Brain & Language 171 (2017) 42–51

Contents lists available at ScienceDirect

Brain & Language

journal homepage: www.elsevier.com/locate/b&l

Longitudinal decline in speech production in Parkinson's disease spectrum disorders

Sharon Ash *, Charles Jester, Collin York, Olga L. Kofman, Rachel Langey, Amy Halpin, Kim Firn, Sophia Dominguez Perez, Lama Chahine, Meredith Spindler, Nabila Dahodwala, David J. Irwin, Corey McMillan, Daniel Weintraub, Murray Grossman

Department of Neurology, Perelman School of Medicine, University of Pennsylvania, United States

ARTICLE INFO

Article history:
Received 6 September 2016
Revised 5 May 2017
Accepted 8 May 2017

Keywords:
Parkinson's disease
Longitudinal studies
Language
Speech
Spontaneous discourse

ABSTRACT

We examined narrative speech production longitudinally in non-demented (n = 15) and mildly demented (n = 8) patients with Parkinson's disease spectrum disorder (PDSD), and we related increasing impairment to structural brain changes in specific language and motor regions. Patients provided semi-structured speech samples, describing a standardized picture at two time points (mean ± SD interval = 38 ± 24 months). The recorded speech samples were analyzed for fluency, grammar, and informativeness. PDSD patients with dementia exhibited significant decline in their speech, unrelated to changes in overall cognitive or motor functioning. Regression analysis in a subset of patients with MRI scans (n = 11) revealed that impaired language performance at Time 2 was associated with reduced gray matter (GM) volume at Time 1 in regions of interest important for language functioning but not with reduced GM volume in motor brain areas. These results dissociate language and motor systems and highlight the importance of non-motor brain regions for declining language in PDSD.

1. Introduction

The term Parkinson's disease spectrum disorder (PDSD) covers a range of progressive neurodegenerative conditions characterized by the presence of synuclein histopathologic inclusions. These include Parkinson's disease (PD) without cognitive impairment, PD with mild cognitive impairment (PD-MCI) that typically affects a single domain of cognition such as executive or visuospatial functioning, PD with dementia (PDD) and dementia with Lewy bodies (DLB). Besides the motor deficits present in all PD and most DLB patients, up to 80% of PD patients and all DLB develop dementia (Aarsland, Andersen, Larsen, Lolk, & Kragh-Sorensen, 2003; Buter et al., 2008; Hely, Reid, Adena, Halliday, & Morris, 2008), including deficits in executive function, memory, visuospatial perception, and language.

With regard to verbal communication, investigations of language in PDSD have reported impairments in voice and articulation, which may be attributed to declining motor function (Cummings, Darkins, Mendez, Hill, & Benson, 1988; Ho, Iansek, Marigliani, Bradshaw, & Gates, 1998). Other areas of difficulty reported for language include sentence comprehension (Grossman, Carvell, Stern, Gollomp, & Hurtig, 1992; Lieberman, Friedman, & Feldman, 1990) and verbal fluency (Crescentini, Mondolo, Biasutti, & Shallice, 2008; Obeso, Casabona, Bringas, Alvarez, & Jahanshahi, 2012). However, there are few reports of spontaneous speech production in PDSD (Robinson, 2013).

Rare studies have examined the decline of different aspects of cognitive functioning over time in PDSD (de Lau, Schipper, Hofman, Koudstaal, & Breteler, 2005; Janvin, Aarsland, & Larsen, 2005; Marder, Tang, Cote, Stern, & Mayeux, 1995; Shoji et al., 2014), but we are not aware of any studies that have examined the trajectory of speech production difficulties in PDSD over time. Spontaneous language production is critical to the ability of a person to communicate with family, caregivers, and medical providers. An improved understanding of the language production capabilities of PDSD patients and the evolution of these capabilities over time has the potential value of informing speech therapy interventions for PD, facilitating accurate prognosis, and improving endpoints in treatment trials. The present report provides the first longitudinal study of impairments in speech production in PDSD, and we examine the contributions of motor and cognitive impairments to speech deficits in these patients. We hypothesized that language impairments in PDSD are not exclusively a consequence

* Corresponding author at: Department of Neurology, 3 West Gates, Hospital of the University of Pennsylvania, 3400 Spruce St, Philadelphia, PA 19104-4283, United States.
E-mail address: ash@upenn.edu (S. Ash).

http://dx.doi.org/10.1016/j.bandl.2017.05.001
0093-934X/

Table 1
Means ± SD demographic and clinical characteristics of patients and controls.

	Non-demented	Demented	Controls
Number (M)	15 (13)	8 (5)	20 (9)
Education (y)	17.1 ± 2.1	15.0 ± 1.5	16.0 ± 2.5
Age of onset (y)	59.8 ± 8.9	61.6 ± 8.1	n/a
Age at Time 1 (y)	68.9 ± 5.3	69.1 ± 8.6	68.6 ± 8.2
Disease duration at Time 1 (y)	9.2 ± 6.8	7.1 ± 4.4	n/a
Time 1 to Time 2 interval (mos)	37.7 ± 23.6	36.7 ± 25.4	n/a
Clinical measures			
UPDRS I Motivation/Initiative, Time 1 (max = 4)	0.23 ± 0.44 (13)	0.33 ± 0.58 (3)	–
UPDRS I Motivation/Initiative, Time 2 (max = 4)	0.64 ± 0.63 (14)	1.00 ± 0.82 (4)	–
UPDRS II: oral motor score, Time 1 (max = 12)	1.69 ± 1.70 (13)	1.33 ± 1.53 (3)	–
UPDRS II: oral motor score, Time 2 (max = 12)	2.00 ± 1.78 (13)	3.50 ± 2.65 (4)	–
UPDRS III, Time 1	24.4 ± 9.5 (14)	27.7 ± 18.8 (3)	–
UPDRS III, Time 2	31.9 ± 16.2 (14)[@]	38.8 ± 8.8 (4)	–
Hoehn & Yahr stage, Time 1	2.71 ± 0.47 (14)	3.50 ± 1.05 (6)	–
Hoehn & Yahr stage, Time 2	2.71 ± 0.47 (14)	3.83 ± 0.75 (6)[#]	–
Cognitive measures[1,2,3*]			
MMSE, Time1	28.5 ± 1.4 (15)	25.2 ± 3.2 (8)	29.3 ± 1.1 (19)
MMSE, Time2	27.9 ± 2.5 (15)[^]	20.4 ± 3.9 (7)[#@]	
BNT, Time 1	28.8 ± 1.6 (14)	25.0 ± 3.6 (8)[#]	28.6 ± 1.5 (17)
BNT, Time 2	28.7 ± 2.2 (13)	23.1 ± 5.7 (7)	
FAS Total, Time 1	45.6 ± 12.1 (14)	29.4 ± 11.1 (8)[#]	43.3 ± 10.6 (17)
FAS Total, Time 2	41.9 ± 11.2 (12)	21.8 ± 7.4 (6)[#]	
Reverse digit span, Time 1	5.4 ± 1.3 (14)	4.0 ± 1.1 (7)	5.6 ± 1.5 (14)
Reverse digit span, Time 2	4.9 ± 1.1 (9)	3.3 ± 1.1 (7)	

Notes:
FAS: letter-guided fluency – executive functioning.
Reverse digit span – working memory.
[1] We provide in parentheses the numbers of participants for whom scores were obtained if less than the total, due to technical limitations in recovering some clinical features.
[2] BNT: a 30-item version of the Boston Naming Test – lexical access
[*3] DEM differ from NON-DEM and controls at $p < 0.05$ for all cognitive measures at Time 1 and Time 2.
[#] DEM differ from NON-DEM at $p < 0.01$.
[^] NON-DEM differ from controls at $p < 0.05$.
[@] Time 2 differs from corresponding Time 1 at $p < 0.05$.

of motor impairments, and we found evidence substantiating this hypothesis by observing specific changes in features of speech production over time and the association of those changes with neuroanatomic atrophy.

Language is classically thought to be supported by *peri*-Sylvian regions of the left hemisphere (Damasio & Geschwind, 1984; Geschwind, 1970). Inferior frontal regions have been associated with grammatical features of speech production such as mean length of utterance (MLU) (Borovsky, Saygin, Bates, & Dronkers, 2007; Grossman et al., 1996; Grossman et al., 2013), and posterior-superior temporal regions have been associated with lexical retrieval and the expression of meaningful language content (Borovsky et al., 2007; Troiani et al., 2008). It has become clear in more recent studies that some aspects of language receive bilateral support. For example, speech rate recently has been associated with bilateral frontal regions, particularly in individuals who are aging or have a neurodegenerative disease (Ash et al., 2012; Grossman et al., 2013; van Oers et al., 2010). In the present study, we investigate whether atrophy at baseline in brain regions important for language predicts longitudinal speech production deficits in PDSD.

2. Materials and methods

2.1. Subjects

We conducted a longitudinal study of 23 patients with PDSD, diagnosed in the Cognitive Neurology or Movement Disorders clinics of the Department of Neurology at the University of Pennsylvania by experienced neurologists according to published criteria (Emre et al., 2007; Hughes, Daniel, Kilford, & Lees, 1992; Litvan et al., 2007; McKeith et al., 2005). We examined two groups of patients and assessed each patient twice (Time 1 and Time 2). A non-demented group (NON-DEM, n = 15) consisted of a combined cohort of 9 patients with PD and no recorded cognitive impairment and 6 patients with PD-MCI, who exhibited impairment in only a single cognitive domain (Litvan et al., 2007). The second group, patients with dementia (DEM, n = 8), consisted of 3 patients with PDD and 5 with DLB, diagnosed according to criteria for PDD (Emre et al., 2007) and DLB (McKeith et al., 2005). Patients whose cognitive status declined during the interval between assessments were assigned to the group corresponding to their first assessment (Time 1). Three PD patients with no cognitive impairment at Time 1 were judged to have MCI at Time 2. Since the NON-DEM group consisted of both unimpaired PD patients and patients with MCI, these three participants were assigned to the NON-DEM group despite their change in cognitive status. One patient with PD-MCI at Time 1 was diagnosed with PD-PDD at Time 2. The analyses reported below were conducted with this patient assigned to the NON-DEM group, in accordance with the principle stated above. However, to test the validity of this classification, all significance tests were also run both with this patient assigned to the DEM group and with this patient omitted altogether. These different assignments produced no change to the significance of any of the results reported below. Features such as fluctuating cognition, attention, alertness, and visual hallucinations were mild and did not interfere with performance at the time of testing. Exclusionary criteria included other causes of dementia, such as metabolic, endocrine, vascular, structural, nutritional, and infectious etiologies and primary psychiatric disorders. Each of the 2 subgroups of patient participants was compared to a group of 20 healthy control subjects. These healthy controls were examined only once, since pilot work indicated that there is little change over this brief