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"She will drive the ______": Verb-Based Prediction in Individuals with Parkinson Disease

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A thesis submitted in partial fulfillment of the requirements for the degree in Master of Science

"SHE WILL DRIVE THE _____": VERB-BASED PREDICTION IN INDIVIDUALS WITH PARKINSON DISEASE.

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by

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Abstract

Cognitive changes in Parkinson disease (PD) affect language processing, including sentence comprehension impairments, difficulties with processing verbs, and discourse impairments. In many theories of language comprehension, efficient language processing depends on successful implicit prediction of upcoming concepts and grammatical structures. Such prediction processes, in part, may be regulated by the neural dopaminergic system, which is markedly impaired in PD. In non-language tasks, persons with PD (PwPD) are impaired in prediction, sequencing, and probabilistic learning. However, the contributions of these dopaminergic-mediated prediction and probabilistic learning processes to language processing impairments in PD remain unexplored. We tested whether PwPD are impaired in implicit prediction during auditory language processing. The visual-world paradigm was used to investigate implicit predictive eye movements based on verb meaning. Participants listened to semantically predictive and non-predictive sentences while viewing picture stimuli. Both PwPD and controls showed prediction of upcoming nouns from verbs when hearing sentences like “She will drive the car.” Furthermore, PwPD performed equivalently to controls. These results are surprising given the literature, suggesting either that PwPD have normal linguistic prediction, or that more challenging conditions for prediction are required to reveal PD impairments.

Keywords: Parkinson disease, implicit prediction, language comprehension

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Introduction

It is now clear that persons with Parkinson disease (PwPD) have problems with language comprehension in addition to their primary motor symptoms. In the clinic, PwPD often complain that they find it difficult to keep up with conversations. Backing up these clinical observations, a great deal of research has shown that PwPD have issues with both sentence comprehension (Angwin, Chenery, Copland, Murdoch, & Silburn, 2006; Hochstadt, Nakano, Lieberman, & Friedman, 2006; Longworth, Keenan, Barker, Marslen-Wilson, & Tyler, 2005; Lee, Grossman, Morris, Stern, & Hurtig, 2003) and word processing (Fernandino et al., 2012; Peran et al., 2003). Given that language comprehension is multi-faceted, depending on a number of cognitive operations and abilities, understanding the roots of language comprehension deficits in PwPD is complex and may benefit from a number of theoretical and empirical approaches. The goal of the present thesis is to understand impairments in sentence comprehension that result from PD, although word processing is certainly relevant as well.

The vast majority of sentence comprehension research on PD has focused on impairments in understanding sentences with complex syntax. These studies have been motivated by theories that emphasize syntactic (rather than semantic) processing. In many cases, difficulties with sentence processing have been explained in terms of impairments in cognitive functions that are important for language comprehension, such as reduced working memory capacity (Hochstadt et al., 2006) and executive resource limitations (Grossman et al., 2003). Because properly recovering the structure of a sentence is an important aspect of understanding language, these studies have provided valuable insight into PD language processing.

On the other hand, understanding the meaning of a sentence depends on much more than processing complex syntax. Numerous theories of sentence comprehension emphasize how people construct the meaning of an utterance, rather than focusing on syntactic processing per se. As part of this, some researchers have implicated thematic role assignment as a potential sentence processing deficit in PwPD (Angwin et al., 2006). Assigning thematic roles involves determining, for example, that in “Sally kicked the ball.”, *Sally* is the agent (she is doing the kicking), and the *ball* is the patient (it is being kicked). In addition, implicit prediction of upcoming concepts (such as predicting a certain type of patient given an agent and a verb) plays a key role in many recent theories of sentence comprehension (Altmann & Mirkovic, 2009; Federmeier, 2007; Van Petten & Luka, 2012). For example, a comprehender might implicitly predict a concept such as *ball* following "Sally kicked the". A large number of studies have shown that people implicitly predict concepts (and syntactic structures) as a natural component of language understanding (Altmann & Kamide, 1999; DeLong, Urbach, & Kutas, 2005).

The present research took a novel approach to sentence comprehension deficits in PD. Rather than focusing on syntactic processing, I tested whether PwPD predict upcoming concepts when hearing syntactically simple sentences such as "She will drive the car." That is, I tested whether PwPD would predict (or anticipate) an upcoming noun concept (*car*) based on the meaning of the verb (*drive*). I used a visual world paradigm experiment in which implicit prediction was measured by eye movements to pictures of objects on the screen. To determine prediction, the critical time window began when participants heard the verb, and ended at the point in time corresponding to onset of the spoken noun. In the restrictive condition, only one of four objects that were depicted on a computer screen fit semantically with the verb. For example, when participants heard "She will drive the car.", only one picture corresponded to something that can be driven. The restrictive condition was compared to a non-restrictive one, in which all four objects plausibly fit with the verb. Surprisingly, PwPD performed equivalently to controls, as measured by the proportion of fixations to the target object (the car). That is, both PwPD and control participants showed anticipation of the upcoming noun, and their fixation proportions to the target were remarkably similar.

In the remainder of the Introduction, I first discuss the general neurobiology and symptoms observed in PD. This is followed by a targeted review of the language impairments experienced by PwPD. I then discuss the role of implicit prediction in efficient sentence processing. Finally, I present studies demonstrating prediction deficits in non-linguistic tasks in PD. These studies provide motivation for testing whether impaired implicit prediction contributes to language impairments that have been observed in PwPD.

Parkinson Disease

PD is a neurodegenerative disease that uniquely affects the dopaminergic pathways in the basal ganglia (BG) nuclei. Proper excitation and inhibition of inputs and outputs of BG pathways is controlled predominantly by the production and uptake of the neurotransmitter dopamine (Hornykiewicz, 2001). As a result of the loss of dopaminergic neurons in PD, particularly in the substantia nigra and the ventral tegmental area, the indirect and direct pathways in BG malfunction, leading to the progressive impairments in motor function (Alexander & Crutcher, 1990; Bartels & Leenders, 2009; Helmich, Hallett, Deuschl, Toni, & Bloem, 2012; Liu et al., 2006; Rosin, Topka, & Dichgans, 1997). Motor symptoms that primarily characterize the presence of PD are bradykinesia (i.e., slowness of movements), rigidity, tremor (common, however, not in all cases), and asymmetrical gait and postural changes. The clinical presentation of PD symptoms vary substantially between individuals due to the diverse pattern of dopaminergic neuron loss in the substantia nigra (Hornykiewicz, 2001). This in part accounts for the differences observed in age of onset, the dominant modality of deficit (motor versus cognitive), and whether the motor impairments are mainly tremor or gait (Bartels & Leenders. 2009). Despite differences in the symptoms experienced, the BG nuclei are the area most affected and source of primary neurochemical changes in PD.

The motor symptoms of PD are predominantly managed by dopaminergic medications that act as supplementation for the lack of dopamine production in BG (i.e., levodopa, Goetz et al., 2005). Additionally, the neural changes in PD result in cognitive deficits that can be present from the earliest stages of the disease (Elgh et al., 2009). The presence of cognitive impairments has been positively correlated with the increase in dopaminergic neuronal loss in the medial substantia nigra (German, Manaye, Smith, Wooward & Saper, 1989; Rinne, Rummukainen, Paljarvi, Rinne, 1989). Due to this relationship, it has been proposed that bradyphrenia (i.e., cognitive slowing) mirrors that of bradykinesia (Brown & Marsden, 1998; Rogers, Lees, Smith, & Stern, 1987). Brown and Marsden (1998) suggest that the BG circuits provide the fundamental ability to integrate input to output information, which allows for the proper sequencing of motion and of thought, and as a consequence of damage to BG nuclei, PD symptoms arise. This is crucially supported by the literature identifying the role that BG play in initiating and sequencing movements (Bartels & Leenders, 2009; Menon, Anagnoson, Glover, &

Pfefferbaum, 2000). Even more important is the literature that suggests their role in making use of advance information regarding future motor movement to speed up motor initiation; which has been found to be a deficit in PwPD (Bloxham, Mindel, & Frith, 1984; Sheridan, Flowers, & Hurrell, 1987). Even though PD symptoms and treatments historically have focused on the motor domain, recent investigations have shifted to appreciating the cognitive processing challenges that coexist with motor challenges. The cognitive changes are important to consider both clinically in terms of potential earlier diagnostic markers, and therapeutically, to target rehabilitation programs closer to the source of the impairments.

Parkinson Disease and Language Processing

Language impairments are apparent in PwPD regardless of the presence of dementia (Cummings, 1988). Some researchers have accredited these language issues to motor deficits and in particular, articulatory issues (Critchley, 1981, Darley, Aronson & Brown, 1975, Illes, 1989). However, Grossman et al. (1991) argued that language impairments extend well beyond production related difficulties. They, in addition to other researchers (Lieberman, Friedman & Feldman, 1990; Natsopoulos et al., 1991), have suggested that PwPD have greater difficulty comprehending sentences that contain grammatically complex clausal structures, as compared to sentences composed of simpler clausal structures. In Grossman et al. (1991), PwPD listened to sentences varying in complexity (e.g., *"The eagle chased the hawk"* vs. *"The car that hit the tree was green"*). Each sentence was followed by a simple comprehension question (e.g., *"Which bird was chased?"* vs. *"What was hit?"*). The PD group was slower in general at responding to the comprehension questions, and response latency significantly increased with increases in grammatical complexity. In a follow-up study, Grossman et al. (1992) performed a similar experiment with the addition of a regression analysis that indicated attentional and grammatical factors contribute to PD sentence comprehension impairments. Although the basis for the language impairments in PD remain unclear, some investigators have suggested that it is due strictly to a grammatical processing deficit (Cohen, Bouchard, Scherzer, & Whitaker, 1994; Lieberman, Kako, Friedman, Feldman, & Jiminez, 1992; Natsopoulos et al., 1991; Ullman et al., 1997). However, others argue that it is due to a deficit in executive functions and working memory (Geyer & Grossman, 1994; Grossman, Carvell, Stern, Gollomp, & Hurtig, 1992; Lee et al., 2003; Waters & Caplan, 1997), as a result of a dysfunction of fronto-stratal-thalamic pathways in PD (Grossman et al., 2003).

In addition to sentence processing difficulties identified in PD, early stage patients have also shown deficits in action-verb naming (Bertella et al., 2002; Cotelli et al., 2007; Peran et al., 2009) action-verb identification (Boulenger et al., 2008), and action-verb processing (Fernandino et al., 2012; Herrera, Rodriguez-Ferreiro & Cuetos, 2012). Bertella et al. (2002) conducted a picture-naming task in which PwPD and controls named 52 objects and 50 actions. A verb-naming deficit in PwPD was found when performance was compared to controls. Boulenger et al. (2008) provided further support for verb processing issues in PD using a masked priming experiment (70 action verbs and 70 concrete nouns). PD participants had longer response latencies than did controls, and this effect was exaggerated when PD participants were off versus on dopaminergic medication. Furthermore, Herrera et al. (2012) found that PwPD were more impaired in naming action-verbs that encompass higher motor content (*kick*) compared to lower motor content (*sleep*). Therefore, it has been suggested that the verb processing difficulties in PwPD are due to a strong interaction with the motor system in action-verb processing (Booth, Wood, Lu, Houk, & Bitan, 2007; Fernandino et al., 2012; Herrera et al., 2012; Ibanez et al., 2012; Pulvermuller, Hauk, Nikulin, & Ilmoniemi, 2005).

Even though semantic knowledge is an important component of sentence processing, there has been minimal work investigating semantic aspects of sentence comprehension in PwPD, such as the use of real world knowledge during sentence interpretation. A number of studies have, however, investigated semantic processing of words outside of sentence contexts. For example, Angwin et al. (2007) conducted a semantic priming experiment with PD patients 'on' and 'off' dopminergic medications. Participants were presented with related (e.g., crab - lobster) and unrelated (e.g., kilt - lobster) prime-target pairs with varying inter-stimulus intervals (500 ms, 1000 ms, 1500 ms). Automatic lexical activation in PD patients 'on' medication was delayed significantly compared to controls, and the difference was larger when patients performed the task 'off' medication.

In summary, research suggests that PwPD have impairments in understanding sentences containing complex syntactic structures. Furthermore, verb processing and semantic priming studies provide evidence of impairments in semantic processing outside of sentence contexts. In the present research, I took a novel approach to the study of sentence comprehension impairments in PD. Rather than focusing on syntactic processing, I used data and theories regarding implicit semantic-based prediction to motivate the present study.

Implicit Prediction and Language Comprehension

Both spoken and written language unfold over time. For over 40 years, it has been known that language processing is incremental in that people interpret language immediately as it unfolds continuously over time. In fact, normally functioning adult (and even child) language users may go one step further than keeping up with linguistic input in that they may anticipate what words, types of concepts, or syntactic structures may come next. In many current theories of language comprehension, rapid and efficient sentence processing is dependent on successful implicit prediction of upcoming concepts and syntactic structures, both of which can be constrained by prior sentence, discourse, and real-world contexts (Altmann & Mirkovic, 2009; Federmeier, 2007; Levy, 2008; Van Petten & Luka, 2012). These predictions may take the form of a specific word if the preceding context is sufficiently constrained, as in "I was late for work this morning because while I was driving in, I had a flat ___." Predictions may also take the form of a type of concept, such as types of food following, "The boy will eat a". Predictions also may be more general, such as predicting that a noun should occur following, "She saw a green". Altmann and Mirkovic (2009) present a theory of language comprehension in which such anticipations are the natural product of the integration of the previous linguistic input, the current real world context, knowledge about how the real world works, and knowledge about the syntax of language. Computational models, primarily based on Elman's (1990, 1993) simple recurrent network models, provide mechanistic insight into how prediction can underlie language learning and moment-to-moment processing.

A number of studies have provided evidence for prediction in language comprehension (Altmann & Kamide, 1999; DeLong, Urbach, & Kutas, 2005; Van Berkum, Brown, Zwitserlood, Kooijman, & Hagoort, 2005). In many studies, researchers design stimuli to test whether participants predict a noun patient (e.g. *cake*) that directly follows a verb (e.g. *eat*). This strategy has been used often because many verbs constrain what patients are likely to follow, and constraints can be strengthened by the combination of a verb and the previous linguistic context. For example, Altmann and Kamide (1999) performed a visual-world paradigm eyetracking study in which they presented sentences with a verb that either restricted (e.g., *eat*) or did not restrict (e.g., *move*) upcoming context for a noun (e.g., *cake*). The sentences accompanied a visual scene. For example, *"The boy will eat the cake"* was presented with a scene that included a boy, a cake, a train, a car, and a ball. Thus, only one object in the scene was edible. In contrast, in the non-restrictive case, a number of objects fit the verb in that they were moveable. The visual world paradigm is particularly advantageous for studying prediction in language comprehension. Eye movements can be continuously measured during the unfolding language stimulus, and thus they provide a temporally sensitive measure of language comprehension. Eye movements are relatively unconscious, automatic, implicit, computationally cheap, and rapid. Furthermore, people move their eyes approximately once every 250 ms, and typically are not aware that they are doing so. Altmann and Kamide found that listeners showed a significantly higher probability of launching a saccadic eye movement to the target (*cake)* when the verb restricted the context (only one edible object). Critically this difference occurred during the time window that began when participants heard *eat*, and ended before they heard *cake*. In other words, participants' eye movements revealed anticipation of the upcoming patient of the verb. Altmann and Kamide interpreted their results in terms of the information used for assigning nouns to thematic roles of the verb. They suggested that these predictive saccades are indicative of listeners using thematically appropriate real world knowledge about the action denoted by a verb. Their explanation was based on McRae, Ferretti, and Amyote (1997), who argued that upon encountering a verb, a comprehender is able to access event-specific knowledge about *who does what to whom*.

A number of visual world studies have now shown evidence of prediction during sentence comprehension (Borovsky, Elman, & Fernald, 2012; Kamide, Altmann, & Haywood, 2003). For example, Kamide, Altmann, and Haywood (2003) presented visual scenes that contained both sentence subjects (e.g., *girl* and *man*) and objects (e.g., *carousel* and *motorbike*) while simultaneously presenting a sentence such as *"The girl/man will ride the carousel/motorbike*". Predictive eye movements mirrored the fact that a young *girl* is more likely to ride a carousel, whereas an adult man is more likely to ride a motorbike. The results suggest that listeners combine information based on real-world knowledge and the current visual context to selectively restrict post-verbal arguments.

Clear evidence for prediction has also been provided by event-related potential (ERP) studies (DeLong, Urbach, & Kutas, 2005; Van Berkum et al., 2005; Wicha, Moreno, & Kutas, 2004). For example, DeLong, Urbach and Kutas (2005) tested whether prior context would promote prediction of upcoming articles such as "a" versus "an" preceding a predictable noun. They presented readers with highly constraining sentences such as, "*The day was breezy so the boy went outside to fly...a kite/an airplane"*, while simultaneously measuring ERPs using EEG. Sentences were read from a computer screen, and there was no co-present visual stimuli. The interest point is a negative component that peaks around 400 ms after stimulus-onset corresponding to processing of semantic information. When sentences that are presented vary in semantic congruency (e.g., She likes her coffee with cream and sugar/puppy), a difference in N400 amplitude is observed. The N400 is greater for words that are less expected. The results demonstrated the well-known N400 amplitude difference at the highly expected "kite" compared to the less expected "airplane". More importantly, this difference was also found between the expected "a" versus the unexpected "an", providing clear evidence of prediction. These results show that prediction is driven at least in part by real-world knowledge, such as what a boy is likely to fly on breezy day.

In summary, based on real-world everyday experiences, as well as hearing and reading about many types of events, activities, and situations, people have developed extensive conceptual knowledge that can be applied to thematic role processing. This knowledge is an important source of information that allows people to constrain the conceptual and syntactic properties of upcoming information in a sentence. One way in which this type of implicit prediction during language comprehension is important is that it allows for faster processing of incoming input (Dikker & Pylkkanen, 2013; Federmeier, 2007; Federmeier et al., 2010; Wlotko, Federmeier, & Kutas, 2012). If an individual’s predictive processes were impaired, it seems likely that they would have trouble keeping up with the pace of conversation. Therefore, I hypothesized that PwPD may be impaired at implicit prediction (based on verbs) during sentence processing. Another reason to suspect that this is the case is that PwPD have presented with challenges in processing verbs, as discussed above. Considering that verbs are often strong cues for what is to come up next, if the thematic knowledge associated with those verbs is not being used to anticipate the meaning of upcoming words, language impairments would result. Furthermore, PwPD have been shown to have issues with prediction and probabilistic processing in non-linguistic tasks. Thus, it also is possible that these issues extend to the linguistic domain. Ullman et al. (1997) have suggested that perhaps the difficulty with rules underlying syntactic dependencies in sentences may be a specific instance of a broader deficit in procedural learning and rule-based processing associated with disorders of the BG. If we take this one step further to suggest that perhaps both syntactic and semantic dependencies in sentences may be a particular example of a more general probabilistic learning deficit with disorders of the BG, this may be a plausible source for the language impairments in PD.

Non-linguistic Prediction Tasks

Predictive processes are suggested to be impaired in PD. The motor domain has been heavily studied, and research strongly suggests impairments in premotor preparation (Bloxham et al.,1984; Sheridan, Flowers, & Hurrell, 1987), initiation of movement (Flowers 1978; Menon, 2000), and motor sequencing (Menon, 2000). Movement is sequentially and temporally based, and thus requires smooth transitions between actions. As a result, prediction is a necessary component of motor behaviour to properly execute motor tasks. Flowers (1978) suggests that PwPD are less able to use predictive control when engaging in motor tasks, leading to the motor symptoms characteristic of PD. It has been more broadly suggested that PwPD may not employ predictive processes for future events in external situations on both a motor and thought basis (Flowers, 1978).

Investigations have extended into other domains, apart from motor, to further explore this apparent prediction deficit. PwPD have shown deficits in cognitive tasks requiring the integration of multiple cues to correctly predict an upcoming event based on probabilistic information (Shohamy, Myers, Onlaor, & Gluck, 2004; Shohamy, Myers, Hopkins, Sage, & Gluck, 2009). PwPD have difficulty using advance cue information to correctly predict a target's future movements (Schnider, Gutbrod, & Hess, 1995). They also demonstrate impairments in prediction during the Iowa Gambling task (Kobayakawa, Koyama, Mimura, & Kawamura, 2008; Peretta, Pari, & Beninger, 2005), and the weather prediction task (Shohamy, Myers, Onlaor, & Gluck, 2004; Shohamy, Myers, Hopkins, Sage, & Gluck, 2009). Furthermore, Shohamy (2009) has shown that PwPD have difficulty making use of probabilistic information as integration complexity increases with the weather prediction task. Note that these tasks primarily test explicit predictive abilities. Researchers have also investigated probabilistic learning in PwPD using artificial grammars (Smith & McDowall, 2006). Statistical language learning is an implicit process that requires probabilistic information to correctly develop knowledge of grammatical structure (Saffran, Newport, & Aslin, 1996; Saffran, Newport, Aslin, Tunick, & Barrueco, 1997). Smith and McDowall (2006) show that PwPD have difficulty learning artificial grammars, lending support to the hypothesis that the BG play a significant role in probabilistic learning tasks.

Deep brain stimulation studies elaborate the BG's role in probabilistic tasks. Wilkinson et al. (2011) suggest that the subthalamic nucleus plays an important part in implicit probabilistic classification learning. They found stimulation of the subthalamic nucleus improves implicit learning of necessary cue integration for more implicit compared to explicit related cues on the weather prediction task. Courthard et al. (2012) further support this finding with a deep brain stimulation study targeting the subthalamic nucleus in PD patients on and off medication. They found that PD participants off medication had impaired memory for probabilistic information, whereas stimulation of the subthalamic nucleus enhanced the ability to integrate multiple pieces of information.

In summary, PwPD demonstrate deficits in recruitment of probabilistic information and integrating events, which are both necessary for prediction to occur in real-world situations. Given that implicit prediction of upcoming information is also required for efficient sentence processing, because PwPD are impaired on prediction tasks in the motor domain and other non-linguistic cognitive tasks, deficits in implicit prediction may contribute to language impairments in PD.

The Present Study

The primary goal was to assess whether PwPD are impaired at implicit prediction during sentence processing. I focused on the ability to use a verb to predict an upcoming noun patient. In line with the deficits in predictive and probabilistic learning of non-linguistic information in PD, I predicted that similar impairments would be found in linguistic processing. Specifically, I predicted that PwPD would be less able than matched control participants to anticipate an upcoming target noun (e.g., *car*) following the onset of a constraining verb (e.g., *drive*). The experiment was approved by, and conducted in compliance with, the Health Science Research Ethics Board at the University of Western Ontario, and the Lawson Health Research Institute.

Experiment: Prediction Based on Simple Sentences in Persons with Parkinson Disease and Matched Controls

The purpose of this experiment was to test whether PwPD are impaired in implicit prediction during auditory language processing. The visual world paradigm was used to investigate implicit predictive eye movements based on verb meaning. This experiment consisted of two parts, which I call the predictive trials and the directive trials. In the predictive trials, PwPD and matched control participants listened to semantically restrictive and non-restrictive sentences (canonical, future-simple sentences such as *"She will drive the car"*). While doing so, they viewed four picture stimuli arranged in quadrants on the computer screen. In the restrictive sentences, the verb fit unambiguously with one of the objects on the screen (*drive* - car), but not the others (e.g., hat, banana, and flashlight). In the non-restrictive sentences (control trials), the verb plausibly fit with all of the pictured stimuli.

The directive trials were the same except that the sentences were all of the form, *"Look at the flower"*. That is, participants were directed to look at a picture, and there was no predictive component in these trials. The directive condition was included to aid in understanding any differences between PwPD and controls in the case that such differences were found. For example, if eye movements to the target in the restrictive sentences were delayed for PwPD relative to controls, this might be due to motor issues in terms of planning and executing saccades given acoustic cues. The directive condition would then provide insight into this possibility. That is, if the results for PwPD and controls were identical in the directive condition (in which prediction was not an issue), potential motor differences could then be ruled out as an explanation for any differences found in the predictive condition.

Method

Participants

Twenty-three PwPD (9 females) and 21 healthy matched controls (9 females) were recruited. On the day of testing, one PwPD (male) and one control (female) were excluded due to an inability to track their pupil after having cataracts surgery. This surgery involves the removal of the eye lens, and replacement with an artificial lens. The eyetracker is sensitive to reflective material, and the artificial lens acted as a second pupil, therefore preventing the camera from focusing on one 'pupil' long enough to track. Two PwPD (one female and one male) were excluded due to additional symptoms that questioned the PD diagnosis. On performing the cognitive measures, the speech language-pathologist reported that one individual showed symptoms more akin to progressive supranuclear palsy, which can be misdiagnosed as PD. The second individual disclosed that they had symptoms akin to narcolepsy, which was an issue when attempting to focus on the passive language listening task.

The demographic data exclude those four individuals. PwPD ranged in age from 52 to 77 years (*M* = 64.6, *SD* = 6.3), and controls ranged in age from 55 to 80 (*M* = 67.2, *SD* = 7.2). PwPD were recruited from the Movement Disorders Clinic at the University Hospital in London, Ontario. Healthy older adults were recruited as members of the London community from the London Healthy Aging Center, or community centers.

All participants were screened to have no history of major psychiatric illness (i.e., schizophrenia, psychosis or bipolar disorder), neurological illness (i.e., stroke, multiple sclerosis, etc.), neurosurgical procedure, or traumatic brain injury. All participants self-rated proficiency in speaking and understanding English with 7 or higher on the modified LEAP-Q (Language Experience and Proficiency Questionnaire, ONDRI manual). All participants attended school through at least grade 12, (PwPD, *M* = 15.2 years of education, *SD* = 2.1; Controls, *M* = 16.0 years, *SD* = 2.5).

All participants were screened for visual or oculomotor dysfunction (visual acuity of 20/50 or worse [with corrected lenses], convergence insufficiency, supranuclear gaze palsy) by a neuro-ophthamologist. No participant was found to have convergence insufficiencies at 70 cm. A distance of 70 cm was used because participants’ eyes were positioned 70 cm from the display during the eye tracking experiment. Participants with corrected visual acuity were asked to wear their lenses for the duration of the experiment

(7 PwPD, 2 Controls). Eye movements were also evaluated in the neuro-ophthalmology clinic by asking the participant first to make large-amplitude saccades (of about ninety degrees), using the examiner's left thumb and right index finger as targets, from left to right and back several times (to assess horizontal saccades), and then up and down and back several times (to assess vertical saccades). Smooth pursuit eye movements were evaluated by asking the participant to hold their head immobile while following the examiner's finger with their eyes. The examiner's finger moved smoothly, at a distance of about 1.5 meters from the participant's face, in a cross-shaped trajectory. This was done first horizontally from left to right and back (about ninety degrees) and then vertically upwards and downwards and back (about ninety degrees), along the two major orthogonal meridians bisecting the neutral position of gaze. Saccadic eye movements were monitored for hypometria (systematic undershooting of the intended target), hypermetria (systematic overshooting of the intended target), and dysmetria (over- or undershooting of the intended target with random but equal frequency). Smooth pursuit eye movements were monitored for saccadic pursuit - a series of "catch-up" saccades necessary when smooth pursuit velocity is inadequate to keep up with the examiner's finger. Both saccades and smooth pursuit were used to assess the range of extraocular motility and to ensure there were no unexpected limitations of eye movements that might indicate an underlying diagnosis other that Parkinson disease (e.g., progressive supranuclear palsy, which is characterized by vertical gaze limitation). The eye movement results are reported in Table 1, showing normal smooth pursuit in all participants and some hypometric behaviour in saccadic movement. However, the neuro-opthamologist reported that each participant was able to perform the eyetracking task, as the small saccadic hypometria noted was accommodated by large target images and corresponding areas of interest in the eyetracking analyses.

Participants who, at the time of the study, were not currently wearing a hearing amplification device (e.g., hearing aids) completed a hearing screening protocol to ensure sufficient hearing acuity for completing study tasks (35 completed; 5 participants [1 PwPD, 4 Controls] had existing amplification). Pure tone hearing screenings were conducted by a registered speech-language pathologist in accordance with the American Speech-Language-Hearing Association Guidelines for Audiologic Screening for adults

Table 1. Summary of saccadic and pursuit eye movements for PwPD and controls.

	PwPD		Controls	
	Vertical	*Horizontal*	*Vertical*	*Horizontal*
SACCADIC				
Normal	8	13	15	18
Hypometric (up only)	4		1	
Hypometric (both)	8	7	4	2
SMOOTH PURSUIT				
Normal	20	20	20	20

(ASHA, 1997). A single, calibrated, GSI-18 Screening Audiometer (Grason-Stadler Incorporated, Eden Prairie, MN, USA) with TDH-39 headphones was used for screening. Fourteen participants (6 PwPD, 8 Controls) failed the hearing screening and were referred for further audiologic testing. Participants who failed the hearing screening were fitted with a Bellman Audio Maxi Personal Amplifier (Bellman & Symfon, Gothenburgh, Sweden) for the cognitive testing and eyetracking procedure.

The Dementia Rating Scale (DRS) was used to provide a baseline measure of cognitive abilities for each individual. It also was administered by a speech-language pathologist, and is reported as DRS-2 age and education-corrected Mayo's Older Americans Normative Studies (MOANS) scaled scores (Jurica, Leitten, & Mattis, 2001). The standard score cut-off for discriminating normal cognition in PD from PD-dementia and PD-Mild Cognitive Impairment (MCI) is $\leq$ 123 (Llebaria et al., 2008), whereas the cut-off in controls is $\leq$ 129 (Monsch et al., 1995). All individuals were above these criteria for their group on the DRS (PwPD: *M* = 138, *range* =132-143; controls: *M* = 141, *range* =132-144).

At time of testing, PwPD averaged 8.3 years (*SD* = 3.7) since time of diagnosis of PD. All PwPD were optimally medicated at the time of testing. Levodopa Equivalent Dose (LED) was calculated using the formula proposed in Tomlinson et al. (2010; *M* = 551 mg, *SD* = 327, *Range* = 200 - 1596 mg). All PD participants were tested at their individual optimal time of day (Morning [n = 9]; Afternoon [n = 11]). The neurologist administered the Movement Disorders Society-Unified Parkinson disease Rating Scale (MDS-UPDRS, Goetz et al., 2008) on the day of testing to collect information concerning motor symptoms (*M* = 25.7, *SD* = 8.4). These scores indicate that the PD participants demonstrated mild to moderate motor symptoms (Goetz et al. 2008). Hoehn and Yahr (1967) scores were collected by the neurologist to classify disease severity (*M* = 2, *Range* = 1-3). The scores range from 1 (unilateral involvement only usually with minimal or no functional disability) to 5 (confinement to bed or wheelchair unless aided). Therefore the scores on the MDS-UPDRS and Hoehn and Yahr coincide, with both motor symptoms and disease severity consistently within the range of mild to moderate.

Stimuli & Apparatus

Sentences. Sixty sentences of the form "*She will [verb] the [noun]*" (see Appendix A) were presented auditorially over speakers with accompanying visual stimuli. Predictive trials consisted of 30 sentences for each of the restrictive and non-restrictive conditions. In the restrictive sentences, the verb fit unambiguously with one of the objects on the screen (*drive* - car), but not the others (e.g., hat, banana, and flashlight). In the non-restrictive sentences (control trials), the verb plausibly fit with all of the pictured stimuli. Target words were 30 common nouns, and each was presented once in the restrictive and once in the non-restrictive condition. Because the goal was to investigate prediction based solely on the meaning of the verb, we used sentences with an initial noun or pronoun that carried little semantic information (i.e., She).

In the directive trials, the sentences followed the template "*Look at the [noun]*". Target words were 20 common nouns. Four visual stimuli were included on each trial, one of which corresponded to the noun, with the other three being unrelated. See Appendix B for complete stimuli.

Visual Stimuli. All images were presented at 300 x 300 pixels as black and white line drawings selected from the International Picture Corpus (Szekely et al., 2004) and Snodgrass and Vanderwart (1980). The pictures used in the predictive part of the experiment were the same as in Nozari and Mirman (2015). The pictures used in the directive part were not used in the predictive part. Each of the four pictures were placed in a different quadrant of the screen at a 45 degree angle from the center of the screen. The position of the images were randomized over trials and participants.

Auditory Stimuli. The digital sound files were played by a PC computer (Windows XP) with an Audiomedia II sound card, through Logitech X-120 speakers (120V ~ 60Hz). All sentences were recorded by a native English female speaker, with a mean intensity of 77 dB (range = 74 - 80 dB). The sentences were recorded in a sound proof booth, with an AKG 520C head worn condenser microphone with a Sound Devices USB Pre2 preamp on a MacBook Air OSX. The sentence stimuli were recorded using Audacity, Version 2.0.6, set for mono channel recording at a 44100 sampling rate. To ensure that the sentence files were consistent across all stimuli, relative to intensity and pausing, the audio files were root mean compressed using Audacity, and were digitally edited to remove silence at the beginning and end. All sentences had the same duration from the beginning of the sentence to the verb onset (750 ms), with 300 ms of silence following the noun offset. The sound file adjustments were constructed using a customized Praat script, Version 5.3.84.

Eyetracker. A desktop mounted Eyelink 1000 eyetracker was used to record all eye movements. Calibration was performed prior to beginning the test trials, and at any point in time that the participant took their head out of the chin rest. Before the start of every trial, the fixation point acted as a calibration check. If the camera lost the pupil, the program automatically went to camera setup to allow for a calibration to be completed. Monocular gaze position was recorded at 2000 Hz. The camera lens was positioned 60 cm away from the participant’s head, with a 35 degree angle to their eyes. The participant’s head was positioned 70 cm away from the 16-inch monitor with the resolution set to 1024 x 768 dpi. Stimuli were presented using Experiment Builder, Version 1.10.1241 software.

Procedure

Eye Tracking Procedure. For each trial, a fixation cross was presented for up to 10 s. Once the participant focused on the fixation cross for 3 s, the cross disappeared, and four pictures were presented. The four pictures (one in each quadrant) were presented for 2 s to allow participants time to familiarize themselves with the objects, and their positions on the screen. Following the preview period, the pictures remained on the screen while the sentence was played over speakers, with the critical verb onset at 750 ms after the onset of the sentence. Figure 1 illustrates the trial procedure.

There were three blocks of trials. Block 1 began with six practice trials (three restrictive and three non-restrictive), and then continued to the predictive experimental trials (15 restrictive and 15 non-restrictive). All sentences followed the format, "*She will [verb] the [noun]*." Block 2 included an additional 30 predictive trials (15 restrictive and 15 non-restrictive). For all trials, participants were instructed to "Listen to the sentence and look wherever you would like at the pictures on the screen." Block 3 began with three practice trials, and then continued to the 20 directive trials, all using the sentence format, "*Look at the [noun]*." In this block, participants were instructed to "Listen to the sentence and look wherever you would like at the pictures on the screen."

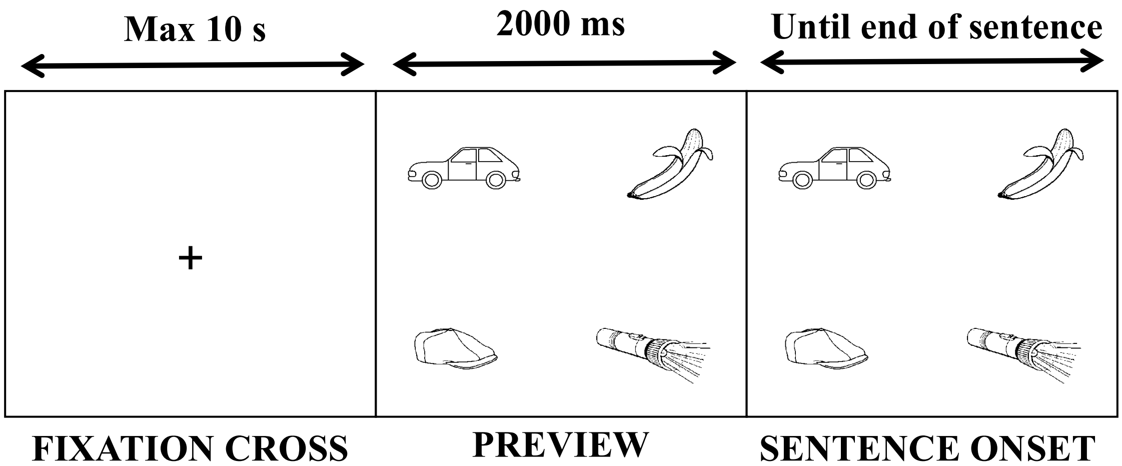

Figure 1. Illustration of the trial procedure for the predictive and directive trials.

Results

The predictive and directive trials were both analyzed using Growth Curve Analysis (GCA). Thus, for each set of comparisons a model was created to best-fit the behavioural data. The best-fit model is indicated by running ANOVA comparisons between each model level. A p-value based on the parameter estimates of the best-fit model is the measure of statistical significance. For further detail on GCA see below.

Growth Curve Analysis

GCA is a statistical approach used to analyze visual world eyetracking data (Mirman, 2014; Mirman, Dixon, & Magnuson, 2008). In a visual world experiment, small increments of time (ms) are the necessary unit for an accurate measure of eye movements made during any given trial. Growth curve analysis involves hierarchical modeling of orthogonal polynomials, which allows for discrete analyses of fixation proportions over time. Compared to natural polynomials, orthogonal polynomials account for more of the subtleties of processing by allowing individual time terms (i.e., intercept, linear, quadratic, cubic, and quartic) to be independent of one another, thus avoiding correlated measures (Mirman, Yee, Blumstein, & Magnuson, 2011). The polynomial order necessary to capture the data is dependent on the behavioural curve attributes. That is, the greater the number of inflection points, the higher the order of the polynomial used to model the data. Another determinant of choosing the polynomial order is the time-window chosen for analyses. For visual world experiments, generally cubic and quartic time terms are not particularly informative, and the common practice is to include only the intercept, linear, and quadratic polynomial terms (Mirman et al., 2008).

Each time term provides a slightly different understanding of the modeled curve. The intercept term denotes the average y-value of the curve across the analysis window. It is important to note that the intercept term is comparable to the standard visual world paradigm comparisons of overall fixation proportion, while the higher-order terms provide more detailed information regarding the time course (Mirman et al., 2011). The linear term accounts for monotonic change in fixation proportion by providing a function that preserves the given order of observations, which allows observations to remain time-dependent in the model. The linear term denotes the average slope across the analysis window. The quadratic, cubic, and quartic terms all provide analyses of inflection points (e.g., an increase followed by a decrease in fixation proportion, or vice versa). However, the cubic and quartic terms capture details observed in the asymptotic tails, as compared to the quadratic term, which is concerned with the center driven inflection point. The curves are illustrated in Figure 2, which is taken from Mirman (2014).

The models are able to incorporate main effects, interactions and individual variability by manipulating the fixed and random effects. The fixed effects in the current models were condition, group, and object type. Therefore, the fixed effects provide information regarding overall differences between conditions (restrictive vs. non-restrictive sentences), participant groups (PwPD vs. controls), and object (target vs. distractors). The residual effects are captured through the addition of random effects to the models and capture individual participant deviation from the means across participants and conditions.

Analyses were performed using three time-windows. For the predictive trials, two time-windows were analyzed. The first began 200 ms following verb onset (2950 ms) and finished 200 ms following noun onset (4440 ms). This time-window included the time that is required to program and launch a saccade, which is approximately 200 to 250 ms. The addition of 200 ms is standard in visual world experiment analyses. It was important to isolate this time period in the restrictive and non-restrictive conditions because prediction of the noun was the key issue (i.e., the time between hearing the verb and hearing the noun). Polynomial models up to the quadratic term were used to analyze fixation proportions during this shorter time-window because fixation proportions were not at asymptote. The second time-window included fixation proportions from the verb onset (2750 ms) to the asymptote (6000 ms; which was determined by observing the behavioural data) to capture the data patterns over the trial from the critical point to the end of the sentence. Cubic orthogonal polynomial models were used to analyze the data during this longer time-window. Analyses of this longer time-window were included for completeness. They are not as theoretically central as are the analyses of the predictive time-window. For the directive trials, one time-window was sufficient to capture the behavioural data. It began at noun onset (3900 ms) and continued to the asymptote (6500 ms; which also was determined by observing the behavioural data). Cubic orthogonal polynomial models were used to analyze the data during this time-window.

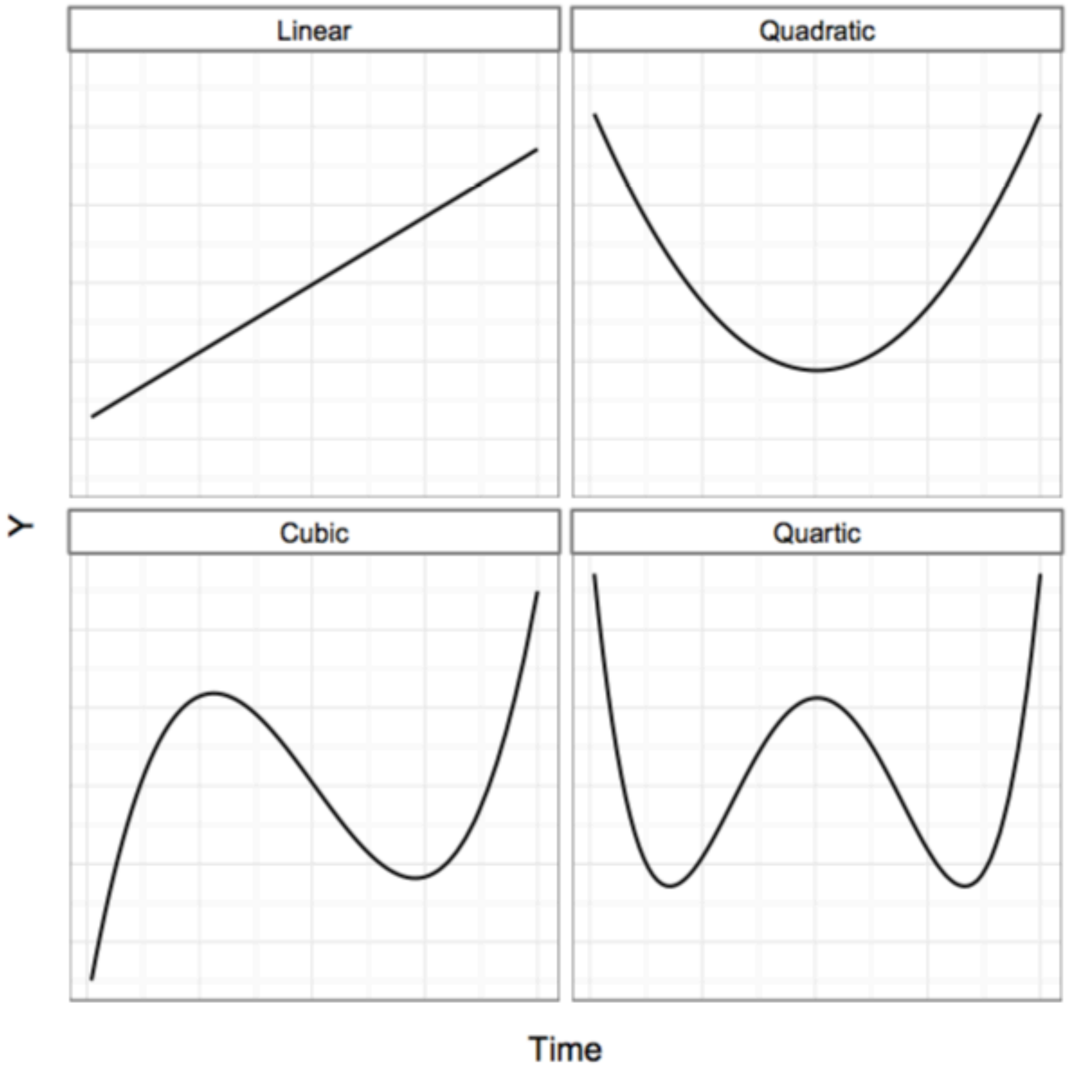

Figure 2. This illustration is taken from Mirman (2014) to elicit how each polynomial time term will model the behavioural data differently. It is important to observe the behavioural data, and select the appropriate polynomial order to use.

Each comparison model was based on nested model testing to determine the best polynomial degree. The nested model testing consisted of reaching the highest polynomial degree at which the model converged. The model was tested against a nested model, this being a model with one fewer polynomial degree. The models were compared using chi-square and log likelihood scores. Parameter-specific *p*-values were estimated using the normal approximation (*t*-value treated as a *z*-value). If the model significantly increased fit as compared to the nested model, the higher polynomial degree model was adopted. This pattern continued testing up to the quadratic or cubic polynomials, depending on the time-window. All models incorporated full random effect structure of participants (i.e., up to the quadratic term or cubic term given the model being used). Additionally, random effects of participant by condition or participant by object on time terms up to the quadratic were added when condition or object was included as a fixed effect. All analyses were conducted in R version 3.0.2 using the lme4 package (version 1.0-5).

Predictive Trials

Restrictive and Non-restrictive Conditions

Persons with Parkinson Disease. The effect of condition was analyzed using a second-order (quadratic) orthogonal polynomial with fixed effects of condition (restrictive vs. non-restrictive) on all time terms, and participant and participant-by-condition random effects on all time terms. The time-window of analysis was 200 ms following verb onset to 200 ms following noun onset (i.e., prediction time-window). The data were best fit when the fixed effect of condition was added to the quadratic term ($\chi^2(1) = 17.44$, $p < .0001$). The fixed effect parameter estimates of the quadratic model on condition were significant on all time terms. The significant intercept term indicates that PwPD had higher overall fixation proportions to the target for restrictive relative to non-restrictive sentences (*Estimate* = 0.038, *SE* = 0.015, $t = 2.53$, $p = .011$). The significant linear term indicates a steeper slope for the restrictive condition (*Estimate* = 0.298, *SE* = 0.053, $t = 5.58$, $p < .0001$). The quadratic term indicates a significantly steeper curve for the restrictive condition (*Estimate* = 0.212, *SE* = 0.041, $t = 5.20$, $p < .0001$). These results indicate a difference in the increasing fixation proportions to the target between the restrictive and non-restrictive conditions for PwPD during the prediction period. That is, PwPD showed prediction based on the meaning of the verb. The full fixed effect parameter estimates and their standard errors, *t*- and *p*-values can be found in Table 2 for the prediction and post-prediction periods. The behavioural data are illustrated in Figure 3.

Although not as important theoretically, the main effect of condition also was analyzed from verb onset to the observed asymptote (i.e., post-verb onset time-window). A third-order (cubic) orthogonal polynomial with fixed effects of condition on all terms, and random effects of participants (all terms) and participant-by-condition (up to quadratic). The data were best fit when the fixed effect of condition was added to the cubic term ($\chi^2(1) = 42.55$, $p < .0001$). The estimated parameters indicate that from the verb onset to noun offset (i.e., end of sentence), PwPD produced significantly higher fixation proportions to the target in the restrictive compared to the non-restrictive condition. The effect of condition was significant on the intercept ($p < .02$), as well as on the quadratic and cubic terms ($p < .0001$ in both cases). The linear term, however, was nonsignificant. These results indicate that the pattern observed in the prediction period is found also during this longer time-window that extends until the end of the sentence. Refer to Table 2 for full parameter estimates, and Figure 3 for the modeled and observed data.

Controls. The same analyses were conducted on the data from control participants. As with PwPD, the data were best fit when the fixed effect of condition was added to the quadratic term ($\chi^2(1) = 9.89$, $p < .002$). The fixed effect parameter estimates of condition in the quadratic model demonstrate a significant effect on all time terms. The significant intercept term indicates that, as was the case for PwPD, controls had higher overall target fixation proportions for the restrictive relative to non-restrictive sentences (*Estimate* = 0.058, *SE* = 0.015, $t = 3.82$, $p < .0001$). The significant linear term indicates an increased slope rate for restrictive sentences (*Estimate* = 0.354, *SE* = 0.057, $t = 6.17$, $p < .0001$). Finally, the quadratic term shows a significantly steeper curve (*Estimate* = 0.188, *SE* = 0.056, $t = 3.36$, $p = .0007$).

The main effect of condition from verb onset to the observed asymptote did not converge past the linear model ($\chi^2(1) = 7.01$, $p < .009$). There was a significant effect of condition on the intercept time term (*Estimate* = 0.027, *SE* = 0.011, $t = 2.47$, $p < .013$), and on the linear time term (*Estimate* = 0.480, *SE* = 0.073, $t = 6.59$, $p < .0001$). These results indicate that controls produced significantly more fixations on the target in the restrictive compared to non-restrictive sentences during the prediction period, and this remains true for the remainder of the trial. The full fixed effect parameter estimates can be found in Table 3, with the behavioural data illustrated in Figure 3.

Persons with Parkinson Disease and controls. The interaction of condition by group was analyzed using a second-order (quadratic) orthogonal polynomial with fixed effects of condition (restrictive vs. non-restrictive) and group (PwPD vs. controls) on all time terms, and random effects of participants and participant-by-condition on all time terms. During the prediction time-window, the data were best fit when the fixed effects were added to the quadratic term ($\chi^2(1) = 24.84$, $p < .0001$). In terms of the fixed effect parameter estimates of the quadratic model for the interaction, no significant differences were found between groups ($p > .3$ for all time terms). Therefore, there is no evidence of differential prediction for PwPD and controls. This lack of a difference is clear in the data shown in Figure 3.

The pattern remained when the interaction was tested using data from the longer time-window. The data were best fit when the fixed effects were added to the cubic term ($\chi^2(1) = 135.25$, $p < .0001$). The estimated parameters of the cubic model indicate no interaction between group and condition (all time terms, $p > .09$). This indicates that PwPD and controls did not differ on target fixation proportions during the prediction period or throughout the entire trial post verb onset. The full fixed effect parameter estimates can be found in Table 4, with the behavioural data illustrated in Figure 3.

Target and Distractor Objects

Persons with Parkinson Disease. For the prediction time-window, the interaction of object and condition was analyzed using a second-order (quadratic) orthogonal polynomial. The fixed effects of object (target vs. the average of the three distractors) and condition (restrictive vs. non-restrictive) with participant, participant-by-object, and participant-by-condition random effects were added on all time terms. The data were best fit by a model that included the quadratic term ($\chi^2(1) = 47.57$, $p < .0001$). The interaction parameter estimates of the quadratic model demonstrate a significant effect on all time terms ($p < .002$) in the prediction period, suggesting differences in the time course of the proportions of fixations on the objects given the condition.

The pattern changed when the interaction was tested using data from the verb onset to asymptote time-window. The data were best fit when the fixed effects were

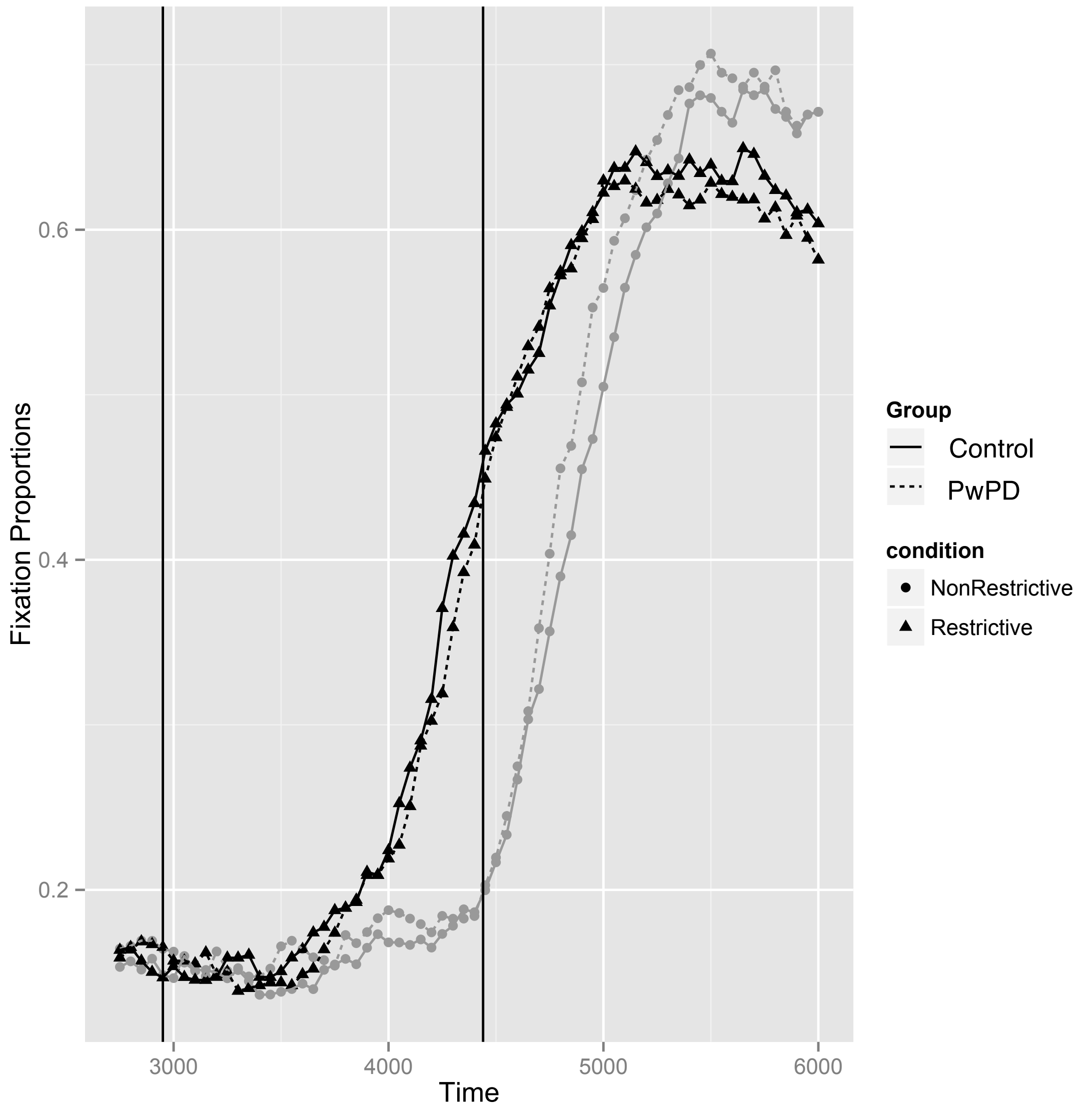

Figure 3. The average proportion of looks to the target in the restrictive and non restrictive conditions for PwPD and Controls. The start of the graph is at the verb onset. The first vertical line denotes verb onset plus 200 ms (2950 ms) and the second vertical line denotes noun onset plus 200 ms (4440 ms), and time scale continues until asymptote.

Table 2. Condition GCA results for restrictive and non-restrictive sentences in PwPD. The left section shows the quadratic model estimates for the condition effect for the prediction period, while the right section shows the cubic model estimates for the post-prediction period.

	Prediction Period				Post-Prediction Period			
	Estimate	*SE*	*t*	*p*	Estimate	*SE*	*t*	*p*
Intercept	0.038	0.015	2.53	.011	0.031	0.012	2.53	.011
Linear	0.298	0.053	5.58	< .0001	-0.122	0.096	-1.27	.204
Quadratic	0.212	0.041	5.20	< .0001	-0.539	0.061	-8.85	< .0001
Cubic	-	-	-	-	-0.147	0.023	-6.55	< .0001

Table 3. Condition GCA results for restrictive and non-restrictive sentences in controls. The left section shows the quadratic model estimates for the condition effect for the prediction period, while the right section shows the linear model estimates (no convergence greater than linear) for the post-prediction period.

	Prediction Period				Post-Prediction Period			
	Estimate	*SE*	*t*	*p*	Estimate	*SE*	*t*	*p*
Intercept	0.058	0.015	3.82	< .0001	0.027	0.011	2.47	.013
Linear	0.354	0.057	6.17	< .0001	0.480	0.073	6.59	< .0001
Quadratic	0.188	0.056	3.36	.0007	-	-	-	-

Table 4. GCA results for the interaction between group (PwPD vs. controls) and condition (restrictive vs. non-restrictive). The left section shows the quadratic model estimates for the interaction for the prediction period, while the right section shows the cubic model estimates for the post-prediction period.

	Prediction Period				Post-Prediction Period			
	Estimate	*SE*	*t*	*p*	Estimate	*SE*	*t*	*p*
Intercept	-0.019	0.021	-0.93	.352	-0.028	0.016	-1.67	.094
Linear	-0.055	0.079	0.07	.481	-0.089	0.127	-0.71	.479
Quadratic	0.023	0.071	0.33	.739	0.056	0.081	0.69	.487
Cubic	-	-	-	-	0.045	0.032	1.41	.158

added to the cubic term ($\chi^2(1) = 1378.62$, $p < .0001$). The parameter estimates of the cubic model indicate no interaction between group and condition on overall average fixation proportion ($p = .11$) and slope ($p = .49$) time terms. However, an interaction existed on the quadratic (*Estimate = 0.665* , *SE* = 0.028, $t = 23.12$, $p < .0001$), and cubic terms (*Estimate = 0.195* , *SE* = 0.028, $t = 6.79$, $p < .0001$), indicating a later rising and longer lasting effect for target objects in non-restrictive compared to restrictive sentences. The full fixed effect parameter estimates can be found in Table 5, with the behavioural data illustrated in Figure 4.

Controls. The same analyses were conducted on the data from control participants. As with PwPD, the data were best fit when the fixed effect of condition was added to the quadratic term ($\chi^2(1) = 35.84$, $p < .0001$). The interaction parameter estimates of the quadratic model demonstrate a significant effect on all time terms ($p < .0001$) during the prediction period, suggesting that controls also show differences in the time course of fixations to objects given the condition (restrictive relative to non-restrictive).

The pattern changed when the interaction was tested using data from the verb onset to asymptote time-window. The data were best fit when the fixed effects were added to the cubic term ($\chi^2(1) = 1459.11$, $p < .0001$). The parameter estimates of the cubic model indicate a significant interaction on the overall average fixation proportion to the target compared to distractors given the condition ($p = .0117$). The slope did not differ ($p = .49$). However, a significant interaction was found on the quadratic and cubic terms ($p < .0001$ in both cases), indicating a later rising and longer lasting effect for target objects in non-restrictive compared to restrictive sentences. The post-prediction curve steepness is comparable to PwPD data. The full fixed effect parameter estimates can be found in Table 6 for the prediction and post-prediction periods, with behavioural data illustrated in Figure 5.

Directive Trials

Persons with Parkinson Disease and controls. The effect of group was analyzed using a third-order (cubic) orthogonal polynomial with fixed effects of group (PwPD vs. controls), and participant random effects on all time terms. The time window of analysis was 200 ms following noun onset to the observed asymptote. Fixation proportions to the target object was the dependent variable. The data were best fit when the fixed effect of group was added to the quadratic term ($\chi^2(1) = 6.47$, $p < .02$). The fixed effect parameter

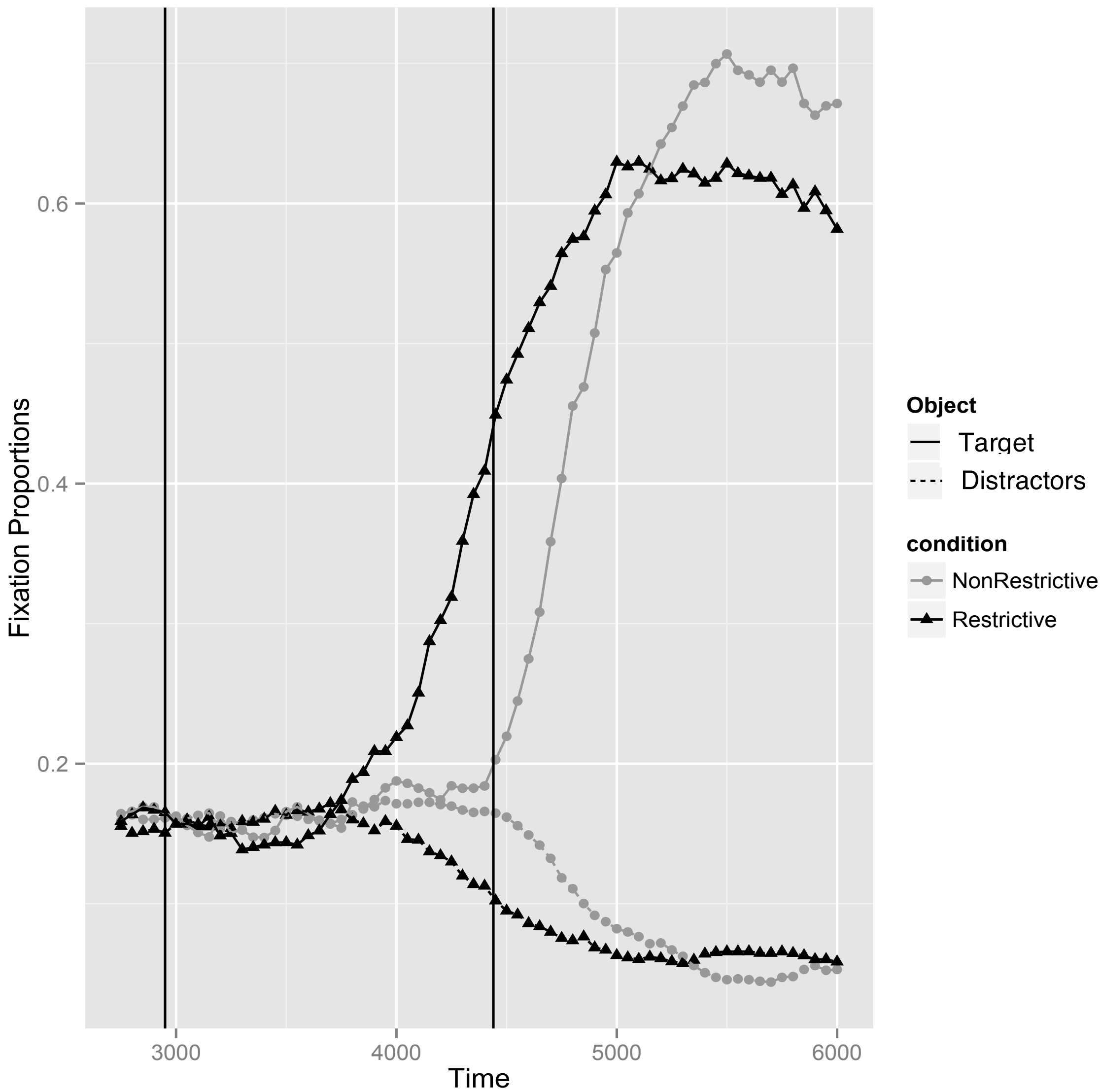

Figure 4. The average proportion of looks to the target versus distractors (averaged) in the restrictive and non-restrictive conditions for PwPD. The start of the graph is at the verb onset. The first vertical line denotes verb onset plus 200 ms (2950 ms) and the second vertical line denotes noun onset plus 200 ms (4440 ms), and time scale continues until asymptote.

Table 5. GCA results for the interaction between object (target vs. distractors [averaged]) and condition (restrictive vs. non-restrictive) for PwPD. The left section shows the quadratic model estimates for the interaction for the prediction period, while the right section shows the cubic model estimates for the post-prediction period.

	Prediction Period				Post-Prediction Period			
	Estimate	*SE*	*t*	*p*	Estimate	*SE*	*t*	*p*
Intercept	-0.051	0.015	-3.26	.0011	-0.042	0.027	-1.59	.11
Linear	-0.374	0.064	-5.80	< .0001	0.145	0.210	0.69	.49
Quadratic	-0.273	0.054	-5.08	< .0001	0.665	0.028	23.12	< .0001
Cubic	-	-	-	-	0.195	0.028	6.79	< .0001

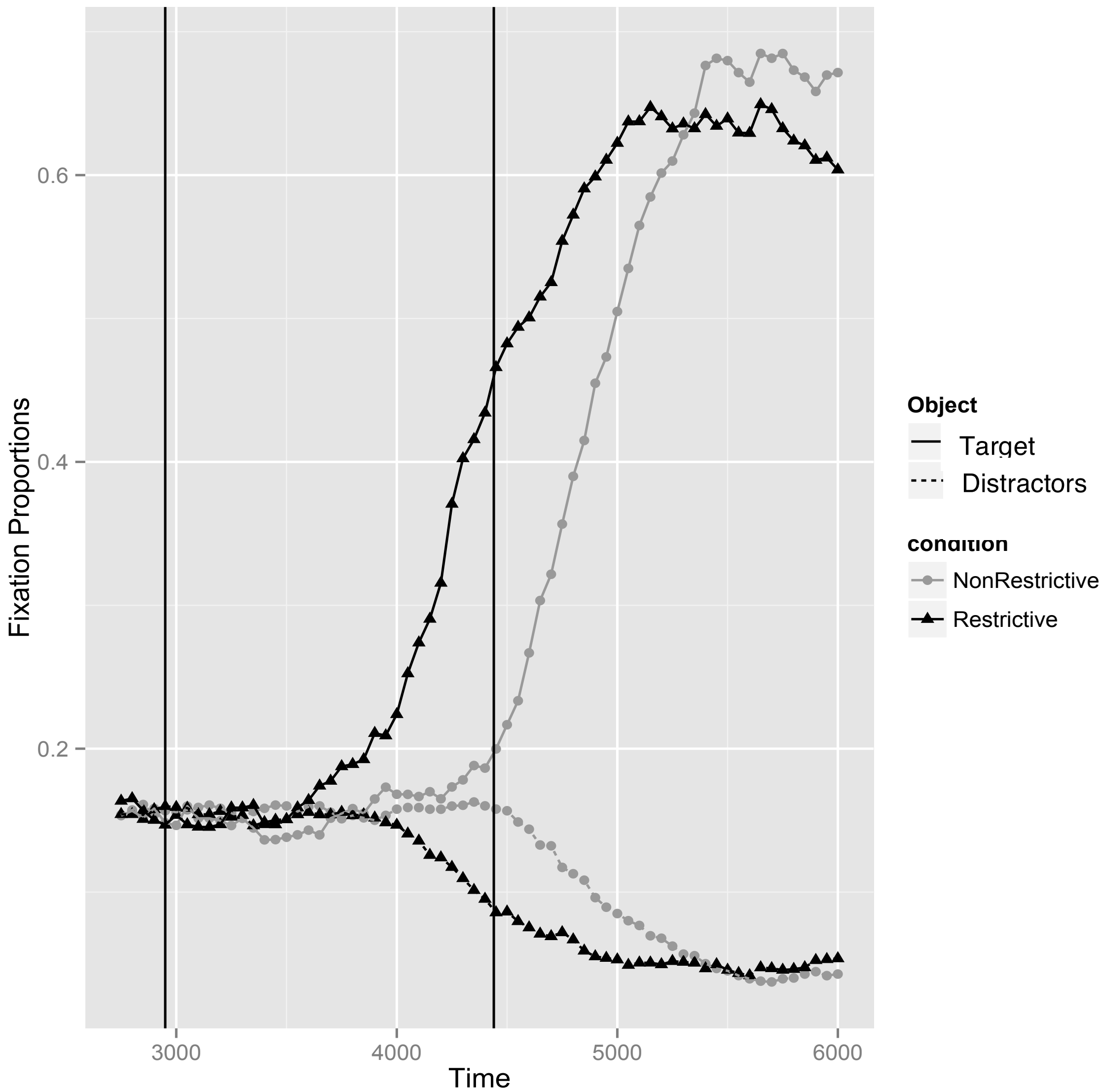

Figure 5. The average proportion of looks to the target versus distractors (averaged) in the restrictive and non-restrictive conditions for controls. The start of the graph is at the verb onset. The first vertical line denotes verb onset plus 200 ms (2950 ms) and the second vertical line denotes noun onset plus 200 ms (4440 ms), and time scale continues until asymptote.

Table 6. GCA results for the interaction between object (target vs. distractors [averaged]) and condition (restrictive vs. non-restrictive) for controls. The left section shows the quadratic model estimates for the interaction for the prediction period, while the right section shows the cubic model estimates for the post-prediction period.

	Prediction Period				Post-Prediction Period			
	Estimate	*SE*	*t*	*p*	Estimate	*SE*	*t*	*p*
Intercept	-0.071	0.016	-4.22	< .0001	-0.075	0.029	-2.52	.0117
Linear	-0.432	0.065	-6.60	< .0001	0.022	0.226	0.09	.9228
Quadratic	-0.243	0.061	-3.96	< .0001	0.736	0.094	7.79	< .0001
Cubic	-	-	-	-	0.256	0.025	10.25	< .0001

estimates of the quadratic model show a significant effect of group only on the quadratic time term (*Estimate* = -0.242, *SE* = 0.08, t = -2.73, p = .0063). This suggests a significantly earlier rising curve for fixation proportions to target images for PwPD compared to controls. However, overall PwPD and controls did not differ on their overall average fixation proportion or average slope to the target. The full set of statistics can be found in Table 7. The behavioural data are illustrated in Figure 6.

Target and Distractor Objects

Persons with Parkinson Disease. The effect of object was analyzed using a third-order (cubic) orthogonal polynomial with fixed effects of object (target vs. distractors), and participant random effects on all time terms. The time-window was the same as in the previous analysis. The data were best fit when the fixed effect of object was added to the cubic term ($\chi^2(1) = 774.175$, $p < .0001$). The fixed effect parameter estimates of the cubic model were significant for all time terms ($p < .0001$). Thus, PwPD were more likely to fixate on the target than on the distractor images in directive sentences. The full set of statistics can be found in Table 8, and the behavioural data are illustrated in Figure 6.

Controls. The same model structure was used to analyze the effect of object for the control group. As with PwPD, the data were best fit when the fixed effect of object was added to the cubic term ($\chi^2(1) = 805.94$, $p < .0001$). The fixed effect parameter estimates of the cubic model showed comparable results to PwPD. All time terms for the object effect were significant ($p < .0001$). Similar to PwPD, controls were more likely to fixate on the target than on the distractor images in directive sentences. The full set of statistics can be found in Table 8, and the behavioural data are illustrated in Figure 6.

Persons with Parkinson Disease and controls. The group by object interaction was analyzed using a third-order (cubic) orthogonal polynomial with fixed effects of group and object on all time terms, and random effects of subject (all time terms) and subject-by-object (up to quadratic). The data were best fit when the fixed effect of object was added to the cubic term, ($\chi^2(1) = 1590.12$, $p < .0001$). The fixed effect parameter estimates of the cubic model show a significant interaction on the quadratic (*Estimate =0.171* , *SE* = 0.076, $t = 2.24$, $p < .03$) and cubic terms (*Estimate =-0.119* , *SE* = 0.019, $t = -6.22$, $p < .0001$). These results indicate that target compared to distractor fixation proportions diverge earlier for PwPD than for controls. Additionally, the difference between target and distractor fixations decreases earlier for PwPD compared to controls, indicating that PwPD significantly decrease looks to the target compared to controls closer to the noun offset. The full fixed effect parameter estimates can be found in Table 9.

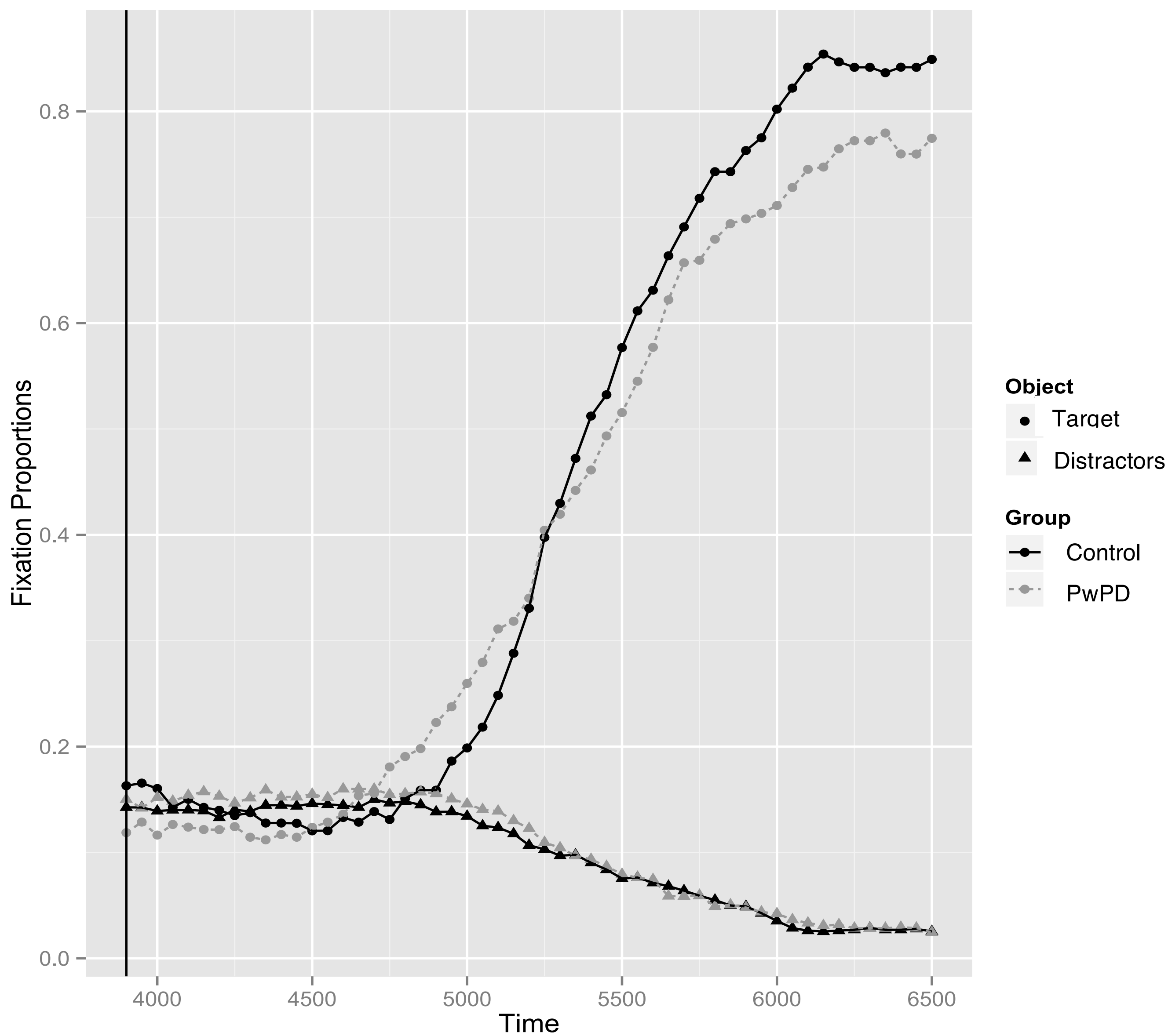

Figure 6. The average proportion of looks to the target versus distractors (averaged) in the directive condition for PwPD and controls. The start of the graph is at the verb onset, noun onset is denoted at 3900 ms, and time scale continues until asymptote.

Table 7. Group (PwPD compared to controls) GCA results for the directive condition ("*Look at the flower*"). The estimates are from the quadratic model for the noun onset to the observed asymptote time window.

	PwPD vs. Controls			
	Estimate	*SE*	*t*	*p*
Intercept	0.007	0.026	0.26	.7903
Linear	0.046	0.11	0.42	.6749
Quadratic	-0.242	0.08	-2.73	.0063

Table 8. Object (target compared to distractor) GCA results for the directive condition ("*Look at the flower*"). The estimates are for the noun onset to the observed asymptote time window. The left section shows the cubic model estimates for the object effect for PwPD, the right section is for matched controls.

	PwPD				Controls			
	Estimate	*SE*	*t*	*p*	Estimate	*SE*	*t*	*p*
Intercept	-0.303	0.017	-17.19	< .0001	-0.335	0.021	-15.60	< .0001
Linear	-2.171	0.111	-19.51	< .0001	-2.339	0.135	-17.34	< .0001
Quadratic	-0.297	0.064	-4.60	< .0001	-0.468	0.075	-6.22	< .0001
Cubic	0.477	0.015	30.77	< .0001	0.596	0.018	31.53	< .0001

Table 9. GCA results for the interaction between group (PwPD vs. controls) and object (target vs. distractor) for the directive condition ("*Look at the flower*"). The estimates are from the cubic model for the noun onset to the observed asymptote time window.

	PwPD vs. Controls			
	Estimate	*SE*	*t*	*p*
Intercept	0.032	0.022	1.49	.135
Linear	0.168	0.142	1.18	.236
Quadratic	0.171	0.076	2.24	.025
Cubic	-0.119	0.019	-6.22	< .0001

Discussion

The current study took a novel approach to investigating sentence comprehension impairments in PD. I tested the hypothesis that PwPD may have issues with implicit prediction in language comprehension. Rather than focusing on syntactic processing, my hypothesis was motivated by theories of implicit semantic-based prediction that posit a central role for anticipation in sentence comprehension (Altmann & Mirkovic, 2009; Federmeier, 2007; Van Petten & Luka, 2012). My study was motivated in part by previous demonstrations that PwPD have issues with prediction and probabilistic processing in non-linguistic tasks such as the Iowa Gambling and weather prediction tasks. Furthermore, there are several studies showing that PwPD have impairments in verb processing (Boulenger et al., 2008; Fernandino et al., 2012; Herrera et al., 2012). This is important in the context of implicit prediction because verbs often carry rich thematic information which highly constrains the upcoming linguistic input. Indeed, some researchers have speculated that PD sentence comprehension deficits may be due, in part, to thematic role processing (Angwin et al., 2006, 2007). In this experiment, I tested specifically prediction of patients (e.g., *car*) from verbs (e.g., *drive*) using the visual world paradigm. In the current study, PD participants' prediction of a patient from a verb, as measured by their predictive eye movements, did not differ from controls. This suggests that fundamental prediction processes in a linguistic task remain intact, at least during comprehension of short syntactically simple sentences that are accompanied by relevant visual cues.

Surprising Results

These results are surprising for a few reasons. First, despite evidence demonstrating that PwPD are impaired at verb processing, they showed normal prediction of patients from verbs denoting actions. The literature on PD verb impairments is somewhat mixed (Kemmerer, Miller, Macpherson, Huber, & Tanel, 2013). Some studies of verb comprehension have shown deficits in PwPD (Fernandino et al., 2013, Peran et al., 2003), whereas others have not. It appears that the most consistent evidence of verb processing impairments has been found with production tasks in which PwPD are required to name a depicted action (Bertella et al., 2002; Cotelli et al., 2007; Rodriguez-Ferreiro, Menendez, Ribacoba, & Cuetos, 2009), or in which they are required to generate a verb given a noun (Crescentini, Mondolo, Biasutti, & Shallice, 2008; Peran et al., 2009). However, in the present study, participants did not produce verbs.

Due to the nature of my task, perhaps no group difference was found because participants were not predicting verbs. Rather, they predicted the patient noun following the verb. The clearest evidence of verb processing deficits is found in studies in which PD generate verbs (Crescentini et al., 2008; Peran et al., 2009). Perhaps there are some parallels to these verb generation tasks in terms of predicting a verb from a context. Therefore, it possibly could be illuminating to design a study in which the target words are verbs. One could design such a study by using structures that allow for additional constraining information to be presented prior to a verb. For example, sentences could be used in which an agent and an instrument precede a verb (e.g., *The lumberjack used the axe to* ____). PD participants' prediction of a verb could be measured in an ERP or a reading time study. In this design, participants would have to access their semantic knowledge for *lumberjack* and *axe* to predict *chop* as the probable verb.

It has also been argued that action-verb comprehension deficits in PD occur for only certain types of verbs, primarily physical action verbs (Fernandino et al., 2012). For example, Herrera et al. (2012) found that PD participants made more errors in picture naming on verbs with greater motor content (e.g., *dig*) versus those with less motor content (e.g., *sleep*). Furthermore, Nguyen, Roberts, Orange, Jog, and McRae (2015) divided PwPD into those with greater upper versus lower limb motor impairments. They found that PD patients with greater upper limb impairment were slower in processing upper-limb versus lower-limb verbs, whereas patients with greater lower limb impairment performed similarly on both verb categories. These studies were motivated by findings suggesting co-activation of the basal ganglia and primary motor regions during action-verb semantic tasks, which has led researchers to propose that these areas work in synchrony to integrate motor-semantic information (Crosson et al., 2003). Assuming that processing of physical action verbs may be impaired, it is surprising that the PD participants could not only understand the meaning of the verbs in my study, but also use the meaning to predict a patient. In the current study, the restrictive verbs consisted of 16 upper-limb action verbs (e.g., She will light the candle), 9 whole-body action verbs (e.g., She will hunt the deer), 2 oral action verbs (e.g., She will taste the pie), 2 oral/upper action verbs (e.g., She will eat the pear), and 1 abstract verb (e.g., She will read the book). Given that these verbs are predominantly physical action verbs of high motor content, one would have suspected processing issues to be observed. Perhaps an avenue to address concerns whether implicit prediction of verbs differentiating in high versus low motor content for both upper and lower limb recruitment (Nguyen et al., 2015) would show deficits in PwPD based on their dominant limb impairment.

A second issue that arises from the current results is that PwPD demonstrate difficulties with non-linguistic prediction tasks, suggesting that a prediction deficit exists. However, PwPD performed like controls on my task, even though it required the use of predictive/probabilistic information. The weather prediction task is one example of a probabilistic learning task in which PwPD are impaired. Participants in such a task are not given any explicit information about the probabilistic nature of the cues and outcomes, but rather participants begin by guessing the outcome (sun or rain). In Shohamy et al. (2004), participants were tested on 200-trial sessions over 3 consecutive days. The measure of interest was the improvement on the percentage of correct trials seen across each day of testing. This task recruits implicit probabilistic learning, however once the patterns are acquired, it depends on explicit prediction and explicit responses. One potential explanation as to why I did not find differences between PwPD and controls is that the non-linguistic predictive tasks used previously tend to involve learning of new probabilistic information and explicit, thoughtful prediction responses. However, the implicit prediction involved in language comprehension depends on previously learned probabilistic information. In addition, the present study did not require a verbal response, unlike these other prediction tasks. Rather, I measured prediction based on automatic, non-conscious eye movements. A potential linguistically-based study that could test probabilistic language learning followed by prediction would be to expose participants to new non-existing verb and/or noun concepts and contingencies among them. A learning task could be implemented that is similar in nature to that of Shohamy et al. (2004), with a testing phase that uses similar eyetracking measures as the present study.

An additional factor to consider is that PwPD have motor issues. My study involved measuring participants automatic eye movements to various objects on a screen. It is important to note that the oculomotor circuit (controlling saccadic eye movements) connects the basal ganglia to the thalamus and cortex (Alexander, Delong, & Strick, 1986). PD patients have been identified with visuoperceptual impairments (Levin et al., 1991; Taylor, Saint-Cyr, & Lang, 1986), related to object tracking and antisaccades (i.e., looking away from a stimulus). Matsumoto et al. (2011) investigated these impairments by measuring eye movements of PwPD during visual scene exploration. They showed that as scene complexity increases, the eye movement patterns of PwPD become more similar to controls. In my study, although complex scenes were not presented, there were four line drawings of objects on the screen, thus providing a relatively complex visual stimulus. In studies that have investigated the language impairments in PD, many have used sentence-picture matching paradigms. Grossman et al. (1993) suggested that the deficit in sentence-picture matching is unrelated to visuoperceptuospatial deficits observed in PD. This conclusion is supported by Matsumoto et al. (2011). Importantly, to verify that no major oculomotor issues were present in any of my participants (PwPD and controls), a neuro-opthomologist performed an eye movement screening. Apparently, this screening was successful because PwPD performed comparably to controls. Even though eyetracking methods are common in language comprehension research, the visual world paradigm that I used has been used only once to study language impairments in PwPD (Hochstadt, 2009). This is presumably due to concerns that oculomotor deficits might make any differences between PwPD and controls difficult to interpret. Hochstadt (2009) investigated impairments in syntax, and found that PD participants were impaired in processing sentences such as “The queen was kicking the cook who was fat.” Thus, in terms of methodological issues, my study provides additional support that the visual world eyetracking paradigm can be used to study language comprehension in PwPD.

Finally, PwPD have presented with issues in activating word meaning. Angwin et al. (2006) used a semantic priming task whereby two prime words were presented prior to a target at stimulus onset asynchronies (SOA: the time between the onset of one stimulus and the onset of the next) of 250 ms and 1,200 ms. Primes were either both related to the target (*summer* - *snow* - *winter*), related-unrelated (*summer* - *hill* - *winter*), unrelated-related (*island* - *snow* - *winter*), or both unrelated to target (*island* - *hill* - *winter*). PD participants 'on' medication demonstrated comparable priming patterns to controls for all related conditions for both short and long SOAs. In contrast, when performing the task 'off' dopaminergic medication, PD participants showed different priming effects at the 250 ms SOA, specifically decreased priming effects in the related-unrelated condition. This research was driven by the work suggesting the influence the striatum has on information processing speed (Harrington, Haaland, & Hermanowicz, 1998; Schubotz, Friederici, & von Cramon, 2000). The present research also can be viewed as measuring the speed with which PwPD can activate and use semantic knowledge. One potential explanation for the difference in results between Angwin et al. (2006, 2007) and the current study is that PwPD were not tested 'off' dopaminergic medication in my study. For this reason, a prediction deficit in sentence processing may not have been elicited due to supplementation of dopamine levels. Therefore, my findings may be consistent with Angwin et al. (2006) in the sense that PwPD with dopamine supplementation were able to perform the semantic prediction task comparably to controls.

Although investigating language impairments 'on' and 'off' dopaminergic medication is important to consider, there are a few reasons as to why I chose to test PD participants only when they were optimally medicated. First, some studies investigating language impairments in PwPD have found deficits in verb processing (Fernandino et al. 2012; Herrera, Rodriguez-Ferreiro & Cuetos, 2012), and in sentence processing (Angwin et al., 2006; Hochstadt et al., 2006; Longworth et al., 2005; Lee et al., 2003), regardless of whether they were 'on' or 'off' their medication. This is the same trend observed in studies of prediction in nonlinguistic tasks in PwPD. Finally, in terms of clinical applications, PwPD do take their medication when performing everyday tasks outside of clinical or experimental settings. Therefore, it is important to understand their cognitive abilities when they are on the normal medication.

Other Potential Explanations

Because this was the first investigation of this type, I used syntactically and semantically simple sentences. The semantic cues for prediction were based on the verb alone. In typical conversation and reading, language is much more complex. It is possible that when cues need to be combined and are possibly competing, as is the case in more natural everyday language, impaired prediction might be observed. In fact, this is what I am planning to test in my next study. Borovsky et al. (2012) used a visual-world paradigm that requires the integration of multiple cues to arrive at the correct target. In comparison to the current experiment, prediction would be based on the integration of the agent and verb versus solely on the verb. In Borovsky et al. (2012), they presented sentences such as, "*The pirate hides the treasure",* while simultaneously presenting four pictures: the target (e.g., treasure), an agent-related distractor (e.g., ship), an action-related distractor (e.g., bone), and an unrelated distractor (e.g., cat). Thus, two of the pictures are related to *pirate* (treasure and ship), and two are related to *hide* (bone and treasure). To anticipate the upcoming patient, a listener must activate and integrate *pirate* and *hide.* Listeners are required to draw upon real world knowledge and integrate information from both cues to arrive at the object that a pirate would most likely hide (i.e., treasure versus bone). With this additional complexity of the task, prediction deficits during sentence processing may be elicited in this population.

Another factor to consider is that in visual-world paradigm experiments, pictures are provided, thus giving an additional cue to participants. In addition, there was a preview period of two seconds, so that participants were able to familiarize themselves with the objects on the screen and their positions (this is standard practice in visual world studies). Much of every day conversation and written text is about topics that have nothing to do with co-present objects. Thus, because this type of contextual information may not be present, the relevant context is the product of the discourse and the integration of the comprehender's background world knowledge. Therefore, it is possible that impaired prediction might be observed when language is comprehended in the absence of relevant visual cues. This could be tested using reading time measures or ERPs. For example, Kutas and Federmeier (2000) studied word expectancy in language comprehension by analyzing the N400. They presented short two-sentence discourses such as, *"They wanted to make the hotel look more like a tropical resort. So along the driveway they planted rows of...tulips/pines/palms".* To properly anticipate the correct target *palms*, the reader must activate thematic information and integrate multiple cues (Kutas & Federmeier, 2000). Presenting two-sentence discourses to PwPD may introduce ambiguities in interpretation because, although the syntax need not be complex, it may be the case that integration of material across multiple sentences taxes working memory. However, such an experiment would more closely relate to the complexity of everyday language.

Conclusion

At this point, a number of researchers have argued that sentence comprehension impairments in PwPD are due to deficits in syntactic computations, working memory, and/or executive functioning. My study did not tax any of these prior cognitive functions. Sentences were syntactically simple, and the identical structure was repeated throughout the experiment. Sentences were short, and therefore performance was not influenced by any potential limitations in working memory or executive functioning. Fixation proportions were the dependent variable, so there were no explicit responses that potentially might depend on working memory or executive functioning. In summary, it might be the case that implicit linguistic prediction is not impaired in PwPD. That is, sentence comprehension deficits may be due to issues with syntactic computations, working memory, and/or executive functioning. On the other hand, further research in which such prediction depends on the integration of more complex linguistic cues is required before firm conclusions can be drawn about its potential role in PD sentence comprehension deficits.

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Appendix A

Stimuli used in part one.
All sentences followed the same structure, "*She will* [verb] *the* [noun]".

Sentence	Target	Distractor 1	Distractor 2	Distractor 3
Non-restrictive				
bring	candle	doll	hat	guitar
describe	flower	banana	horse	gun
draw	bus	window	present	doll
examine	deer	pool	car	bow
eye	bow	ladder	pear	watch
forget	ladder	bow	watch	pipe
gaze	pool	horse	car	whistle
get	banana	candle	hat	bow
hate	boat	dog	pool	kite
hold	hat	flower	book	pie
imagine	gun	fish	doll	boat
keep	present	watch	baby	fish
leave	flashlight	gun	pie	banana
like	watch	guitar	shirt	car
look	pear	dog	whistle	hat
move	towel	kite	flashlight	pipe
need	shirt	baby	horse	gun
notice	pipe	book	dog	window
observe	window	kite	pipe	ladder
paint	dog	pool	banana	boat
picture	guitar	bus	deer	flower
point to	horse	window	flashlight	towel
recognize	whistle	book	present	baby
remember	doll	pie	fish	shirt
see	book	whistle	deer	flashlight
sketch	kite	guitar	bus	pear
spot	baby	candle	towel	deer
stare	fish	candle	present	bus
study	car	flower	pear	boat
take	pie	shirt	towel	ladder
Restrictive				
blow	whistle	shirt	ladder	horse
button	shirt	pipe	bus	fish
climb	ladder	hat	pie	bow
close	window	flower	dog	gun
cradle	doll	window	horse	bus
drive	car	hat	banana	flashlight
eat	pear	boat	doll	car
fire	gun	towel	hat	baby
fly	kite	fish	book	gun

fold	towel	guitar	whistle	pool
fry	fish	pipe	ladder	book
hunt	deer	watch	candle	banana
light	candle	bow	present	fish
nurse	baby	kite	whistle	pear
peel	banana	horse	doll	shirt
play	guitar	towel	shirt	ladder
pluck	flower	window	bus	candle
read	book	pear	kite	doll
ride	bus	guitar	watch	pie
saddle	horse	banana	flower	present
sail	boat	pear	watch	deer
smoke	pipe	baby	guitar	towel
swim in	pool	present	book	kite
take off	hat	candle	dog	pool
taste	pie	dog	boat	window
tie	bow	gun	pool	car
turn off	flashlight	bow	deer	whistle
unwrap	present	deer	flashlight	car
walk	dog	flashlight	pie	boat
wind	watch	flower	pipe	baby

Appendix B

Stimuli used for part two. All sentences followed the structure, "*Look at the* [noun]".

Target	**Distractor 1**	**Distractor 2**	**Distractor 3**
balloon	drum	helmet	log
rope	bathtub	clock	mailbox
slide	strawberry	drum	helmet
clock	fan	tape	shovel
drum	log	brush	tractor
bathtub	dress	violin	slide
lamp	crib	strawberry	feather
squirrel	rollerskate	belt	fan
fan	mailbox	slide	tractor
log	scarf	fan	tape
scarf	violin	tractor	rollerskate
feather	drum	log	balloon
dress	tape	mailbox	clock
brush	shovel	lamp	pumpkin
pumpkin	balloon	helmet	violin
shovel	pumpkin	bathtub	lamp
mailbox	crib	belt	rope
strawberry	tractor	dress	mailbox
rollerskate	helmet	squirrel	brush
crib	tape	shovel	dress

Curriculum Vitae

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