The roles of sequencing and verbal working memory in sentence comprehension deficits in Parkinson’s disease

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Abstract

Studies of sentence comprehension deficits in Parkinson’s disease (PD) patients suggest that language processing involves circuits connecting subcortical and cortical regions. Anatomically segregated neural circuits appear to support different cognitive and motor functions. To investigate which functions are implicated in PD comprehension deficits, we tested comprehension, verbal working memory span, and cognitive set-switching in a non-linguistic task in 41 PD patients; we also obtained speech measurements reflecting motor sequencing processes that may be involved in articulatory rehearsal within working memory. Comprehension of sentences with center-embedded or final relative clauses was impaired when they could not be understood from lexical semantic content alone. Overall comprehension error rates correlated strongly with impaired set-switching and significantly with reduced working memory span and speech motor sequencing deficits. Correlations with comprehension of different sentence structures indicate that these impairments do not represent a single deficit; rather, PD comprehension deficits appear to arise from several independent mechanisms. Deficits in cognitive set-switching or underlying inhibitory processes may compromise the ability to process relative clauses. Deficits in verbal working memory appear to impair comprehension of long-distance dependencies. Speech sequencing correlated with neither set-switching nor verbal working memory span, consistent with their being supported by independent, segregated cortico-subcortical circuits.

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1. Introduction

The traditional view of the neural bases of language has focused on neocortical regions—predominantly Broca’s and Wernicke’s areas and adjacent perisylvian regions. However, current neurophysiological and neuro-anatomical data suggest that not only do cortical “language” regions serve other roles as well (e.g., Rizzolatti & Arbib, 1998), but linguistic function also draws on subcortical regions (Lieberman, 2000, 2002). Like many other complex behaviors, language appears to be regulated by distributed networks linking multiple anatomical regions (Mesulam, 1990). In one class of neural circuits, regions of neocortex send convergent projections to the striatum—the primary input structure of the basal ganglia—and the basal ganglia in turn send projections back up to the cortex (Lehéricy et al., 2004; Middleton & Strick, 2000). Cortico-striato-cortical circuits are involved in aspects of behavior that include motor control, learning, reasoning, planning, dual-task performance, obsessive-compulsive disorder, and mood (Brainard & Doupe, 2000; Brown & Marsden, 1988, 1991; Cools, Barker, Sahakian, & Robbins, 2001; Cools, Stafanova, Barker, Robbins, & Owen, 2002; Cummings, 1993; Cummings, Darkins, Mendez, Hill, & Benson, 1988; Dallymple-Alford, Kalder, Jones, & Watson, 1994; Flowers & Robertson, 1985; Gotham, Brown, & Marsden, 1988; Graybiel, Aosaki, Flaherty, & Kimura, 1994; Greenberg, Murphy, & Rasmussen, 2000; Hayes, Davidson, Keele,

The functional basis of PD patients’ comprehension deficits remains uncertain. Increased confrontation naming errors have been observed in late-stage patients with parkinsonian dementia (e.g., Cummings et al., 1988). To avoid confounding effects of semantic deficits (and other cognitive deficits associated with dementia), studies of comprehension have focused on mildly and moderately impaired PD patients, in whom naming has generally been found to be intact (e.g., Cummings et al., 1988; Grossman et al., 1991, 1992; Kensinger, Shearer, Locascio, Growdon, & Corkin, 2003; Levin et al., 1989). PD may affect the temporal dynamics of lexical activation. For example, semantic priming studies indicate that automatic semantic activation may be delayed in PD (Angwin, Chenery, Copland, Murdoch, & Silburn, 2004; Arnott, Chenery, Murdoch, & Silburn, 2001; Grossman, Zurif, et al., 2002). PD patients also show deficits in selectively activating the contextually appropriate meaning of homophones (Copland, Chenery, & Murdoch, 2000, 2001).

However, deficits in accessing or selecting word meaning appear to account for at best a small proportion of the comprehension errors PD patients make on syntactically complex sentences. In sentence comprehension tasks that do not use homophones, PD patients show few comprehension errors when individual words provide semantic information that allows sentences to be understood without the use of syntax (Grossman, 1999; Grossman et al., 1991, 1992, 2000, 2001; Grossman, Lee, et al., 2002; Grossman, Zurif, et al., 2002; Kemmerer, 1999; Lieberman et al., 1990, 1992; Natsopoulos et al., 1991, 1993; Skeel et al., 2001). (Note that this result is consistent with relative sparing not only of lexical semantics but also of world knowledge in mildly to moderately impaired PD patients.) Moreover, when sentences differ in syntactic structure (e.g., object-relative vs. subject-relative center-embedded clauses) but not lexical content, PD patients make disproportionately more errors, compared with control subjects, on the syntactically more complex sentences (Grossman et al., 1991, 1992, 2000, 2001; Grossman, Lee, et al., 2002; Grossman, Zurif, et al., 2002).

Thus, proposed explanations of PD sentence comprehension deficits have focused on mechanisms beyond the lexical level. These include impaired cognitive sequencing and switching (Lieberman, 2000), reduced verbal working memory capacity (Caplan & Waters, 1999), impaired art fluent rehearsal processes involved in sentence comprehension (Lieberman, 2000), and reduced capacity and control over “cognitive resources” involved in sentence processing (Grossman et al., 2000; Grossman, Lee, et al., 2002). In the research reported here, we obtained measures reflecting cognitive sequencing abilities, verbal working memory, and articulatory rehearsal on a single, large group of PD subjects. Previous studies have looked, to some extent, at how deficits in these three functions may separately relate to sentence comprehension deficits in PD (e.g., Caplan & Waters, 1999; Grossman et al., 1992, 2001; Lieberman et al., 1992; Skeel et al., 2001). The research reported here allowed us to investigate the inter-relationships of these functions as well. By obtaining these measures in the same session in which we tested comprehension, we maximized the likelihood of finding significant relationships: PD patients’ performance may fluctuate across sessions depending on factors such as when they last took their medication.

1.1. Cognitive sequencing and inhibition

Impaired sentence comprehension in PD could reflect an inability to switch cognitive sets. The basal ganglia are critically involved in sequencing motor behavior; they both “promote automatic execution of routine movement” and, complementarily, “respond to unusual circumstances to reorder the cortical control of movement” (Marsden & Obeso, 1994, p. 889). The circuitry linking the
basal ganglia to prefrontal cortical regions associated with cognitive function (Alexander, Delong, & Strick, 1986; Lange et al., 1992; Malapani et al., 1994; Middleton & Strick, 2000; Naeser et al., 1982) does not differ radically from the cortico-striato-cortical circuitry implicated in motor control (Lieberman, 2000; Marsden & Obeso, 1994). This suggests that “loss of basal ganglia contribution ... would lead to inflexibility of mental and motor response” (Marsden & Obeso, 1994, p. 893). Consistent with this prediction, cognitive set-switching is impaired by PD (Flowers & Robertson, 1985; Lange et al., 1992; Lieberman et al., 1992; Marsden & Obeso, 1994; Owen et al., 1993), bilateral lesions of the striatum (Pickett et al., 1998), and surgical lesions of the globus pallidus, the principal output structure of the basal ganglia (Scott et al., 2002). The basal ganglia are selectively activated in association with switching cognitive set (Monchi et al., 2001) and appear also to subserve the resolution of competing possibilities in language: Basal ganglia activation is seen in association with the processing and disambiguation of syntactically ambiguous sentences (Stowe et al., 2004).

PD might also impair cognitive sequencing by affecting frontal lobe function. Dopamine depletion is sometimes found in cortical regions in PD (Scatton, Rouquier, Javoy-Agid, & Agid, 1982), and the disease can cause deficits in various “executive” cognitive processes—including set-switching—that are affected by frontal lobe lesions (Lange et al., 1992; Taylor et al., 1990).

Either of these two possible effects of PD on cognitive sequencing is consistent with the fact that withdrawing PD patients from dopamine supplementation medication typically worsens set-switching performance (e.g., Cools et al., 2001; Gotham et al., 1988; Hayes et al., 1998; Lange et al., 1992).

The comprehension deficits of patients with basal ganglia dysfunction are consistent with a set-switching deficit. PD patients and a subject with bilateral striatal damage had high error rates when answering voice-switched questions—i.e., questions posed in the passive voice concerning information presented in the active voice or vice versa (Pickett et al., 1998). PD patients have difficulties comprehending sentences that contain embedded relative clauses, like The king that is pulled by the cook is short (Grossman, 1999; Grossman et al., 1991, 1992, 2000, 2001; Grossman, Lee, et al., 2002; Grossman, Zurif, et al., 2002; Lieberman et al., 1990; Pickett et al., 1998; Sceel et al., 2001). Processing these sentences may require the listener to switch away from the “canonical” subject–verb–object order of English sentences at the boundary between the main and the embedded clause.

Set-switching depends on several processes, including the ability to inhibit the now-irrelevant set. In addition to set-switching studies, a variety of other studies indicate that PD patients have deficits in inhibitory processes, as evidenced, for example, by difficulties in ignoring distractor items or irrelevant aspects of stimuli (e.g., Maddox et al., 1996; Sharpe, 1990), increased interference effects in dual or divided-attention tasks (e.g., Brown & Marsden, 1991; Dalrymple-Alford et al., 1994; Malapani et al., 1994), difficulties in inhibiting prepotent responses in Stroop-type tasks (e.g., Brown & Marsden, 1988, 1991), and the aforementioned deficits in selecting appropriate homophone meanings (Copland et al., 2000, 2001).

This suggests a somewhat different possible mechanism for PD sentence comprehension deficits. Several models of sentence processing (e.g., MacDonald, Pearlmuter, & Seidenberg, 1994; Vosse & Kempen, 2000) propose that as listeners hear a sentence, they activate multiple possible syntactic structures that are consistent with the current input. When information later in the sentence proves inconsistent with an activated structure, it is inhibited. A deficit in inhibitory processing would thus impair the ability to select from among competing structures. For example, in the case of center-embedded relative clauses, both a main-clause SVO and a center-embedded structure (among others) might be “proposed” based on the initial noun phrase, but the relative pronoun would rule out the simple SVO structure. Weakened inhibition would prevent this ruling-out—especially given that, under most models, the initial activation of the SVO would be higher than that of the center-embedded structure, owing to its higher frequency in the language. Correlations have been observed between measures of inhibition and the ability to resolve syntactic ambiguities in healthy young subjects (Mendelson, 2002) and between Stroop task performance and sentence comprehension in PD patients (Grossman, Lee, et al., 2002).

1.2. Verbal working memory: The executive component

Prefrontal dopamine depletion also might impair sentence comprehension in PD by affecting the executive component of verbal working memory. Verbal working memory is essentially an individual’s capacity to hold and manipulate verbal material in the short term. According to the well-tested model of Baddeley (1986), the verbal working memory system consists of a phonological loop, which stores a limited amount of verbal material in raw phonological form for a short time, and a “central executive,” which manipulates the material. Children and adults exhibit strong correlations between verbal working memory capacity and syntactic proficiency (Baddeley, 1986; Carpenter, Miyake, & Just, 1994; Gathercole & Baddeley, 1993), and under conditions that strain verbal working memory, normal adults exhibit syntax comprehension difficulties similar to those of aphasics (Blackwell & Bates, 1995; Carpenter et al., 1994). The sentence structures on which PD patients show comprehension deficits may have significant working memory demands, requiring listeners to resolve long-distance dependencies or to leave thematic roles (i.e., whether a named entity is performing or “receiving” the action of the verb) indeterminate while other material is processed.
Dorsolateral prefrontal cortex is implicated in the executive components of both visuospatial (Courtney, Petit, Jose, Ungerleider, & Haxby, 1998; Petrides, 2000) and verbal working memory (Awh et al., 1996; Smith, Jonides, Marshuetz, & Koepp, 1998). Dopamine depletion reduces the capacity of frontal executive systems (Brozoski, Brown, Rosvold, & Goldman-Rakic, 1979; Robbins, 2000) and modulates frontal neuronal activity related to spatial working memory (Williams & Goldman-Rakic, 1995). Detrimental effects of PD on spatial working memory are well known (e.g., Kensinger et al., 2003; Owen, Iddon, Hodges, Summers, & Robbins, 1997). Patients with mild-to-moderate PD typically do not show deficits in simple short-term memory tasks like forward digit span, but may show reductions in backward digit span, which reflects manipulation as well as storage demands (Lieberman et al., 1992). Studies addressing verbal working memory in PD have generally found deficits (Caplan & Waters, 1999; Gilbert, Belleville, Bherer, & Chouinard, 2005; Kensinger et al., 2003).

Verbal working memory, like set-switching, may also be related to sentence comprehension via inhibition. Inhibition plays a role in several analyses of working memory (or at least of tasks by which it is commonly operationalized). Analysis of errors on verbal working memory span tasks, such as Reading Span (Daneman & Carpenter, 1980), that require subjects to recall the last words of sets of successive read sentences shows that lower-span individuals are particularly susceptible to intrusions of words from the parts of the sentences that they were not required to remember (De Beni, Palladino, Pazzaglia, & Cornoldi, 1998). A relationship between working memory span and inhibition is seen even when the latter is measured using relatively simple non-verbal tasks. Poorer performance on anti-saccade tasks, which require the inhibition of reflexive saccades, has been observed for individuals with lower verbal working memory spans (Kane, Bleckley, & Conway, 2001) or maintaining a concurrent verbal working memory load (Roberts, Hager, & Heron, 1994).

Studies of how verbal working memory deficits may relate to sentence comprehension in PD have yielded somewhat equivocal results. Caplan and Waters (1999) found that PD patients who had reduced verbal working memory spans compared with controls also were impaired on comprehending sentences containing two propositions, but not on simple sentences. Grossman et al. (2001), however, found that taking PD patients off dopamine supplementation medication led to poorer comprehension of syntactically more complex sentences without reducing verbal working memory span. Skeel et al. (2001) found that while comprehension was impaired in PD patients and correlated with span scores, span was not reduced compared with controls. However, Skeel et al. used a novel working memory measure that may not be comparable to more common measures and, as they acknowledge, may not reflect aspects of working memory important to syntactic processing.

1.3. Verbal working memory: Articulatory sequencing and rehearsal

The phonological loop component of Baddeley’s working memory model consists of a limited-capacity phonological store and an articulatory rehearsal mechanism. The latter allows people to extend the duration of their memory for verbal material by, in essence, repeating it to themselves overtly or covertly. Covert rehearsal activates frontal and subcortical neural mechanisms that regulate overt speech (Awh et al., 1996; Smith et al., 1998). Listening to sentences activates these same areas, to an extent proportional to the structural complexity of the sentences (Just, Carpenter, Keller, Eddy, & Thulborn, 1996), indicating that articulatory rehearsal plays a role in sentence comprehension. Impairment of the neural mechanisms that regulate speech could therefore interfere with verbal working memory, and thereby with sentence comprehension, by affecting rehearsal. Howard et al. (2000) found reduced verbal working memory in PD patients with speech apraxia.

Some PD patients show deficits in motor sequencing in speech production. “Voiced” and “voiceless” stop consonants in word-initial position differ in voice-onset time (VOT) – the time that elapses between the acoustic “burst” as the oral cavity of the supralaryngeal vocal tract opens and the start of laryngeal phonation (Lister & Abramson, 1964) (see Supplementary Fig. 1). To produce these contrasts a speaker must precisely regulate the sequence of lip or tongue gestures that open the oral cavity relative to the laryngeal maneuvers that initiate phonation. When words are spoken in isolation by neurologically intact English speakers, VOTs for the voiceless consonants, [p], [t], and [k], are rarely less than 20 ms longer than the longest VOT produced for the corresponding voiced stop consonants, [b], [d], and [g] (e.g., Lieberman, Kanki, & Protopapas, 1995; Pickett, 1998; Pickett et al., 1998) (see Supplementary Fig. 2). In Broca’s aphasics (Baum, Blumstein, Naeser, & Palumbo, 1990; Blumstein, Cooper, Goodglass, Statlender, & Gottlieb, 1980) and PD patients (Lieberman et al., 1992), this temporal distinction (“minimal distance”) may be reduced; in extreme cases the VOT ranges may overlap, such that the shortest voiceless VOT is shorter than the longest voiced VOT (see Supplementary Fig. 3). In running speech, especially at higher speech rates, VOT overlap occurs occasionally even in healthy individuals (Miller, Green, & Reeves, 1986).

PD patients who exhibit difficulties regulating VOT are more likely to exhibit sentence comprehension deficits than those without such speech motor deficits (Lieberman et al., 1992). Irregularities in VOT control were also noted in tandem with deficits in sentence (but not word) comprehension in a patient with bilateral striatal damage (Pickett et al., 1998).
A similar relationship between sentence comprehension and speech motor control has been observed in studies in otherwise fit subjects of the effects of hypoxia (Cyerman et al., 2002; Lieberman, Kanki, Protopapas, Reed, & Youngs, 1994; Lieberman et al., 1995; Lieberman, Morey, Hochstadt, Larson, & Mather, 2005)—to which the globus pallidus, the principal basal ganglia output, is particularly sensitive (Brierly, 1976; Chie et al., 2004; Jeong, Kwon, Chin, Yoon, & Na, 2002; Kuoppamaki, Bhatia, & Quinn, 2002; Laplane et al., 1989).

In short, at least three cognitive mechanisms might contribute to sentence comprehension deficits in PD:

- If cognitive sequencing abilities involved in (for example) switching syntactic operations at clause boundaries are impaired, we should expect correlated impairments in sentence comprehension—especially for sentences containing relative clauses—and in set-switching on non-linguistic tasks.
- If the capacity of the executive component of verbal working memory is diminished, we should expect correlations between impaired comprehension and measures of reduced verbal working memory span.
- If disrupted functioning of speech motor control circuitry affects the rehearsal component of the phonological loop, we should expect comprehension deficits to correlate with VOT measures indicating degraded articulatory sequencing.

These three mechanisms need not be correlated with one another. Cortico-striato-cortical circuits are typically structured so that within a given subcortical structure, neuronal populations that project to different parts of the brain are segregated from each other (Middleton & Strick, 2000). These segregated circuits regulate different aspects of behavior and cognition. Thus, focal damage to any such structure may produce varying deficits in different individuals, depending on which neuronal populations have been affected. To the extent that our proposed mechanisms depend on anatomically segregated cortico-striato-cortical circuits, they may be separately impaired in PD patients with different patterns of focal damage.

On the other hand, set-switching and the executive component of verbal working memory may be related to sentence comprehension because they involve common inhibitory processes—and common associated neural circuitry. If that is the case, not only should we expect correlations between measures of all three, but we should also expect set-switching and executive working memory to be related to the same aspects of sentence processing.

2. Materials and methods

2.1 Subjects

Forty-five subjects with PD were recruited from the Movement Disorders Unit of Memorial Hospital of Rhode Island. All were screened by one of the authors (J.F.), who was then the unit’s primary neurologist. All volunteered for and gave written informed consent to this study. The subjects were at stages 0–3 on the Hoehn and Yahr (1967) scale. Most were on medication for PD at the time of testing. However, four subjects (8, 27, 29, and 34) were not taking medication. (Subjects 29 and 34 were receiving placebo as part of a double-blind study of l-dopa medication on which the blind has since been broken.) All but one subject were native English speakers. Subject 31 had immigrated from Italy at age 8. In previous work, we found no significant differences in performance on a similar sentence comprehension task between native English speakers and subjects who had begun acquiring English at ages 7–16 years (Lieberman et al., 1992).

Testing was done at Memorial Hospital, in a single session typically lasting less than an hour. Before the main testing, we administered the Mini-Mental State Exam (MMSE) (Folstein, Folstein, & McHugh, 1975) to exclude possible dementia. Four subjects were excluded because they had MMSE scores below 25. Table 1 lists relevant clinical and personal information about the remaining 41 subjects.

2.2 Test battery and procedures

After the MMSE, subjects were tape-recorded while twice reading aloud a list of 30 monosyllabic English words consisting of an initial stop consonant, a vowel, and a final stop consonant (e.g., bad, tag, and keep). Subjects were instructed to read the list slowly, saying each word as if it were a separate sentence.

We then administered the Reading Span test of verbal working memory (Daneman & Carpenter, 1980). The subject reads aloud a series of sentences and is then asked to recall the last word of each, without starting with the last word of the very last sentence. The test begins with five sets of two sentences each; if a subject correctly recalls the last words of at least three sets, the subject moves on to five sets of three sentences, and if successful at that, to sets of four sentences, and so on. Reading Span is graded as the highest level at which a subject gets at least three sets correct, with half-credit for getting two correct.²

² Phonetic distinctions that do not depend critically on proper motor sequencing are not compromised in subjects with PD (Lieberman, 2000) or focal lesions of the basal ganglia (Pickett et al., 1998). These subjects preserve differences in the “intrinsic” durations of vowels and properly produce variations in formant frequency. Nor is the deficit in the representation of speech sounds, because these subjects correctly produce the differences in vowel length that signal whether a word-final stop consonant is voiced or voiceless.

³ Waters and Caplan (2000) have raised concerns about the stability of Reading Span. However, for our purposes we are less concerned with whether verbal working memory capacity is a stable characteristic of an individual than whether it relates to sentence processing at a given time. Since we tested comprehension and span in the same session, reliability across sessions is not an issue.
Table 1
Personal characteristics and test results of Parkinson’s disease patients

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<th>Subject</th>
<th>Sex</th>
<th>Age</th>
<th>Hoehn-Yahr stage</th>
<th>Reading span</th>
<th>Mean TMS error (%)</th>
<th>Odd Man Out error, mean blocks 3 and 4 (%)</th>
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<th>Mean VOT Separation (ms)</th>
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<td>2</td>
<td>2</td>
<td>1.7</td>
<td>10</td>
<td>Yes</td>
<td>51.4</td>
</tr>
<tr>
<td>28</td>
<td>M</td>
<td>79</td>
<td>2</td>
<td>2</td>
<td>0.0</td>
<td>5</td>
<td>Yes</td>
<td>29.3</td>
</tr>
<tr>
<td>29</td>
<td>F</td>
<td>67</td>
<td>NA</td>
<td>3</td>
<td>0.0</td>
<td>0</td>
<td>No</td>
<td>41.4</td>
</tr>
<tr>
<td>30</td>
<td>M</td>
<td>82</td>
<td>2</td>
<td>2</td>
<td>3.3</td>
<td>10</td>
<td>No</td>
<td>59.1</td>
</tr>
<tr>
<td>31</td>
<td>M</td>
<td>73</td>
<td>2</td>
<td>2</td>
<td>0.0</td>
<td>5</td>
<td>No</td>
<td>57.1</td>
</tr>
<tr>
<td>32</td>
<td>F</td>
<td>67</td>
<td>2</td>
<td>2</td>
<td>3.3</td>
<td>5</td>
<td>No</td>
<td>57.3</td>
</tr>
<tr>
<td>33</td>
<td>M</td>
<td>78</td>
<td>2</td>
<td>2</td>
<td>8.3</td>
<td>20</td>
<td>Yes</td>
<td>45.7</td>
</tr>
<tr>
<td>34</td>
<td>M</td>
<td>76</td>
<td>2</td>
<td>2.5</td>
<td>3.3</td>
<td>0</td>
<td>No</td>
<td>71.3</td>
</tr>
<tr>
<td>35</td>
<td>M</td>
<td>79</td>
<td>2</td>
<td>2</td>
<td>1.7</td>
<td>40</td>
<td>Yes</td>
<td>46.5</td>
</tr>
<tr>
<td>36</td>
<td>M</td>
<td>74</td>
<td>1</td>
<td>3</td>
<td>0.0</td>
<td>5</td>
<td>No</td>
<td>57.8</td>
</tr>
<tr>
<td>37</td>
<td>F</td>
<td>76</td>
<td>2</td>
<td>2</td>
<td>1.7</td>
<td>5</td>
<td>No</td>
<td>54.7</td>
</tr>
<tr>
<td>38</td>
<td>M</td>
<td>60</td>
<td>1</td>
<td>2</td>
<td>1.7</td>
<td>10</td>
<td>No</td>
<td>52.4</td>
</tr>
<tr>
<td>39</td>
<td>F</td>
<td>47</td>
<td>0</td>
<td>2</td>
<td>0.0</td>
<td>10</td>
<td>No</td>
<td>85.5</td>
</tr>
<tr>
<td>40</td>
<td>M</td>
<td>76</td>
<td>3</td>
<td>1</td>
<td>10.0</td>
<td>20</td>
<td>Yes</td>
<td>35.6</td>
</tr>
<tr>
<td>41</td>
<td>M</td>
<td>51</td>
<td>2</td>
<td>3</td>
<td>0.0</td>
<td>5</td>
<td>No</td>
<td>55.6</td>
</tr>
</tbody>
</table>

NA, information not available; TMS, Test of Meaning from Syntax; VOT, voice-onset time.

* As assessed on date nearest to testing.

Next we administered the sentence–picture matching version of the Test of Meaning from Syntax (TMS) (Pickett, 1998). One of three line drawings depicted the meaning of a sentence read aloud by the experimenter; the other two matched the sentence only partially. The subject had to point to or state the number that identified the target drawing. Before taking the test, subjects were familiarized with the depicted characters and objects and given practice in doing the task.

Sentences varied in structural complexity, voice, and semantic constraint. They either were simple one-clause sentences or contained a relative clause in center-embedded or sentence-final position; they were in either the active or the passive voice; and their content was such that subjects could or could not use real-world knowledge to aid their comprehension. Crossing these factors yielded 12 conditions. The same five verbs were used in each condition—chase, kick, poke, pull, and push—and each verb was associated with two characters and two objects that likewise recurred across the conditions. (Objects appeared only in the semantically constrained condition.) The resulting 60 sentences were presented in quasi-randomized order. Table 2 shows the complete set of sentences for the verb pull. In trials with semantically non-constrained sentences, one of the distracter pictures depicted a situation in which the agent–patient relationship (i.e., who is doing what to whom) was reversed relative to the test sentence.

This stimulus set extends the range of sentence structures for which comprehension deficits have been investigated in PD. Past studies (Grossman, 1999; Grossman et al., 1991, 1992, 2000; Grossman, Lee, et al., 2002; Grossman, Zurif, et al., 2002) have manipulated the complexity of center-
Table 2
Example sentences used in the Test of Meaning from Syntax

<table>
<thead>
<tr>
<th>Complexity</th>
<th>Voice</th>
<th>Semantically constrained</th>
<th>Semantically non-constrained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple</td>
<td>Active</td>
<td>The cook pulls the box</td>
<td>The cook pulls the king</td>
</tr>
<tr>
<td></td>
<td>Passive</td>
<td>The box is pulled by the cook</td>
<td>The king is pulled by the cook</td>
</tr>
<tr>
<td>Final relative clause</td>
<td>Active</td>
<td>The cook pulls the box that is full</td>
<td>The cook pulls the king that is short</td>
</tr>
<tr>
<td></td>
<td>Passive</td>
<td>The box is pulled by the box that is short</td>
<td>The king is pulled by the box that is short</td>
</tr>
<tr>
<td>Center-embedded</td>
<td>Active</td>
<td>The cook that is short pulls the box</td>
<td>The cook that is short pulls the king</td>
</tr>
<tr>
<td></td>
<td>Passive</td>
<td>The box that is pulled by the box is full</td>
<td>The king that is pulled by the box is short</td>
</tr>
</tbody>
</table>

embedded sentences by using active-voice “subject relative” (e.g., the eagle that chased the hawk) and “object relative” clauses (the eagle that the hawk chased), but not by changing the voice of the verb. (Pickett et al. (1998) obtained pilot results for a small group of PD patients on sentences similar to the ones we used here, but did not report a statistical analysis.)

The Odd Man Out (OMO) test (Flowers & Robertson, 1985), which assesses the ability to form and switch mental sets, was then administered. Subjects are shown a series of cards, each of which depicts three items (either shapes or letters). The subject must choose one item that “does not belong” with the other two. Two possible choice rules are applicable to any card: one based on size, the other on form. After choosing an item on the first card, the subject is asked to use the same choice rule on the next nine cards. On the 10 cards after that, the subject is asked to choose the odd item by a different rule. The first 10 cards are shown again, and the subject is asked to switch back to the first rule. Finally, the subject is shown the second set of cards and asked to switch again to the second rule. Whenever the subject uses the incorrect rule, the experimenter points out the error, without ever explicitly articulating the rules, and asks the subject to try again.

Finally, each subject once again read the list of 30 monosyllabic words aloud twice.

Throughout the session, subjects’ responses were tape-recorded using a condenser microphone and a digital audio recorder. Responses on the MMSE, Reading Span test, TMS, and OMO test were also recorded on response sheets.

VOTs were measured using the Brown Lab Interactive Speech System (Mertus, 1998). Cursors were placed at the beginning of the noise burst that occurs on the release of a stop consonant and at the onset of phonation (see Supplementary Fig. 1). A computer program measured the cursor-marked intervals and produced histograms of the VOT results.

3. Results

Table 1 summarizes subjects’ performance on the Reading Span test, the Test of Meaning from Syntax, and the Odd Man Out task, and gives data on their speech performance. If fatigue had affected performance on later tests within a session, relationships among the factors being explored might be distorted. As a check that performance was consistent within a session, we compared the VOT min-

Fig. 1. Mean percentage errors for each condition of the Test of Memory from Syntax. Dashed lines and open symbols, semantically constrained conditions; solid lines and filled symbols, semantically non-constrained conditions; diamonds, active voice; circles, passive voice. Bars indicate standard error.

Fig. 1 plots the mean error percentage for each condition of the Test of Meaning from Syntax.5 A three-way repeated-measures ANOVA showed significant main effects of semantic constraint (F(1,40) = 25.35, p < .001), voice (F(1,40) = 8.56, p < .005), and complexity (F(2,80) = 19.13, p < .001). There were significantly more errors on semantically non-constrained than constrained sentences, and passive sentences were more difficult than active sentences. Post hoc analysis showed that simple sentences were easier to comprehend than sentences with final (F(1,40) = 20.06, p < .001) or center-embedded relative clauses (F(1,40) = 34.81, p < .001).

---

4 Unless otherwise noted, significance values are for one-tailed tests of anticipated effects.

5 One item from the passive constrained center-embedded sentence condition was used for an example trial, and the non-constrained simple sentence conditions each contained one item on which subjects exhibited excessively high errors. These items were removed from the analysis.
A significant interaction of semantic constraint with complexity \(F(2, 80) = 9.55, p < .001\) reflected the fact that non-constrained sentences were more difficult than their constrained counterparts only when they contained final \((F(1, 40) = 20.16, p < .001)\) or center-embedded relative clauses \((F(1, 40) = 16.47, p < .001)\). Semantic constraint also interacted with voice \((F(1, 40) = 6.91, p < .01)\); Passive sentences were harder than active ones only in the absence of constraint \((F(1, 40) = 10.04, p < .005)\). A significant interaction of complexity and voice \((F(2, 80) = 4.92, p < .01)\) indicated further that passive sentences were harder than active only when they contained a center-embedded relative clause \((F(1, 40) = 8.70, p < .005)\).

Finally, the three-way interaction of constraint, voice, and complexity was significant \((F(2, 80) = 4.76, p < .01)\). The greater difficulty of passive compared with active non-constrained sentences obtained only for center-embedded sentences \((F(1, 40) = 8.83, p < .005)\). Passive non-constrained sentences with center-embedded clauses were marginally more difficult than those with final relative clauses \((F(1, 40) = 2.56, p = .059)\). There were more errors for active non-constrained sentences with final relative clauses than for their center-embedded counterparts; however, this unexpected difference did not approach significance at the two-tailed level. The latter sentences were still harder than active non-constrained simple sentences \((F(1, 40) = 12.36, p < .001)\) or active constrained center-embedded sentences \((F(1, 40) = 3.09, p < .05)\).

To give some idea of the prevalence among our patients of the major patterns seen in the ANOVA, of the 33 subjects with non-zero TMS error rates, 27 showed equal error rates on simple sentences in the constrained and non-constrained conditions, with five showing higher rates on non-constrained simple sentences. But for final-relative-clause sentences, 21 of these 33 subjects showed higher error rates on non-constrained sentences, and 10 equal error rates in both semantic conditions. For center-embedded sentences, 24 subjects showed higher error rates on non-constrained sentences, and only 5 equal rates. Similarly, of the 32 patients with non-zero error rates on semantically non-constrained sentences, 17 had greater error rates on both final-relative-clause and center-embedded sentences than on simple sentences, 9 had higher error rates just on center-embedded sentences, and 4 showed higher error rates just on final-relative-clause sentences. Finally, of the 28 subjects with non-zero error rates on center-embedded non-constrained sentences, 21 showed greater error rates when these sentences were in the passive voice than in the active voice, and 2 equal error rates.

### 3.2. Relationship of cognitive and speech measures to sentence comprehension

Table 3 lists the Pearson coefficients for the correlations among our cognitive, speech, clinical, and sentence comprehension measures. Errors on the first two 10-card blocks of the Odd Man Out test may reflect difficulty in setting or recognizing a choice criterion. Errors on the third and fourth blocks, however, reflect a cognitive switching deficit per se.

Table 3

<table>
<thead>
<tr>
<th></th>
<th>Reading Span</th>
<th>VOT mean separation</th>
<th>Hoehn-Yahr stage</th>
<th>Mean TMS error (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odd Man Out error, mean</td>
<td>-.33*</td>
<td>.18</td>
<td>.38**</td>
<td>.67***</td>
</tr>
<tr>
<td>blocks 3 &amp; 4 (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reading Span</td>
<td>.14</td>
<td>-.31*</td>
<td>-.39*</td>
<td></td>
</tr>
<tr>
<td>VOT mean separation</td>
<td>-.19</td>
<td>-.29*</td>
<td>.31*</td>
<td></td>
</tr>
<tr>
<td>Hoehn-Yahr stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TMS, Test of Meaning from Syntax; VOT, voice-onset time.

- * \(p < .05\)
- ** \(p < .01\)
- *** \(p < .001\)

The rate of the latter errors (which for simplicity we shall refer to as OMO errors) correlated strongly with the overall error percentage on the Test of Meaning from Syntax (see Fig. 2).

Our measures reflecting different aspects of verbal working memory also showed significant (if not as strong) relationships to comprehension. Reading Span correlated significantly with overall sentence comprehension error rate. With respect to articulatory sequencing, 12 subjects exhibited overlap in one or more VOT histograms (see Supplementary Fig. 3 for an example). The difference in sentence comprehension performance between the overlap and non-overlap groups was not significant \((t(39) = 0.64, p = 0.26)\). However, only subjects with extreme deficits in speech motor sequencing are likely to produce more than a few overlapping tokens in the course of reading 60 words; a subject with a milder impairment may produce none. We thus calculated an alternative measure. For each consonant pair, we subtracted the mean VOT for the voiced tokens (excluding cases of pre-voicing, i.e., phonation beginning before the “burst”) from the mean voiceless VOT. We then averaged over all three pairs to obtain a “mean VOT separation.” The more tokens a subject produces with VOTs that approach the boundary between voiced and voiceless consonants, the shorter the mean separation should be. Mean VOT separation correlated with overall TMS performance.

Although each of our three measures showed some relation to sentence comprehension, their contributions might
not be independent. OMO errors correlated significantly with Reading Span. Mean VOT separation, however, did not correlate significantly with Reading Span or OMO errors. In a multiple regression analysis, OMO errors, Reading Span, and mean separation collectively gave a correlation coefficient of \( r = .71 \) (\( p < .001 \)) with overall TMS performance. The partial correlations of OMO errors, Reading Span, and mean separation with TMS errors (reflecting the extent to which variance associated with each factor is uniquely associated with sentence comprehension) were .62, -.23, and -.23, respectively; only the first value is significant (\( p < .001 \)).

Table 4 shows the degree to which performance on each condition of the TMS correlated with our cognitive and speech measures. We calculated Spearman correlation coefficients because data in some conditions did not meet the assumptions for parametric tests. Even so, the correlations in some low-error conditions must be interpreted with caution. (For example, the significant correlations with comprehension of simple constrained sentences are due entirely to errors by one subject.) Bearing this in mind, several aspects of these correlations are noteworthy.

OMO performance correlated most broadly across sentence types. Despite correlating poorly with each other, mean VOT separation and Reading Span tended to correlate most strongly and most weakly with the same sentence types. OMO correlation coefficients did not follow this same pattern, even though OMO errors were significantly correlated with Reading Span.6

### Table 4

<table>
<thead>
<tr>
<th>Semantic constraint</th>
<th>Complexity</th>
<th>Voice</th>
<th>OMO</th>
<th>Reading span</th>
<th>VOT mean separation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constrained</td>
<td>Simple</td>
<td>Active</td>
<td>0.27*</td>
<td>−0.30*</td>
<td>−0.27*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passive</td>
<td>0.27*</td>
<td>−0.30*</td>
<td>−0.27*</td>
</tr>
<tr>
<td></td>
<td>Final</td>
<td>Active</td>
<td>0.10</td>
<td>−0.24</td>
<td>−0.16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passive</td>
<td>0.34*</td>
<td>−0.34*</td>
<td>−0.11</td>
</tr>
<tr>
<td></td>
<td>Center</td>
<td>Active</td>
<td>0.24</td>
<td>0.00</td>
<td>−0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passive</td>
<td>0.37***</td>
<td>−0.34*</td>
<td>−0.29*</td>
</tr>
<tr>
<td>Non-constrained</td>
<td>Simple</td>
<td>Active</td>
<td>0.32*</td>
<td>−0.07</td>
<td>−0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passive</td>
<td>0.24</td>
<td>−0.22</td>
<td>0.10</td>
</tr>
<tr>
<td></td>
<td>Final</td>
<td>Active</td>
<td>0.51***</td>
<td>−0.25</td>
<td>−0.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passive</td>
<td>0.49***</td>
<td>−0.33*</td>
<td>−0.33*</td>
</tr>
<tr>
<td></td>
<td>Center</td>
<td>Active</td>
<td>0.44***</td>
<td>−0.21</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passive</td>
<td>0.30*</td>
<td>−0.34*</td>
<td>−0.30*</td>
</tr>
</tbody>
</table>

OMO, mean % error on blocks 3 and 4 of Odd Man Out task; VOT, voice-onset time.

* \( p < .05 \).

** \( p < .01 \).

*** \( p < .005 \).

### 3.3. Correlations with clinical status

The Hoehn–Yahr stages of 38 subjects had been assessed sufficiently closely to the time of testing to allow correlational analysis with our measures. Hoehn–Yahr stage correlated significantly with overall TMS performance, OMO errors, and Reading Span, but not with mean VOT separation. When added to the multiple regression analysis described above, Hoehn–Yahr stage had a partial correlation coefficient with TMS performance of only −.01.

### 4. Discussion

The results of our sentence comprehension task replicate, for a new set of sentence structures, the general finding about patients with mild-to-moderate PD established in past comparisons with control subjects (Caplan & Waters, 1999; Grossman, 1999; Grossman et al., 1991, 1992, 2000; Grossman, Lee, et al., 2002; Grossman, Zurif, et al., 2002; Lieberman et al., 1990, 1992; Natsopoulos et al., 1991; Skeel et al., 2001): in the absence of semantic information that would make it possible to understand a sentence without comprehending its syntax, a subgroup of patients had greater difficulty comprehending more structurally complex sentences containing relative clauses. That the sentence comprehension deficits are due to PD is supported by the significant correlation of TMS errors with Hoehn–Yahr stage. The near-zero partial correlation coefficient of Hoehn–Yahr stage in the multiple regression analysis suggests that the disease process leads to sentence comprehension deficits through its effects on the cognitive functions measured by our tasks.

The order of difficulty observed among our sentence types is consistent with studies of healthy subjects and aphasics (e.g., Carpenter et al., 1994; Just et al., 1996; Stromswold, Caplan, Alpert, & Rauch, 1996), with one exception: among non-constrained sentences, center-embedded sentences in the active voice were not only significantly easier to comprehend than ones in the passive

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6 One indicator of the degree to which measures accounted for performance on the same sentence conditions is the correlation between the correlation coefficients for each measure (i.e., the correlations between the values in the columns in Table 4). The mean separation coefficients correlated significantly with those for Reading span (\( r = .61, p < .05 \), two-tailed). For the OMO correlation coefficients, however, the correlations with the mean separation and Reading Span correlation coefficients were \( r = −.15 (p = .64, \text{two-tailed}) \) and \( r = −.20 (p = .53, \text{two-tailed}) \), respectively.
voice but easier (albeit non-significantly) than sentences with final relative clauses. In previous studies showing
greater difficulty with center-embedded sentences, the embedded clauses have usually consisted of a transitive
verb accompanied by its subject or object. To comprehend
such sentences an individual must determine the thematic
relationship (who is doing what to whom) between the sub-
ject of the sentence and the embedded noun. By contrast,
the relative clauses in our active center-embedded sentences
consist only of an adjective following the simple copular
verb is. In such sentences, it should be relatively easy to rap-
idly “attach” the adjective to the subject. These sentences
should also place fewer demands on verbal working mem-
ory because of the shorter distance between the subject
noun and the main-clause verb. Indeed, Skeel et al. (2001)
found that for non-constrained active center-embedded
sentences whose relative clauses did consist of a transitive
verb plus an object (i.e., whose structure paralleled that of
our passive center-embedded sentences), PD patients made
significantly more comprehension errors than they did on
non-constrained active final-relative-clause sentences iden-
tical in structure to the ones we used.

Because the relative clauses in our passive center-embed-
ded sentences were longer and more complex than those in
other sentences (see Table 2), we cannot attribute the diffi-
culty subjects had with such sentences in the absence of
semantic constraint specifically to center-embedding, the
passive voice, or their interaction. Rather, it could be that
the general difficulty of non-constrained sentences contain-
ing relative clauses was exacerbated when the clause con-
tained more complex (or just more) material. However, other
studies (Hochstadt, 2004) indicate that PD patients have
greater difficulty comprehending passive than active
center-embedded sentences that are otherwise identical in
structure.

We now turn to the central question of our investiga-
tion: when obtained on the same subjects, what do mea-
sures reflecting cognitive set-switching, verbal working
memory, and articulatory rehearsal indicate about the
functional basis of sentence comprehension deficits in PD?
Our results indicate that all three mechanisms contribute to
these deficits—but that they are differentially involved in
different aspects of sentence processing.

As has repeatedly been observed in comparisons with
control subjects (e.g., Flowers & Robertson, 1985; Lange
et al., 1992; Lieberman et al., 1992; Marsden & Obeso,
1994; Owen et al., 1993), PD impaired the ability to switch
cognitive set in some of our subjects. In earlier PD research
using the OMO test, control subjects had an average error
rate of less than 10%, with a standard deviation around the
same magnitude (Flowers & Robertson, 1985). Our
patients’ OMO error rates averaged 19% and ranged as
high as 65%. Moreover, OMO errors correlated signifi-
cantly with disease stage.

Impaired cognitive set-switching appears to have a
strong functional relationship to sentence comprehension
deficits in PD. OMO error rate correlated strongly with
TMS performance, even after any role of the other mea-
sured factors was partialed out. Our results are consistent
with the hypothesis that general cognitive sequencing
capacities that are not specifically linguistic are involved in
switches in processing at boundaries between clauses.
Despite the structural simplicity of the relative clauses in
our active non-constrained center-embedded sentences,
OMO performance correlated as strongly with compre-
henision of those sentences as it did with comprehension of
other non-constrained sentences containing relative clauses.
In other work, we have obtained evidence that the on-line
processing of relative clauses is impaired in PD patients by
tracking eye movements during a sentence–picture match-
ing task (Hochstadt, 2004). Alternatively, the relationship
between set-switching errors and comprehension deficits
may reflect impairment of inhibitory processes involved in
“choosing among” competing grammatical structures. This
explanation, however, seems better suited to explaining
deficits in comprehending center-embedded sentences than
final-relative-clause sentences, since in the latter the subject
can settle on the preferred SVO main-clause structure
before processing the relative clause.

Impaired verbal working memory processes also appear
to be involved in PD sentence comprehension deficits. Our
data suggest that the disease compromised verbal working
memory capacity in some of our subjects, consistent with
previous reports (Caplan & Waters, 1999; Gilbert et al.,
2005; Kensinger et al., 2003). Hoehn–Yahr stage correlated
significantly with Reading Span. Omitting three subjects for
whom age data were unavailable, our subjects had a mean
age of 66.7 years (standard deviation, 10.8) and a mean
Reading Span score of 2.08 (standard deviation, 0.49).
Including all subjects, the mean Reading Span score was
2.11 (standard deviation, 0.50). By contrast, in 11 studies of
neurologically normal subjects over 60 years old reviewed
by Carpenter et al. (1994), the average mean span score was
2.49, and only two studies obtained mean scores less than
2.3.7

Speech motor sequencing, which we have hypothesized
should relate to articulatory rehearsal processes, also
clearly was impaired in many of our subjects, as found in
past research (e.g., Lieberman et al., 1992). As noted earlier,
in healthy individuals the minimal distance between VOTs
for voiced and voiceless consonants is rarely less than
20 ms. Of our 41 subjects, 33 had at least one minimal
distance less than 20 ms, and of those, 12 exhibited VOT over-
lap (i.e., a negative minimal distance).

Both Reading Span and mean VOT separation corre-
lated significantly with sentence comprehension. Moreover,
their tendency to correlate more strongly or weakly with
performance on the same sentence types supports the idea
that both measures reflect aspects of verbal working mem-

7 These comparisons must be made with some caution, as the data re-
viewed by Carpenter et al. include results from an auditory span task relat-
ed to but different from Reading Span, and because span scores can vary
with differences in instructions and procedures.
The similarity is not trivial, since OMO errors did not show the same pattern of correlations, and since Reading Span and VOT separation were not significantly correlated with each other. It may be the case that Reading Span reflects primarily the combined processing capacity of executive working memory and the inherent capacity of the phonological store, with little or no contribution from rehearsal processes. Reading a series of lengthy sentences aloud, as required by the Reading Span task, engages the neurological mechanisms used for articulatory rehearsal. Thus, it may limit or even eliminate subjects' use of rehearsal to remember the final words of those sentences. Similar effects of "articulatory suppression" are seen in behavioral studies of verbal working memory (Gathercole & Baddeley, 1993) when subjects listening to or reading sentences are required to simultaneously hold in memory a random sequence of digits or other "concurrent load."

The role of verbal working memory processes in linguistic processing appears to differ from that of cognitive set-switching. Unlike OMO errors, neither Reading Span nor mean VOT separation correlated with comprehension of our non-constrained active center-embedded sentences, whose short, simple relative clauses, we argued above, place low demands on working memory. By contrast, both working memory measures correlated significantly with comprehension not only of semantically non-constrained passive center-embedded sentences—the hardest sentence type overall—but also of their non-constrained counterparts, whose relative clauses were equally long and complex. Intact verbal working memory processes may be important for resolving the long-distance dependencies between subject noun and main-clause verb phrase in these sentences. Grossman et al. (1992) found that the ability of PD patients to answer questions specifically probing long-distance dependencies was a significant predictor of their overall comprehension of a set of similar sentences. Since the function of rehearsal is to extend the duration of items in working memory (Baddeley, 1986), it may be especially critical for processing long-distance dependencies: VOT mean separation did not significantly correlate with comprehension of semantically constrained passive sentences with final relative clauses, while Reading Span did.

Our data also suggest a possible role for verbal working memory processes in comprehending passive sentences. Reading Span and mean VOT separation showed a tendency, at least in the more difficult sentence conditions, to correlate significantly with comprehension of passive but not active sentences (even when their relative clauses did not differ in length and complexity). OMO errors did not show the same relationship with verb voice. Passive sentences violate the usual association of a clause’s subject with the agent of the action and the object with the patient of the action. On-line eye-tracking data (Hochstadt, 2004) indicate that PD patients with comprehension deficits are overly biased toward taking the subject as the agent. Conceivably, verbal working memory processes are called into play in passive sentences when subjects have to “undo” the canonical thematic role assignment—especially when lexical semantics (in combination with world knowledge) do not constrain who is doing what to whom.

These correlational measures appear inconsistent with the proposal by Caplan and Waters (1999) that working memory includes a “language interpretation resource” that performs automatic syntactic operations and a separate, non-linguistic system that performs controlled, “post-interpretive” operations on linguistic output. According to that proposal, Reading Span and similar measures reflect the operation only of the latter system, which is said to be sensitive to the number of propositions within an utterance but not to syntactic complexity. If that were the case, we would expect Reading Span to correlate significantly with all our non-constrained sentences containing relative clauses, regardless of syntactic structure. It does not.8

The differential roles of impaired set-shifting and articulatory rehearsal in PD sentence comprehension deficits are supported by the absence of significant correlation between OMO performance and mean VOT separation. This is consistent with their being supported by segregated cortico-striato-cortical circuits that will not necessarily be affected together in a given PD patient.

OMO errors did, however, correlate significantly with Reading Span. This relationship could reflect verbal memory demands of the OMO task. Lehto (1996) suggested that correlations he observed in normal subjects between working memory span and performance on a set-shifting task similar to the OMO might reflect the need to “keep activated several aspects of the [task], such as the correct stimulus dimension, feedback given by the examiner, the nature of unsuccessful trials, and so on” (p. 39). Another, not necessarily exclusive possible explanation for the OMO–Reading Span correlation lies in the dual-task nature of Reading Span. Subjects have to divide their attention between the words they are holding in memory and the sentences they are reading. PD patients often have trouble with dual or divided-attention tasks (Dalrymple-Alford et al., 1994; Malapani et al., 1994), particularly when they must generate internal strategies for controlling their attention rather than relying on external cues (Brown & Marsden, 1988, 1991). That is just the difficulty they face in the OMO task, where they must selectively attend to one sorting criterion while inhibiting attention to the other.

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8 It should be acknowledged that there are other debates over both what tasks like Reading Span measure and the nature of verbal working memory, especially as it relates to sentence comprehension. For example, MacDonald and Christiansen (2002) suggest that verbal working memory—or at least whatever span tasks measure—is not a “primitive,” underlying cognitive capacity; instead, individual differences in performance on both span and comprehension tasks reflect differing experiences with language and differences in biological factors associated with, for example, “accuracy of phonological representations” and information processing speed. Data from studies of aphasics have led some researchers (e.g., Martin, 1995) to question the need for a concept of verbal working memory capacity in accounting for sentence comprehension. Our data do not address these controversies.
The relationship between Odd Man Out errors and Reading Span may go deeper than the task demands: as noted in Section 1, inhibition may be an important component of both set-switching and verbal working memory. In point of fact, set-switching, working memory, dual-task performance, and selective attention are among the cognitive capacities commonly grouped under “executive function.” Imaging studies indicate that they involve common cortical tissue, including dorsolateral prefrontal cortex (Duncan & Owen, 2000). However, the differences in the patterns of correlation of OMO errors and Reading Span with different conditions of the TMS suggest that the two measures do reflect mechanisms that are at least partially functionally distinct. This is not to say that altered inhibition is not involved in PD sentence comprehension deficits, or that it is not reflected in one or both measures—only that a shared inhibitory basis for set-switching and verbal working memory does not appear to account for every relationship we see between these factors and comprehension.

Though only a few of our patients were not on PD medication, our results are unlikely to reflect effects of dopamine supplementation medication. Most studies showing sentence comprehension deficits in PD have similarly used predominantly medicated subjects, but a study comparing the same PD patients on and off dopaminergic medication indicated that comprehension of sentences containing center-embedded relative clauses (and not syntactically simpler sentences) worsens when medication is withdrawn (Grossman et al., 2001). Thus, it seems likely that dopamine deficiency is responsible for the sentence comprehension deficits in PD, and that these deficits are only partially masked by medication. Similarly, we cited evidence above that set-switching and verbal working memory worsen when PD patients are taken off medication. We do not know of any “on–off” studies of speech motor sequencing in PD, but of course many other motor symptoms do improve with dopamine supplementation medication.

At the same time, our results do not depend critically on the four unmedicated subjects described in Section 2.1. On none of our measures were the scores for these subjects clustered at any extreme of the distribution. Moreover, analyses performed with these subjects removed from the data set did not render non-significant any results that were found to be significant for the complete subject group (or vice versa), with one minor exception that does not affect our conclusions: the marginally significant difference in error rate between center-embedded and final-relative-clause passive non-constrained sentences became non-significant ($F(1,36) = 1.76, p = 0.097$).

To conclude, the data we have obtained implicate several independent mechanisms in the sentence comprehension deficits that have been repeatedly found among a subgroup of PD patients. Comprehension errors on sentences containing relative clauses appear to derive from domain-general deficits in cognitive flexibility (likely due to impaired basal ganglia sequencing or prefrontal dopamine depletion) or possibly in inhibition. Deficits in two different verbal working memory mechanisms—executive processes and speech motor sequencing processes involved in articulatory rehearsal—may affect the comprehension of long-distance dependencies between sentence elements and possibly of the passive voice. However, these two mechanisms appear to be neurally independent of each other, and speech motor sequencing deficits appear to be independent of cognitive sequencing deficits as well. This independence is explained by the segregated nature of the underlying cortico-striato-cortical circuits: which circuits will be damaged in any given PD patient cannot be predicted.

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**Appendix A. Supplementary material**


**References**


