected) height threshold, 400-voxel extent, and accepted clusters with a peak voxel Z-score > 3.09 ($p < 0.001$).

The regression module in SPM5 was used to relate gray matter atrophy to fluency as expressed by speech rate in words per minute. In order to assess the basis for impaired fluency, we also related gray matter atrophy to the percentage of duration of the narrative occupied by between-utterance pauses of at least 2 seconds. This was the one measure on which all LBSD subgroups were impaired relative to controls. We also related gray matter atrophy to the composite measure of executive functioning and to the composite measure of grammatical competence. We performed a whole-brain analysis but then used an explicit mask so that we could examine the relationship between these features and brain areas known to be significantly atrophied from the prior analysis of whole brain gray matter atrophy. We interpreted only regions where measures of language performance were related to atrophied gray matter areas because these diseased areas were likely to be related to the patients' deficits, and it would be difficult to explain with confidence significant associations between patients' performance and non-atrophied regions. For the regression analyses, we used a height threshold of $p < .05$ (uncorrected), 50-voxel extent, and we accepted clusters with a peak voxel Z-score > 3.09 ($p < .001$). Coordinates for all accepted clusters were converted to Talairach space (Talairach & Tournoux, 1988).

RESULTS

Participant characteristics

The control subjects and patients were matched for age and education, as noted above, although they were not matched for sex. For the measures of speech production investigated in this study, differences in the speech of men and women would not be predicted, and statistical comparison of means confirmed that there was no significant difference between male and female control subjects on any of the language measures under investigation. In addition, there was no correlation of dopaminergic medication with measures of performance on the language task. The effect of anti-cholinesterase medication was not amenable to meaningful statistical comparisons because the number of patients who were taking such medication at the time of the study task was very small, numbering only 4 out of the 32 for whom data were available. Since three of the four patients who received cholinesterase inhibitor medication were in the DLB/PDD group and yet performed significantly worse than PD patients and controls on most measures of language and neuropsychological functioning, it is unlikely that this medication had a beneficial impact on the patients' performance.

Language production measures

Characteristics of the overall speech output of the subjects are summarized in Table 2. Speech rate quantified as raw WPM was significantly reduced in LBSD compared to controls. The speech rate of DLB/PDD patients was about half that of healthy seniors, and it was significantly less than that of PD patients, whose speech rate did not differ from that of controls. For the LBSD patient group as a whole, the average number of words spoken in narrating the story did not differ from the output of controls, but this measure was significantly less for the DLB/PDD patient group than for both PD patients and control subjects [compared to PD, $U = 81.0$; $p < .05$; compared to controls, $U = 51.0$; $p < .05$]. This distinction held for the 6 PDD patients, with a mean number of words produced of 387 ± 88

[$U=14.0$; $p<.02$], though not for the 8 DLB patients, who produced more words (500 ± 381) [$U=37.0$; $p>.10$] but took even more time to do so. Thus, the DLB subgroup had a significantly lower speech rate than PDD patients, PD patients, or controls.

Several additional differences were observed in the speech of patients with LBSD. We consider first the deficits that may be related to motor function or initiation. There were significantly more silent pauses in LBSD than among controls, and pauses between utterances occupied significantly more of the patients' narrations than was the case for healthy subjects. DLB/PDD patients spent more than one-third of their speaking time in silences between utterances, significantly more than the between-utterance pause duration of both PD patients and controls. This was true for both DLB patients [mean (SD) = 44.7 (17.0), $U=1.0$; $p<.001$] and PDD patients [mean (SD) = 27.4 (11.8), $U=3.0$; $p<.001$]. PD patients also produced significantly long silences between utterances, at a rate about three times that of controls [$U=84.0$; $p<.01$]. In order to assess the impact of long between-utterance pauses on speech rate, a measure of "modified WPM" was constructed for all participants. This was derived by subtracting the total duration of between-utterance pauses (that were more than 2 sec long) from the total duration of the narrative. WPM was then calculated based on the total number of words in the narrative and the duration with these long pauses removed. This calculation was motivated by the importance of separating between-utterance pauses from speaking time, because the duration of long pauses between utterances consumed a large proportion of the duration of the narrative of LBSD patients and might give a false representation of the nature of the patients' speech. It was not the case that they proceeded through the narrative with speech that was slowed down but continuous. As has been described elsewhere (Illes, 1989; Sachin et al., 2008), silences were often followed by periods of speech that were spoken either at a normal rate or, sometimes, an accelerated rate.

The calculations of modified WPM are summarized in Table 2. While raw WPM is significantly different for controls compared to the LBSD patient group, modified WPM does not differ between LBSD and controls. Similarly, raw WPM was significantly different for controls compared to the DLB/PDD patient group, but for the modified WPM, the difference between these groups only approaches a level of significant impairment ($p=.077$). We subdivided the DLB/PDD subgroup to investigate the source of the borderline difference between the DLB/PDD subgroup and controls. For the 6 PDD subjects, the modified WPM did not differ significantly from that of controls [PDD mean (SD) = 138 (43); $U=46$; $p>.9$]. However, for the 8 DLB patients, the modified WPM did differ significantly from that of controls [DLB mean (SD) = 97 (44); $U=19$; $p<.01$].

Articulation errors were significantly more frequent in LBSD than in the control group. DLB/PDD patients made more errors of articulation than both PD patients and controls, while DLB [mean (SD) = 17.6 (11.8)] and PDD patients [mean (SD) = 16.8 (13.2)] did not differ from each other [$U=22.0$; $p>.8$]. Articulation was correlated with the UPDRS total motor score in LBSD ($s=.58$, $p<.01$, $n=32$); this was true in both PD ($s=.52$, $p<.05$, $n=18$) and DLB/PDD ($s=.66$, $p<.05$, $n=14$). Total motor score did not correlate with any other measure of speech production.

We also observed difficulty in LBSD in grammatical production. The composite measure of sentence structure, which includes well-formed utterances, syntactically complex utterances, and production of required determiners, was significantly lower in LBSD than in controls. DLB/PDD patients were particularly impaired in comparison to both controls and PD patients on measures of grammaticality. On subdividing the DLB/PDD group, it was found that the deficit was attributable to DLB [$U=16.0$; $p<.01$], but not to PDD [$U=24.0$; $p=.08$].

Access to the lexicon, as reflected by the proportion of open class (content) words, did not differ among subject groups.

Neuropsychological measures

The results of the neuropsychological testing are summarized in Table 1. The LBSD patients differed significantly from controls on most neuropsychological measures. Examination of the demented and non-demented subgroups revealed that the differences between LBSD patients and controls were due largely to substantial deficits within the DLB/PDD subgroup. In the Pyramid and Palm Trees measure of semantic memory, non-demented PD patients were impaired relative to controls, despite a minimal difference in absolute score. It appears that this finding may be due in part to a ceiling effect in controls. The impairment of non-demented PD patients in sentence comprehension has been found in previous work using a variety of techniques (Grossman, 1999; Grossman et al., 2003).

A composite score of executive measures involved in planning and mental organization was constructed using the average Z-scores of the letter-guided naming fluency, category naming fluency, Trails B time, and Stroop time neuropsychological measures (Table 1). The composite Z-score showed that LBSD patients overall are impaired relative to controls [mean (SD) = -2.3 (2.8); $p < .05$]. This result is due to the DLB/PDD group, which was significantly impaired ($p < .001$), while the PD group was not impaired relative to controls ($p > .2$). The DLB [mean (SD) = -5.2 (1.8)] and PDD groups [mean (SD) = -3.8 (1.9)] did not differ from each other on this measure [$U = 9.0$; $p > .2$].

Correlations

Correlations of speech fluency (WPM) with other features of narrative production as well as motor and neuropsychological measures for the LBSD patient group are shown in Table 3. Speech rate in WPM was correlated with long pauses and with frequency of articulatory errors. In addition, WPM was correlated with executive functioning, grammatical comprehension, and memory functioning. The correlations of between-utterance pauses largely overlap those of raw WPM, but they include a relationship of pauses to grammatical structure in speech production and to the measure of initiation. In addition to these findings, examination of the PD and DLB/PDD subgroups reveals that WPM correlates with pauses in each subgroup [in PD, $s = -.53$, $p < .05$; in DLB/PDD, $s = -.55$, $p < .05$].

Imaging

The structural images for 11 LBSD patients exhibited extensive gray matter atrophy compared to healthy seniors (Figure 1). The coordinates of atrophy peaks are given in Table 4. Atrophy was observed bilaterally in medial frontal, ventrolateral, dorsolateral, and insula frontal regions, as well as temporal and inferior parietal regions, hippocampus, and fusiform, lingual, and cuneus regions.

We performed a whole brain regression analysis to relate fluency as measured by speech rate (WPM) to gray matter atrophy. Atrophy was significantly related to overall speech rate in several areas, including left ventromedial, ventrolateral, dorsolateral, and anterior cingulate frontal regions, as well as in right anterior, medial frontal, and insula regions. This relationship to speech rate was also found in superior temporal, inferior parietal, middle occipital, hippocampal, and precuneus regions bilaterally, in left middle temporal and temporoparietal regions, and in right inferior temporal and fusiform regions. To investigate the source of the fluency impairment in these patients, we also performed whole brain regression analyses to relate between-utterance pauses, the composite measure of executive functioning, and the composite measure of grammatical production competence to gray matter atrophy in areas of significant disease. The coordinates of peaks of the correlations

for the three measures of language production and the composite measure of executive functioning are given in Tables A2–A5 of the Appendix.

Most importantly, we identified two significant cortical areas where there was overlap of atrophy related to speech rate, between-utterance pauses, executive functioning, and grammatical production. These two areas are shown in Figure 2 in coronal slices at $y=60$ (Panel A) and $y=14$ (Panel B). In Panel A, overlap of all four measures is seen in a right medial frontal region (BA 10). In Panel B, overlap of all four measures is seen in two areas of left ventrolateral prefrontal cortex (BA 47).

DISCUSSION

We studied 35 patients with LBSD to assess their deficits in speech production and to determine the linguistic, motor and neuropsychological factors contributing to their impaired fluency. We found that linguistic, motor, and cognitive factors all play a role in the reduced fluency of LBSD patients. Factors contributing to reduced fluency include long pauses between sentences as well as articulatory disorders. Cognitive factors contributing to impaired fluency include deficits in executive function involving planning and mental organization, comprehension of complex grammatical structures, and episodic memory. The speech deficits apparent in these LBSD patients are mainly attributable to the DLB/PDD subgroup. These patients have a progressive dementia involving executive functioning, memory, and visuospatial processing (Emre et al., 2007). We found that reduced fluency in LBSD was related to gray matter atrophy in frontal cortex, in particular in left inferior frontal cortex and right dorsal medial frontal cortex. The findings of the present report thus indicate that patients with DLB/PDD are also impaired in aspects of language production.

Motor impairment

In this study, we focused on the impaired fluency of LBSD patients. Articulatory errors were correlated with speech rate (WPM). Patients made numerous errors in the articulation of words, substituting an incorrect phoneme for a correct one, making false starts to words, and repeating words and restarting phrases. Presumably, articulatory errors slowed the speech of these patients. The correlation of articulation with UPDRS total motor score in LBSD supports the view that a mechanical component contributes to reduced fluency in LBSD. Although LBSD patients have been reported to have hypophonic and prosodically monotonous speech, also related to impaired motor functioning (Sachin et al., 2008), such prosodic phenomena were not recorded in the present cohort of LBSD patients. Motor score in PD and in DLB/PDD was related to the frequency of errors of articulation but not to higher levels of language production (morphology or syntax) or to executive functioning.

Motor deficits alone cannot fully explain the impaired speech fluency of LBSD patients. Patients with DLB/PDD and PD have equivalent motor deficits, yet DLB/PDD patients were significantly more impaired in their speech fluency than PD patients. Therefore, other factors are likely to contribute to reduced fluency in LBSD.

Pauses

LBSD patients also exhibited abnormally long pauses in their speech, which contributed to their reduced overall speech rate. Factoring out the long between-utterance pauses eliminated the difference in speech rate between LBSD and controls and between the DLB/PDD and PD subgroups and controls. The abnormally long pauses of DLB/PDD patients amounted on average to more than one-third of the total duration of the narrative. Correspondingly, their rate of speech was slowed to about half that of controls. We found that the speech of non-demented PD patients was also marked by abnormally long silences

within the stream of speech, although their overall speech rate was not significantly different from that of controls.

For these patients, the factors that contribute to the occurrence of these long pauses appear to include a motor component, reflected by articulatory errors and UPDRS total motor score. In addition, long pauses appeared to be related to many of the same factors as WPM, including executive function and grammatical comprehension. They were also correlated with deficits in the spoken production of grammatical structure. This is consistent with the proposal that between-utterance pauses provide time for planning of the upcoming utterance (Illes, 1989). In addition, long pauses between utterances were correlated with motivation and initiative, which is frequently diminished in PD (Pedersen, Larsen, Alves, & Aarsland, 2009). These findings imply that long pauses between sentences in LBSD contribute to the impaired fluency and overall speech rate of these patients.

Grammar

We next consider the linguistic factors that may contribute to reduced fluency in LBSD. These patients had significant difficulty with grammatical structure in their production of a semi-structured speech sample. Their grammatical errors included omitting required determiners, failing to complete sentences, and omitting the verb phrase, among other errors. While linguistic analyses of the speech production of patients are rare, our findings are consistent with those of earlier reports that have showed that increasing dementia severity corresponds to reduced syntactic complexity (Murray & Lenz, 2001). We found that grammatical expression was significantly compromised in DLB/PDD but not in non-demented PD patients. DLB/PDD patients also have impaired grammatical comprehension compared to both controls and PD. This may suggest the presence of a central disorder of grammatical processing in DLB/PDD, but this topic is beyond the scope of the present study. Regardless of the basis for the grammatical deficit, the grammatical difficulty in DLB/PDD is likely to play a role in the reduced fluency of these patients. Fluent speech depends in part on the ability to construct phrases and clauses rapidly, taking into account the grammatical relations among words in a sentence. It is likely that grammatical limitations contribute to reduced fluency in LBSD. By comparison, lexical retrieval did not differ between control subjects and these LBSD patients.

Executive functioning

Reduced fluency appears to be associated with impaired executive resources in LBSD patients. Language impairments of PD patients are often attributed to a cognitive impairment associated with impaired executive function (Bastiaanse & Leenders, 2009; Grossman, 1999; Grossman et al., 2003). This may be related in part to limitations in a patient's ability to plan and organize a spoken narrative (Ash et al., In press). The performance of these patients on neuropsychological tests also reveals deficits in episodic memory and semantic memory, but it is unlikely that these deficits fully explain the speech production difficulty of LBSD patients. Memory and semantic comprehension are unlikely to play a significant role in the task of this study, since the drawings that comprise the story provide support for the narrations. Nevertheless, episodic memory has a borderline correlation with WPM in LBSD, and this may be related in part to the speaker's ability to remember what s/he has already said. The question of whether higher level language production deficits in PD and DLB/PDD are due to an impairment specific to language or to a generalized cognitive deficit has been raised by others (Bastiaanse & Leenders, 2009; Illes, 1989; Murray & Lenz, 2001). The evidence appears to implicate both a linguistic deficit and a generalized cognitive deficit as obstacles to effective communication in these patients.

In sum, the fluency of narrative speech in LBSD patients exhibits marked impairments. These patients make errors in the articulation of words, which is related to their motor deficits. They have difficulty with the construction of sentences, producing an elevated proportion of unelaborated sentence constructions, missing determiners, incomplete sentences, and other grammatical errors. Their utterances are prone to contain abnormally long pauses, which may provide time for the speaker to organize his/her thoughts and to construct a sentence with complex syntax. The performance of DLB/PDD patients on neuropsychological tests reveals deficits in executive function, memory, semantics, and comprehension, but it appears to be the executive deficit that has the greatest impact in reducing speech rate. Slowed speech is particularly prominent in the DLB/PDD subgroup.

Imaging studies

Further evidence of the fluency impairment of LBSD patients comes from the imaging study. While there is widespread atrophy, regression analyses related speech rate, between-utterance pauses, grammatical production, and executive functioning to specific anatomic distributions of cortical atrophy in these patients. There were two cortical areas that appeared to be playing a particularly prominent role in the slowed speech of LBSD patients, because all four of these speech and cognitive measures were related to the same anatomic distribution of disease. One area associated with reduced fluency in LBSD patients was related to disease in a right medial frontal cortical region (BA10). Imaging studies have demonstrated a connection of this area bilaterally to attention, initiation, and working memory (Gilbert et al., 2006; Ramnani & Owen, 2004). We also found that reduced fluency in LBSD was related to disease in left ventrolateral prefrontal regions (BA 47). Several studies have demonstrated a role for ventrolateral prefrontal regions bilaterally in working memory, episodic memory retrieval, and decision-making. Studies of language production also have shown the importance of these regions for the organization of narrative discourse in healthy adults. In one study, bilateral inferior frontal activation was seen during production of a narrative compared to descriptions of single pictures from the same story (Troiani et al., 2008). In a related study, bilateral inferior frontal activation was evoked by judgments of the degree of association of events in a script (Frag et al., 2010). These prefrontal activations overlap with the recruitment seen in fMRI studies investigating executive resources such as working memory in young adults (Smith, Marshuetz, Geva, & Grafman, 2002). In a study of bvFTD patients, prefrontal cortical atrophy in the right hemisphere was found to be related to difficulty in making the logical connection of one event to the next in narrating the story of a wordless picture book (Ash et al., 2006). BA 47 also is a portion of Broca's area, a region traditionally associated with grammatical aspects of sentence processing. Thus the impaired fluency, prolonged silences, and grammatical difficulty demonstrated by LBSD patients in the current study appear to be a reflection of disease in these areas, compromising speech rate from several perspectives.

This examination is limited by the availability of MRI scans for only one-third of the subjects and by the small number of patients with DLB/PDD. The imaged group is representative of the larger set, however, in that the same proportion of patients is demented in both groups. The imaged LBSD patients also exhibited impairment on each of the measures presented in the regression analyses. We did not perform a categorical analysis comparing groups of patients because of the small sizes of these patient subgroups. More importantly, the regression analysis allowed us to relate the range of atrophy across the spectrum of disease to a parametric assessment of the factors contributing to patients' reduced speech fluency. Although the DLB/PDD patients have more advanced disease, the severity of their disease is relatively mild, and there do not appear to be outliers that could skew the imaging analysis. Nevertheless, future work will benefit from expansion of the sample size in the imaging analysis to a much larger number of subjects.

CONCLUSIONS

In this study, we have extended work on speech production to patients with LBSD. They demonstrate a range in quantified measures of language performance, though they share common pathology. Diminished fluency, in the form of reduced speech rate and extended pausing, was related to deficits in executive function and prefrontal atrophy, suggesting that patients require additional time to plan upcoming utterances compared to healthy seniors. Difficulty with articulation and grammar is primarily found in DLB/PDD patients and reflects a dementia that extends to language-internal factors. Consistent with previous reports, we found that the language production of PD patients is virtually intact, with the exception of extended silences which occur between utterances. DLB/PDD patients exhibit this abnormality and also have deficits in speech articulation, executive function, and grammaticality.

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APPENDIX

Table 1

Mean $\pm$ standard deviation of demographic, clinical, neuropsychological, and language characteristics of 35 LBSD patients and the subset of 11 LBSD patients for whom MRI scans were available¹

	Lewy Body Spectrum Disorder	LBSD patients in imaging analysis
N (male/female)	23/12	9/2
Age (yrs)	72.0 $\pm$ 8.4 (35)	73.5 $\pm$ 5.0 (11)
Education (yrs)	15.5 $\pm$ 2.8 (35)	15.5 $\pm$ 2.7 (11)
MMSE (max=30)	25.0 $\pm$ 4.6 (32)	26.4 $\pm$ 3.0 (11)
Disease duration (yrs)	6.2 $\pm$ 2.8 (34)	7.1 $\pm$ 2.8 (10)

	Lewy Body Spectrum Disorder	LBSD patients in imaging analysis
Levodopa equivalent dose	451 ±399 (26)	348 ±264 (9)
UPDRS total motor score	22.9 ±11.5 (27)	23.0 ±9.3 (11)
Hoehn & Yahr stage	2.4 ±0.6 (30)	2.3 ±0.6 (11)
UPDRS Motivation/Initiative (max=4) ²	.33 ± .59 (18)	.33 ± .50 (9)
Memory		
Word list recall	5.2 ±3.1 (17)	7.0 ±2.6 (8)
Executive function		
Executive composite ³	-2.26 ±2.77 (32)	-1.4 ±2.6 (11)
Letter-guided fluency (FAS)	30.2 ±17.0 (32)	39.9 ±17.0 (11)
Category fluency (animals)	13.0 ±7.3 (32)	15.0 ±6.2 (11)
Reverse digit span	4.2 ±1.5 (30)	4.5 ±1.6 (10)
Trails B time (sec)	136 ±48 (29)	127 ±53 (11)
Stroop time (sec)	112 ±50 (24)	92 ±53 (9)
Semantics		
Boston Naming Test (% correct)	88.9 ±8.8 (27)	87.8 ±6.6 (6)
Pyramids & Palm Trees (max=52)	47.6 ±5.1 (25)	49.0 ±3.9 (11)
Comprehension		
Complex sentences (max=48)	37.2 ±7.8 (18)	39.9 ±7.6 (10)
Words and sentences		
	N=35	N=11
Total word count	526 ±251	541 ±264
Words per minute	106 ±45	107 ±43
Modified words per minute ⁴	134 ±42	133 ±41
Pauses		
Between-utterance pause duration (% of total duration)	22.7 ±19.3	22.1 ±19.3
Within-utterance pause duration (% of total duration)	5.9 ±11.3	5.6 ±5.7
Speech sounds		
Articulation errors/100 words	10.8 ±9.9	12.7 ±11.6
Grammar and lexical retrieval		
Sentence structure (maximum=3)	2.12 ±.37	2.27 ±.20
Open class words (%)	41.1 ±3.3	40.7 ±1.7

NOTES

¹ MRI scans were conducted within one year of the present experimental task.

There are no statistically significant differences between groups.

Since not all participants were available for testing on all neuropsychological measures, and because of technical limitations in recovering some demographic and clinical features, we provide the numbers of participants ascertained for each of those characteristics in parentheses. There is no missing data for measures of language production.

² A higher score corresponds to increasing impairment.

³ The composite score of executive function was constructed by averaging the Z-scores of letter-guided naming fluency, category naming fluency, Trails B time, and Stroop time.

⁴This variable was constructed by subtracting the total duration of between-utterance pauses (that were more than 2 sec long) from the total duration of the narrative. WPM was then calculated based on the total number of words in the narrative and the duration with long pauses removed.

Table 2

Regional distribution of significant atrophy in Lewy body spectrum disorder patients related to speech rate in words per minute.

Anatomic locus (Brodmann area)	Coordinates			Z-score	Cluster size (voxels)
	x	y	z		
Left anterior cingulate (32)	-9	42	0	3.36	544
Left ventral medial prefrontal (11)	-32	35	-18	3.25	947
Left ventral lateral prefrontal (47)	-53	15	-1	3.51	97
Left dorsolateral prefrontal (9)	-42	26	35	3.33	600
Left middle temporal (21)	-65	-40	-1	3.25	719
Left superior temporal (22)	-58	-5	4	3.12	448
Left superior temporal (22/42)	-65	-31	9	3.13	240
Left superior temporal (42)	-63	-35	20	3.11	146
Left temporal/parietal (22/40)	-58	-50	22	4.52	1121
Left inferior parietal (40)	-44	-51	49	3.22	311
Left inferior parietal (39)	-49	-71	22	3.65	153
Left middle occipital (19)	-48	-67	-4	3.37	76
Left middle occipital (19)	-24	-89	18	3.14	454
Left hippocampus	-31	-11	-15	3.52	2372
Left hippocampal (36)	-35	-31	-15	3.56	214
Left precuneus (31)	-3	-49	35	3.63	493
Right anterior frontal (10)	42	68	-6	3.94	282
Right medial frontal (10)	6	65	18	3.56	764
Right insula	43	-10	0	4.12	552
Right inferior temporal (37)	59	-56	-11	3.34	483
Right superior temporal (22)	64	-22	5	3.11	241
Right inferior parietal (39)	48	-57	24	3.35	131
Right inferior parietal (39)	50	-65	12	3.44	336
Right inferior parietal (40/7)	37	-67	46	3.5	3695
Right middle occipital (19)	25	-81	21	3.68	145
Right hippocampal (36)	35	-22	-15	3.66	1369
Right precuneus (7)	2	-55	48	3.65	53
Right fusiform (19)	28	-70	-11	4.14	341

Table 3

Regional distribution of significant atrophy in Lewy body spectrum disorder patients related to between-utterance pause time.

Anatomic locus (Brodmann area)	Coordinates			Z-score	Cluster size (voxels)
	x	y	z		
Left anterior frontal (10)	-14	65	6	3.31	281
Left anterior frontal (10)	-41	45	12	3.93	1046
Left medial frontal (10)	-10	56	-5	4.43	213
Left ventral medial prefrontal (11)	-27	60	-11	4.21	784
Left anterior cingulate (32)	-13	42	-2	4.19	836
Left ventral medial prefrontal (11)	-41	38	-17	3.93	985
Left dorsolateral prefrontal (9)	-41	32	32	4.16	1207
Left dorsolateral prefrontal (45/46)	-51	26	14	3.75	808
Left ventral lateral prefrontal (47)	-55	16	-1	3.12	295
Left ventral lateral prefrontal (47)	-26	10	-17	3.93	2157
Left precentral (6)	-63	1	12	3.19	377
Left precentral (6)	-60	1	24	3.46	323
Left inferior temporal (38)	-43	7	-35	4.19	1018
Left inferior temporal (20)	-48	-22	-24	4.26	320
Left middle temporal (21)	-63	-21	-1	4.48	1888
Left middle temporal (21/37)	-65	-45	-3	3.81	645
Left middle temporal (37)	-55	-56	0	3.35	126
Left superior temporal (42)	-65	-31	18	3.36	179
Left posterior temporal (37)	-45	-81	-6	3.36	138
Left temporal/parietal (22/40)	-57	-50	22	3.83	1776
Left middle occipital (18)	-24	-96	12	4.12	648
Left cingulate (24)	-5	-9	38	4.38	509
Left posterior cingulate (31)	-3	-54	23	3.94	561
Left hippocampus	-24	-12	-13	4.12	4898
Left hippocampal (36)	-35	-30	-18	3.59	291
Left precuneus (7)	-13	-62	36	3.32	171
Left cuneus (18)	-37	-92	1	3.29	277
Right medial frontal (10)	7	65	17	3.95	922
Right ventral lateral prefrontal (47)	36	30	-1	3.18	258
Right ventral lateral prefrontal (47)	35	27	-16	3.74	2333
Right dorsolateral prefrontal (46)	45	39	20	3.14	90
Right dorsolateral prefrontal (46)	51	23	23	4.43	365
Right dorsolateral prefrontal (9)	45	22	36	3.68	182
Right medial temporal (34)	21	-1	-14	4.36	8457
Right middle temporal (21)	47	2	-29	4.04	1068

Anatomic locus (Brodmann area)	Coordinates			Z-score	Cluster size (voxels)
	x	y	z		
Right middle temporal (21)	64	-36	-11	3.72	399
Right superior temporal (22)	64	-41	4	3.52	860
Right inferior parietal (39)	44	-65	35	3.99	2591
Right middle occipital (19)	45	-66	-3	3.6	421
Right middle occipital (19)	38	-91	5	3.56	1700
Right hippocampal (36)	31	-28	-19	3.44	348
Right fusiform (19)	30	-70	-11	3.61	877
Right lingual (18)	5	-76	-2	3.7	513
Right cuneus	8	-101	-1	3.27	771

Table 4

Regional distribution of significant atrophy in Lewy body spectrum disorder patients related to composite grammar score.

Anatomic locus (Brodmann area)	Coordinates			Z-score	Cluster size (voxels)
	x	y	z		
Left anterior frontal (10/11)	-44	54	-10	3.51	663
Left ventral lateral prefrontal (10/47)	-52	40	0	3.31	136
Left ventral lateral prefrontal (47)	-45	11	2	3.47	71
Left ventral lateral prefrontal (47)	-22	21	-21	3.34	1014
Left hippocampal (28)	-22	21	-21	3.34	1014
Left dorsolateral prefrontal (46)	-35	29	23	3.31	236
Left dorsolateral prefrontal (45)	-54	23	15	3.53	2502
Left precentral (6/9)	-51	3	42	3.67	235
Left precentral (4)	-60	-3	17	3.16	321
Left precentral (4)	-59	-9	23	3.32	641
Left anterior temporal (38)	-50	18	-10	3.4	730
Left inferior temporal (20)	-44	-5	-37	3.41	527
Left inferior temporal (20)	-66	-44	-16	3.21	362
Left superior temporal (42)	-68	-28	11	3.45	1074
Left superior temporal (22)	-56	5	-4	3.26	1054
Left superior temporal (22)	-64	-48	15	4.31	313
Left inferior parietal (40)	-62	-24	20	3.35	197
Left inferior parietal (40)	-56	-32	45	3.25	1062
Left inferior parietal (40)	-50	-58	46	3.52	938
Left superior parietal (7)	-34	-49	61	3.14	340
Left middle occipital (19)	-42	-77	20	4.09	115
Left middle occipital (19)	-24	-83	22	4.19	859
Left hippocampal	-17	-52	12	3.55	2250

Anatomic locus (Brodmann area)	Coordinates			Z-score	Cluster size (voxels)
	x	y	z		
Left cingulate (24)	-2	-17	40	3.16	469
Left posterior cingulate/precuneus (31/7)	-7	-52	30	4.28	440
Left precuneus	-21	-64	33	4.72	6053
Left lingual (18)	-7	-76	-5	4.14	317
Left cuneus (17)	-13	-84	13	3.23	1216
Left cuneus (17/18)	-6	-92	8	4.47	447
Right medial frontal (10)	2	59	17	4.18	1581
Right ventral medial prefrontal (11/47)	22	30	-10	3.43	644
Right ventral lateral prefrontal (47)	46	33	-15	3.25	783
Right insula	36	6	11	3.95	1650
Right precentral (6)	62	5	21	3.7	2531
Right inferior temporal (20)	46	-7	-34	3.48	666
Right middle temporal (21)	50	-16	-11	3.97	1913
Right middle temporal (21/22)	57	-19	-2	3.26	101
Right middle temporal (21/37)	66	-48	-4	3.77	865
Right inferior parietal (40)	33	-40	50	3.13	633
Right inferior parietal (40)	42	-46	49	3.54	815
Right parietal (7/40)	24	-43	54	3.23	126
Right middle occipital (19)	36	-78	6	3.87	623
Right hippocampal (35)	21	-31	-8	3.59	1348
Right precuneus	22	-56	37	4.45	8213
Right fusiform (37)	39	-61	-14	3.26	209
Right lingual (19)	10	-66	-3	3.32	344

Table 5

Regional distribution of significant atrophy in Lewy body spectrum disorder patients related to composite executive score.

Anatomic locus (Brodmann area)	Coordinates			Z-score	Cluster size (voxels)
	x	y	z		
Left anterior frontal (10)	-12	65	-7	4.07	228
Left anterior cingulate (32)	-11	43	7	3.6	580
Left ventral lateral prefrontal (47)	-54	17	0	3.48	207
Left inferior frontal (6/44)	-61	6	26	3.13	295
Left anterior temporal (38)	-34	6	-15	3.47	1794
Left inferior temporal (20)	-41	-5	-35	3.88	92
Left middle temporal (21)	-46	6	-34	3.16	210
Left superior temporal (22)	-59	4	2	3.2	235
Left cingulate (24)	-6	-17	39	3.4	465

Anatomic locus (Brodmann area)	Coordinates			Z-score	Cluster size (voxels)
	x	y	z		
Left hippocampus	-37	-20	-14	3.48	1730
Right medial frontal (10)	2	64	17	4.23	1354
Right ventral medial prefrontal (11)	47	40	-15	3.65	755
Right dorsolateral prefrontal (9)	44	23	35	3.35	116
Right insula	34	-6	8	3.93	1574
Right insula	35	-10	-5	3.46	3495
Right precentral (4/6)	62	-3	19	3.51	786
Right inferior temporal (20)	59	-13	-20	3.42	117
Right middle temporal (21)	45	0	-28	3.17	406
Right inferior parietal (39)	50	-64	14	3.12	380
Right hippocampus	34	-19	-16	4.28	1984
Right precuneus (7/19)	26	-65	31	3.25	3215
Right lingual (18)	6	-71	-1	3.63	282

We examined speech fluency in patients with Lewy body spectrum disorder (LBSD). LBSD patients showed reduced overall speech rate and long silences between sentences. Articulation and grammar were impaired primarily in LBSD patients with dementia. Impaired speech fluency was associated with deficits in executive functioning. Reduced speech fluency was related to prefrontal cortical atrophy.

Figure 1.
Cortical atrophy in Lewy body spectrum disorder patients.¹

NOTE: 1. Vertical lines show locations of coronal slices displayed in Figure 2: $y = 60$ and $y = 14$.

Figure 2.

Coronal slices showing overlap of correlations of measures of language production and neuropsychological test performance with cortical atrophy. Red shows region of correlation of WPM with cortical atrophy; colored outlines show regions of correlation of performance scores with cortical atrophy. Yellow = between-utterance pause time; blue = composite grammatical performance score; green = composite executive test Z-score.

Table 1

Mean $\pm$ standard deviation of demographic, clinical and neuropsychological characteristics of patients and controls¹

	Lewy Body Spectrum Disorder	DLB/PDD subgroup	PD subgroup	Controls
N (male/female)	23/12	10/4	13/8	5/11
Age (yrs)	72.0 $\pm$ 8.4 (35)	72.6 $\pm$ 9.4 (14)	71.6 $\pm$ 7.8 (21)	68.6 $\pm$ 6.8 (16)
Education (yrs)	15.5 $\pm$ 2.8 (35)	15.6 $\pm$ 3.0 (14)	15.4 $\pm$ 2.7 (21)	15.6 $\pm$ 2.6 (16)
MMSE (max=30)	25.0 $\pm$ 4.6** (32)	20.9 $\pm$ 4.7** (12)	27.4 $\pm$ 2.0* (20)	29.1 $\pm$ 1.2 (13)
Disease duration (yrs)	6.2 $\pm$ 2.8 (34)	6.6 $\pm$ 2.3 (14)	6.0 $\pm$ 3.1 (20)	--
Levodopa equivalent dose	451 $\pm$ 399 (26)	287 $\pm$ 377 (12)	592 $\pm$ 373 (14)	--
Cholinesterase inhibitor use	4 (32)	3 (14)	1 (18)	--
UPDRS total motor score	23.1 $\pm$ 10.8 (32)	24.9 $\pm$ 12.9 (14)	21.7 $\pm$ 9.0 (18)	--
Hoehn & Yahr stage	2.4 $\pm$ 0.6 (32)	2.7 $\pm$ 0.5 (14)	2.2 $\pm$ 0.6 (18)	--
UPDRS Motivation/Initiative (max=4) ²	.33 $\pm$.59 (18)	.60 $\pm$.55 (5)	.23 $\pm$.60 (13)	--
Memory				
Word list recall (max=10)	5.2 $\pm$ 3.1* (17)	2.4 $\pm$ 1.7** (8)	7.7 $\pm$ 1.6 (9)	7.7 $\pm$ 2.0 (9)
Executive function				
Executive composite ³	-2.26 $\pm$ 2.77 (32)	-4.76 $\pm$ 1.86 (12)	-.76 $\pm$ 2.06 (20)	--
Letter-guided fluency (FAS)	30.2 $\pm$ 17.0 (32)	18.3 $\pm$ 10.8** (12)	37.4 $\pm$ 16.2 (20)	43.8 $\pm$ 9.8 (10)
Category fluency (animals)	13.0 $\pm$ 7.3** (32)	7.1 $\pm$ 3.6** (12)	16.6 $\pm$ 6.7* (20)	22.3 $\pm$ 5.1 (12)
Reverse digit span	4.2 $\pm$ 1.5 (30)	3.0 $\pm$ 0.8** (11)	4.9 $\pm$ 1.4 (19)	5.4 $\pm$ 1.6 (9)
Trails B time	136 $\pm$ 48 (29)	174 $\pm$ 16** (11)	114 $\pm$ 47 (18)	109 $\pm$ 44 (10)
Stroop time	112 $\pm$ 50 (24)	160 $\pm$ 33** (9)	83 $\pm$ 35 (15)	76 $\pm$ 19 (10)
Semantics				
Boston Naming Test (% correct)	88.9 $\pm$ 8.8 (27)	84.4 $\pm$ 8.0* (12)	92.4 $\pm$ 8.0 (15)	92.0 $\pm$ 11.7 (10)
Pyramids & Palm Trees (max=52)	47.6 $\pm$ 5.1** (25)	44.5 $\pm$ 6.8** (10)	49.6 $\pm$ 1.8* (15)	51.5 $\pm$ 0.8 (6)
Comprehension				
Complex sentences (max=48)	37.2 $\pm$ 8.1** (18)	29.7 $\pm$ 5.8** (7)	42.0 $\pm$ 4.4* (11)	46.0 $\pm$ 1.2 (5)

NOTES

¹ Pairwise statistical differences between groups: * differs from controls, $p < .05$; ** differs from controls, $p < .01$. Since not all participants were available for testing on all neuropsychological measures, and because of technical limitations in recovering some demographic and clinical features, we provide in parentheses the numbers of participants for which each characteristic was ascertained.

² A higher score corresponds to increasing impairment.

³ The composite score of executive function was constructed by averaging the Z-scores of letter-guided naming fluency, category naming fluency, Trails B time, and Stroop time.

Table 2Mean $\pm$ standard deviation for measures of language and dysfluencies.¹

	Lewy Body Spectrum Disorder (N=35)	DLB/PDD subgroup (N=14)	PD subgroup (N=21)	Controls (N=16)
Output				
Total words	526 $\pm$ 251	452 $\pm$ 291*	576 $\pm$ 214	609 $\pm$ 228
Words per minute	106 $\pm$ 45*	73 $\pm$ 39**	128 $\pm$ 35	140 $\pm$ 22
Modified words per minute ²	134 $\pm$ 42	115 $\pm$ 47	148 $\pm$ 33	146 $\pm$ 19
Pauses				
Between-utterance pause duration (% of total duration)	22.7 $\pm$ 19.3**	37.3 $\pm$ 17.0**	13.1 $\pm$ 14.3**	4.6 $\pm$ 5.8
Speech sounds				
Articulation errors/100 words	10.8 $\pm$ 9.9	17.3 $\pm$ 11.9**	6.4 $\pm$ 5.0	5.9 $\pm$ 6.0
Grammar and lexical retrieval				
Sentence structure (maximum=3)	2.12 $\pm$.37*	1.91 $\pm$.46**	2.27 $\pm$.19	2.35 $\pm$.26
Open class words (%)	41.1 $\pm$ 3.3	41.1 $\pm$ 4.0	41.1 $\pm$ 2.9	42.8 $\pm$ 3.1

NOTES

¹ Pairwise statistical differences between groups: * differs from controls, $p < .05$; ** differs from controls, $p < .01$.

² This variable was constructed by subtracting the total duration of between-utterance pauses (that were more than 2 sec long) from the total duration of the narrative. WPM was then calculated based on the total number of words in the narrative and the duration with long pauses removed.

Table 3

Correlations of language production with language and extra-linguistic measures in LBSD (N=35). Only significant correlations are shown. (For motor and cognitive measures, the number of subjects for whom data are available is given in parentheses at the beginning of each row.)

	Speech production	
	WPM	Between-utterance pauses
Speech production		
Modified WPM	.76 **	--
Between-utterance pauses	-.73 **	--
Articulation errors	-.39 *	.49 **
Grammatical structure	--	-.49 **
Motor and cognition		
UPDRS total motor score (N=32)	--	--
UPDRS initiation (N=18)	--	.67 **
Executive function (N=32)	.69 **	-.75 **
Grammatical comprehension (N=18)	.75 **	-.66 **
Memory: word list recall (N=17)	.51 *	

*
p<.05;

**
p<.01

Table 4
Regional distribution of significant atrophy in Lewy body spectrum disorder patients

Anatomic locus (Brodmann area)	Coordinates			Z-score	Cluster size (voxels)
	x	y	z		
Left anterior frontal (10)	-17	64	4	3.77	495
Left medial frontal (10)	-7	48	11	4.23	799
Left ventral lateral prefrontal (47)	-45	53	-7	3.6	914
Left ventral lateral prefrontal (47)	-56	16	-1	3.34	493
Left dorsolateral prefrontal (45)	-57	27	16	3.54	4530
Left superior frontal (6)	-45	2	50	3.41	431
Left anterior temporal (38)	-22	15	-23	3.9	3566
Left inferior temporal (20/38)	-43	4	-35	3.37	1779
Left inferior temporal (20)	-67	-14	-16	3.74	1791
Left inferior temporal (20)	-50	-19	-28	3.15	551
Left superior temporal (22)	-62	2	-1	4.22	6660
Left inferior parietal (40)	-47	-25	15	3.17	411
Left inferior parietal (40)	-61	-34	37	3.66	1174
Left postcentral (43)	-67	-14	20	3.56	1381
Left cingulate (24)	-4	-13	41	3.44	1135
Left cingulate (31)	-6	-52	30	3.4	848
Left hippocampal (36)	-27	-27	-15	4.12	6538
Left hippocampal (36)	-37	-36	-21	3.32	433
Left fusiform (37)	-51	-56	-17	3.71	885
Left fusiform (18)	-32	-81	-13	3.29	1312
Left precuneus	-3	-75	25	3.32	8781
Left cuneus (18)	-39	-91	3	3.16	525
Right medial frontal (9)	3	55	19	3.41	1488
Right ventral lateral prefrontal (47)	36	29	-17	3.41	3070
Right dorsolateral prefrontal (9)	46	26	35	3.43	425
Right dorsolateral prefrontal (46)	45	48	9	3.49	764

Anatomic locus (Brodmann area)	Coordinates			Z-score	Cluster size (voxels)
	x	y	z		
Right dorsolateral prefrontal (46)	51	31	19	3.65	410
Right dorsolateral prefrontal (45)	56	19	4	3.87	401
Right insula	36	-16	20	4.16	12202
Right precentral (3)	63	-11	25	3.88	3305
Right inferior temporal (20)	46	1	-34	4.05	1214
Right inferior temporal (20)	54	-15	-26	3.35	447
Right middle temporal (21)	68	-29	-10	4.15	2950
Right inferior parietal (40)	27	-34	41	3.34	744
Right inferior parietal (40)	51	-45	36	3.87	783
Right fusiform (37)	40	-56	-16	3.93	1172
Right lingual (18)	8	-73	-3	3.57	668
Right cuneus (18/19)	12	-97	22	4.18	21067