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Intraindividual variability in neurocognitive speed: A comparison of Parkinson's disease and normal older adults

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Abstract

We examined whether intraindividual variability of neurocognitive speed, or inconsistency, is greater in stages of Parkinson's disease (PD) as compared to a matched group of normal older adults. Intraindividual variability was assessed using four reaction time (RT) (simple and complex) tasks. We examined three sets of correlates: executive functioning (Stroop (interference index), Trail Making Test (Part B), and Digit Ordering Test), finger tapping speed, and gait speed. The participants were matched on age, sex, and education, and did not differ in global cognitive functioning. There were 50 patients with a clinical diagnosis of idiopathic PD (29 men and 21 women) who ranged from 65 to 84 years ($M = 71.5$, S.D. = 4.7) and 48 matched healthy older adults who ranged from 65 to 84 years ($M = 71.5$, S.D. = 4.9). Multiple analyses of variance showed that the PD patients were slower on all three complex RT tasks, and more inconsistent than healthy older adults on the most complex (eight-choice) RT task. Individuals with advanced disease had slower neurocognitive speed and more inconsistency than patients with earlier stage PD. Poorer executive functioning was associated with slower neurocognitive performance in healthy older adults, mild PD patients, and especially severe PD patients. Greater inconsistency in speed was related to poorer executive functioning in late stage PD (for the most complex task) and in healthy older adults (for the simplest task), indicating that motor and cognitive domains have functional coupling (i.e., as one becomes compromised so does the other). Intraindividual variability was not correlated with tapping speed and gait speed in any group. Executive functioning and neurocognitive speed may be valid and distinct clinical markers of disease progression in PD.

Keywords: Parkinson's disease; Aging; Variability; Speed; Executive function; Gait

Intraindividual variability, or inconsistency, is a measure of relatively short-term and reversible changes in an individual's performance across trials or occasions of the same task (Fuentes, Hunter, Strauss, & Hultsch, 2001; Hultsch, MacDonald, & Dixon, 2002; Li & Lindenberger, 1999; Stuss, Pogue, Buckle, & Bondar, 1994). Intraindividual variability in neurocognitive speed has been considered a measure of neurobiological disturbance (Henrickson, 1982; Hultsch & MacDonald, 2004; Li & Lindenberger, 1999) and possibly low physical and cognitive capacity in both normal aging adults (e.g., Bunce, MacDonald, & Hultsch, 2004; Fozard, Vercryssen, Reynolds, Hancock, & Quilter, 1994; Hultsch et al., 2002; Li, Aggen, Nesselroade, & Baltes, 2001; West, Murphy, Armilio, Craik, & Stuss, 2002) and individuals with neurodegenerative disorders (Alzheimer's disease: Hultsch, MacDonald, Hunter, Levy-Bencheton, & Strauss, 2000; Murtha, Cismaru, Waechter, & Chertkow, 2002; mild cognitive impairment: Christensen et al., 2005; Dixon et al., in press; epilepsy: Bruhn & Parsons, 1997; traumatic brain injury: Collins & Long, 1996; Stuss et al., 1994; Parkinson's disease (PD): Burton, Strauss, Hultsch, Moll, & Hunter, 2006; Crawford, Goodrich, Henderson, & Kennard, 1989; Reed & Franks, 1998).

Li and Lindenberger (1999) proposed that a neural network model that simulates the effects of decreased catecholamine levels can describe prior research in cognitive aging showing (a) lower performance in older adults than younger adults, (b) dedifferentiation of cognitive functions with aging (i.e., cognitive abilities become progressively more dependent in late adult-

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hood), and (c) interference in cognitive control tasks with aging. As supported by this catecholaminergic modulation model, the release of catecholamines (e.g., dopamine) may moderate a neuron's signal-to noise ratio. The concentration of catecholamines decreases in the basal ganglia with increasing age. The increase in neural noise in processing information would lead to more inconsistency in performance.

The link between cathecholamines and inconsistency in performance can be addressed with a population of individuals with a compromised dopaminergic system, namely PD patients. Recent research by Burton et al. (2006) has suggested greater intraindividual variability in RT in a group of mostly mild stage PD patients ($n = 10$) than in healthy older adults. Earlier studies have also noted more inconsistent response latencies in individuals with PD than controls (Reed & Franks, 1998). One missing link in the present literature is whether severity of PD, the most common pathological movement disorder of aging, influences neurocognitive speed (level and variability). Motor deficits specific to PD pathology are associated with a degeneration of neurons in the substantia nigra that subsequently reduce dopaminergic levels. The correspondence between disease progression and decreasing dopamine production may influence movement by the underactivation of cortical regions involved in motor programming and planning (Reed & Franks, 1998).

A second missing link is whether executive functioning relates to neurocognitive speed (level and variability) in normal aging and PD. Inconsistency in speeded performance could account for poor executive control. West et al. (2002) found that performance variability was greater for healthy older adults than younger adults, for tasks requiring greater executive control. Some studies have reported that greater intraindividual variability is associated with poor cognitive performance (Cattell Culture Fair Intelligence Test; Rabbitt, Osman, Moore, & Stollery, 2001) and cognitive decline (fluid intelligence and episodic memory; MacDonald, Hultsch, & Dixon, 2003; Ram, Rabbitt, Stollery, & Nesselroade, 2005), whereas other studies have not found an association (working memory inconsistency; Robertson, Myerson, & Hale, 2006).

Idiopathic PD is a common neurodegenerative disorder clinically defined by a triad of dopamine responsive signs: tremor, rigidity, and bradykinesia. PD patients also develop clinical changes, such as gait impairment, termed dopamine non-responsive signs that do not respond as well to levodopa (Lang & Lozano, 1998; Lang & Obeso, 2004). A third missing link in the current literature is how performance variability may be related to dopamine response symptoms and dopamine non-response signs. One key symptom of PD is gait disorder which may result from degeneration of non-dopaminergic neural circuitry beyond the midbrain, which is prominent in advanced disease (Braak & Braak, 2000). Other catecholaminergic (e.g., norepinephrine) or non-catacholaminergic changes (e.g., cholinergic, diffuse Lewy bodies) may support the latter association.

Li and Lindenberger's catecholaminergic modulation model (1999) lead to several predictions relevant to the present study. We focused on four main issues using a relatively large sample of PD patients and matched healthy adults. First, we compared neurocognitive speed (level and inconsistency) in healthy older adults and geriatric patients with PD. If reduced speed and increased intraindividual variability is associated with greater central nervous system dysfunction then geriatric PD patients would be expected to be slower and have more inconsistency in performance than healthy older adults. Second, we examined whether disease severity affected speed and variability in RT. We expected patients with severe disease progression to be slower and show more inconsistency in performance than mild cases because of more compromised dopamine (DA) systems. Third, we examined whether neurocognitive speed (rate and inconsistency) were correlated with executive functioning in PD and healthy older adults. We expected that poorer executive functioning would be related to slower latencies and performance variability in PD. Fourth, we examined whether intraindividual variability was more related to dopamine responsive measures (e.g., finger tapping) than to non-dopamine responsive ones (gait). We expected that tapping speed would be more strongly correlated with response speed and variability for PD patients with compromised DA levels than normal older adults.

1. Method

1.1. Participants

There were 50 PD patients (29 men and 21 women) in the present study with a clinical diagnosis of idiopathic PD. The PD patients ranged from 65 to 84 years ($M = 71.5$, S.D. = 4.7); the mean level of education was 14.0 years (S.D. = 2.9). The PD patients were recruited from the Movement Disorders Clinic at the University of Alberta or via advertisement in the Parkinson's Society of Alberta newsletter. Patients with PD met UK brain bank criteria for idiopathic PD (Gibb & Lees, 1988). There were 48 age, sex, and education-matched control volunteers (28 men and 20 women). The healthy older adult controls ranged from 65 to 84 years ($M = 71.5$, S.D. = 4.9); the mean level of education was 14.9 years (S.D. = 3.6). The controls were recruited from the University of Alberta General Medicine Clinics, friends or acquaintances of other volunteers, or respondents to an advertisement in the Society for the Retired and Semi-Retired newspaper. Clinical depression was screened and participants were excluded from the study if their depression could not be managed by drug treatment. The study was approved by the University of Alberta Health Ethics review board and performed in accordance with the Helsinki declaration.

1.2. Assessment

All participants were examined by a neurologist with expertise in aging and PD. The participant and an informant were independently interviewed to determine if cognitive impairment was present. Exclusion criteria included the presence of an unstable medical illness (e.g., active or recent cancer, symptomatic coronary artery disease, renal failure), an illness (other than PD) that could affect thinking or memory (e.g., symptomatic chronic pulmonary disease, epilepsy), or medications that could directly affect cognition (e.g., centrally acting anti-cholinergic medications). General health was graded using the Cumulative Illness Rating Scale (CIRS) (Parmelee, Thuras, Katz, & Lawton, 1995). The Hachinski Ischemic Score was used to rate vascular risk factors (Rosen, Terry, Fuld, Katzman, & Peck, 1980). Severity of cognitive impairment was graded using the Clinical Dementia Rating scale (CDR) (Morris, 1993). Motor function was assessed with the Unified Parkinson's Disease Rating Scale (UPDRS) (Gancher, 1997) and the Hoehn and Yahr staging (Hoehn & Yahr, 1967). Additional assessments included the Mini-Mental Status Examination (MMSE) (Folstein, Folstein, & McHugh, 1975), the Frontal Assessment Battery (FAB) (Dubois, Slachevsky, Litvan, & Pillon, 2000), the Dementia Rating Scale (DRS) (Brown et al., 1999), the National Adult Reading Test-Revised (NART-R) (Blair & Spreen, 1989), and the Geriatric Depression Scale (GDS; 15-item screening version) (Yesavage, 1988). All participants had blood tests to