

Review Article

Verb Generation in Parkinson's Disease Patients

Jie Yang*

ARC Center of Excellence in Cognition and its Disorders, Macquarie University, Australia

*Corresponding author: Jie Yang, ARC Center of Excellence in Cognition and its Disorders, Macquarie University, NSW 2109, Australia

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Abstract

Previous research has shown that people with Parkinson's disease (PD) have deficits in verb processing. However, the interpretation about the deficits is still in controversy. Motor theory suggests that the deficits in PD patients reflect the role of basal ganglia and frontal regions in the semantic representation of verbs. Grammatical view suggests that the deficits in PD patients indicate that basal ganglia and frontal regions play roles in the grammatical processing of verbs. Executive control view claims that PD patients show deficits in verb processing because basal ganglia and frontal regions are involved in executive control functions that are not specific to language processing. This paper reviews current findings about verb generation in PD patients, and discusses the evidence that supports different views and the possible confounding factors that may influence the interpretations.

Keywords: Parkinson's disease; Verb generation; Basal ganglia; Embodied cognition

Introduction

Parkinson's disease (PD) is a neurodegenerative disorder characterized by motor dysfunctions and cognitive deficits related to the death of dopamine-generating cells in the substantia nigra and functional impairment of the basal ganglia [1]. Previous studies have found that PD can affect frontal areas as well as other cortical and subcortical areas involved in action organization and motor control [2]. PD patients also indicate deficits in verb comprehension [3-6] and production [7-16] as compared with noun processing.

Since PD patients indicate verb specific deficits, and the disease mainly affects brain regions related to motor control, research about verb processing in PD patients is supposed to provide evidence for noun/verb distinction in the brain. So far several hypotheses have been claimed. The first hypothesis claims that nouns and verbs are different in their semantic information, i.e. nouns refer to objects, and verbs refer to actions. The verb processing deficits in PD patients suggest that the motor system, including frontal areas and basal ganglia, plays an important role in the semantic representation of verbs. This hypothesis is based on theories of embodied cognition, which claim that the sensory-motor system contributes to the representation of conceptual knowledge [17-19]. The second hypothesis is that nouns and verbs are different in their grammatical category, i.e. nouns often take the role of arguments in sentences (e.g., subject and object), whereas verbs take the role of connecting and organizing these arguments. Thus, the verb processing deficits in PD patients suggest that the frontal areas and basal ganglia play important roles in the grammatical processing of verbs. The third hypothesis is that verb processing requires more executive control than noun processing. This might relate to grammatical differences between verbs and nouns: verbs can have various complex argument structures, so the processing might involve more selection and inhibition as compared with noun processing. According to this hypothesis, the verb processing deficits in PD patients may reflect the impairment of executive control, and they are not language specific.

To test the above hypothesis, and (more importantly) to clarify the role of frontal areas and basal ganglia in verb processing, researchers have conducted numerous studies on verb processing in PD patients. The current review focuses on the research of verb generation in PD patients, mainly because evidence in this area is ample yet quite inconsistent. Findings from relevant studies were reviewed, and then interpretations of these findings were discussed.

Evidence of Verb Generation in PD Patients

Crescentini et al. (2008) investigated verb generation in people with mild to moderate PD. These patients' motor disability was evaluated, and they were screened for not having dementia and depression. All participants were on anti parkinsonian medication, and were tested in the "on" medication state. A control group of right-handed Italian participants were recruited and they were closely matched to the PD patients for age, sex, education, and mental state. The goal of the study is to examine whether basal ganglia plays an important role in verb generation that requires semantic retrieval and the inhibition of competing alternatives. PD patients and control group performed verb and noun production tasks on the basis of presented nouns. A key manipulation of the study is that the presented nouns were divided into three groups based on their selection of an association with verbs. Nouns with low selection- strong association (e.g., pen) have low requirement for verb selection (e.g., it is easy to retrieve the verb to write based on the noun), and have strong association with the selected verbs (e.g., to write and pen are strongly associated). Nouns with high selection - strong association (e.g., lamp) have high requirement for verb selection (e.g., it is hard to retrieve the verb to turn on based on the noun, because there are many alternatives), and have strong association with the selected verbs (e.g., to turn on and lamp are strongly associated). Nouns with high selection - weak association (e.g., sword) have high requirement for verb selection (e.g., it is hard to retrieve the verb to fight based on the noun, because there are many possibilities), and have weak association with the selected verbs (e.g., to fight and sword are weakly associated). Results showed that during verb production, PD patients

had lower accuracy and longer reaction time as compared with the control group. Furthermore, PD patients had lower accuracy and longer reaction time in the high selection weak association condition than in other two conditions. The analysis of error type showed that most errors PD patients made were grammatical errors. The authors suggest that PD patients have deficits in controlling semantic retrieval and semantic inhibition, and that basal ganglia plays an important role in the general executive control functions rather than the routine semantic processes during lexical retrieval.

Macoir et al. (2013) examined PD patients' ability in verb production. These patients performed conjugation tasks on regular verbs and irregular verbs. Results showed that compared with healthy patients, PD patients had lower performance, but there was no difference between regular and irregular verbs. The authors claim that basal ganglia are involved in language processing but not play a specific role in verb production.

Cotelli et al. (2007) investigated action and object naming abilities in PD patients. All patients were assessed for global cognitive decline (Mini-Mental State Examination, MMSE), non-verbal reasoning, verbal fluency, memory, attention, and execution control function. A control group of healthy adults matched on age and education was included. The authors focused on how the degree of manipulation (i.e. whether the named action requires fine hand movements) influences naming performance. For instance, actions to cut and to squeeze require fine hand movements, whereas action to fly does not require hand movements. The authors found that in PD participants, no significant differences between naming manipulable actions and naming non-manipulable actions. This result implies that PD does not influence the retrieval of specific semantic features during action naming. The authors suggest that in PD patients, dopamine depletion in the striatum can disrupt the function of sub cortical prefrontal networks and cause severe impairments in verb retrieval. Several interpretations can explain the results. For instance, the verb retrieval deficit may be because of the impairment of executive control (i.e. PD patients are bad at semantic retrieval and inhibition), or it can be caused by specific language dysfunction. Although PD patients did not show manipulability specific difficulty in verb production and it implies that the verb retrieval deficit might not be specific to semantic processing, the authors suggest that this null effect might relate to the absence of an impairment of simple limb movement in those PD patients.

J. Rodríguez-Ferreiro et al. (2009) explored the impairment of action and object naming in PD patients. Three participant groups were recruited, including 28 PD patients without dementia, 28 patients diagnosed as probable Alzheimer's disease (AD), and 28 healthy seniors as controls. The three groups were matched on age and education, but PD patients and healthy seniors have higher scores than AD patients. The authors hypothesized that due to the generalized degradation of semantic knowledge in PD patients, they will show deficits in verb and noun generation. The results showed that compared with control group, PD patients showed a significant impairment in both naming tasks. Furthermore, they indicated a significant impairment in naming actions than in naming objects. The authors suggest that verb generation is grounded in the neural networks underpinning motor control.

Herrera et al. (2012) tested whether lesion in motor cortices causes verb-relative impairment. A group of PD patients and a group of healthy seniors matched on age, education, and MMSE scores were recruited. All PD patients were taking anti parkinsonian medication and were "on" phase. PD patients and the control group performed a verb naming task based on pictures that contain high motor content (e.g., to dig) and low motor content (e.g., to sleep). The authors predict that if the semantic features of verbs (i.e. motor content) influence PD patients' naming performance, a significant difference on naming would be found between the high and low motor content conditions. On the other hand, if grammatical features affect the naming performance in PD patients, no difference would be found between the high and low motor content conditions. The results showed that PD patients showed significantly lower performance in verbs with high motor content than in verbs with low motor content. However, such a difference was not observed in the control group. The authors claimed that the verb-relative deficit in PD patients has a semantic origin. That is to say, brain regions involved in motor control functionally contribute to the semantic processing of verbs, and thus the degradation of dopaminergic pathways connecting to these motor regions causes deficits in the semantic processing of verbs [9].

Herrera et al. (2012) investigated the influence of on/off dopamine medication on verbal fluency. The aim of the study was to find how dopamine affects PD patients' performance in verbal fluency tasks, especially action fluency. Twenty non-demented PD patients and 20 controls matched on age, sex, age, and MMSE were recruited. All PD patients were taking anti parkinsonian medication, and they performed verbal fluency tasks twice ("on" and "off" dopamine medication). The authors found that PD patients in on and off medication generated different number of words in the phonological and action fluency tasks. In addition, compared with controls, PD patients with off medication produced fewer words in the phonological and action fluency tasks. Furthermore, the verbs produced by PD patients with off medication had higher frequency than the verbs generated by healthy controls. The authors suggest that dopamine affects the normal functioning within the lexico-semantic network of verbs [16].

Herrera and Cuetos (2012) further examined whether on/off dopamine medication in PD patients affects the processing of motor content during action naming. The study recruited a group of non-demented PD patients and a control group of healthy patients. Patients and healthy controls were matched on age, education, and MMSE. The PD patients participated in the experiment twice, once "on" phase, once "off" phase. All participants performed a verb naming task on 25 action pictures with high motor content and 25 pictures with low motor content. The results showed that the two PD patients showed longer RT on both types of pictures as compared with healthy controls, but only the PD off dopamine group showed significant longer RTs in the high motor content condition than in the low motor content condition. The authors claimed that PD patients deprived of dopamine had a selective deficit in naming pictures with high degree of motor content may be due to the relations between motor areas and verb semantic processing. In other words, motor areas functionally contribute to verb semantic representation, and dopamine medication can modulate verb processing through the influence on motor areas.

Peran and colleagues conducted a series of studies to explore verb generation deficits in PD patients [10-12]. Peran et al. (2003) explored if the frontal pathophysiology in PD patients affects verb processing. Thirty-four PD patients and 24 healthy adults were recruited. The two groups were matched on age, sex, education, and MMSE. The authors used word generation tasks that require semantic and syntactic selection. In noun-to-noun and verb-to-verb generation tasks, participants were asked to produce a semantically related noun or verb when listening to a noun or a verb; in noun-to-verb and verb-to-noun generation tasks, participants were instructed to produce a semantically related item from the other category. The result showed that in verb-to-verb and noun-to-verb generation tasks, PD patients made more errors than did control participants. Furthermore, a negative correlation between noun-to-verb generation errors and Dementia Rating Scale scores was found, but no significant correlation was observed between motor deficit and generation performance. The authors claim that non-demented PD patients may present a particular difficulty to produce verbs in a word generation task.

Peran et al. (2009) using fMRI technique tested two alternative explanations for the verb generation deficit in PD patients. The authors aimed to distinguish the motor theory and the grammatical theory. They investigated brain activations involved in the generation of action-verbs (Gen A) and object naming (ON) in PD patients. The two tasks involve a common set of object drawings: manipulable man-made objects (MMO), which are consequently to specific action verbs; and manipulable biological objects (MBO), which are not closely related to specific actions. The authors hypothesized that the prefrontal cortex plays an important role in the motor representation of verbs, and that motor representation is thus disturbed in PD patients. In this study, no control group was included. The brain activation result showed that PD patients had similar activations in the Gen A and ON tasks on both MMO and MBO. The common activations were in the bilateral pre- and post-central gyrus, bilateral superior temporal gyrus, bilateral occipital gyrus, and cerebellum. Moreover, correlative analysis showed that similar areas had correlations with motor deficit in the Gen A and ON tasks, including left pre central gyrus (BA 6). Nevertheless, the authors claim that a relationship exists between motor system dysfunctions in PD patients and verb generation, and that the verb generation task implies in-depth semantic processing of actions.

Peran et al (2013) further examined whether levodopa could modulate verb-related brain activity in PD patients. PD patients in "ON" and "OFF" levodopa-therapy status participated in an fMRI experiment in which they performed verb generation and motor imagery tasks. No control group was included. The authors predicted that dopaminergic modulation could influence striato-frontal loops, especially the motor-putaminal loops. These cortico-subcortical loops are involved in the semantic representation of action concepts. The behavioral results showed no significant effect for levodopa-therapy status, but the brain results showed that "ON" levodopa-therapy status increased activation in the right post central gyrus in the generation task, and that in the left superior and middle frontal gyrus, left SMA, right post central gyrus, bilateral post central gyrus and right cerebellum, the activation increased in the motor imagery task. The authors claimed that these results support the motor theory of verb processing.

Silveri et al. (2012) investigated whether deep brain stimulation (DBS) of the sub thalamic nucleus (STN) influences verb generation in PD patients. In the study, 7 PD patients started the experiment in ON stimulation and 5 patients in OFF stimulation. A control group of healthy adults was included. Patients and controls were matched on age and education. Participants viewed pictures describing objects and actions and then generated nouns and verbs. The results showed that both control and PD patient groups had longer reaction times in verb generation as compared with noun generation. PD patients with ON condition had higher accuracy, shorter RTs, and less semantic errors as compared with patients in the OFF condition. The authors suggest that stimulation ON can improve verb processing by facilitating the motor components in verb naming and reading, and that it can restore the corticostriatal activity important for semantic selection (e.g., decreasing semantic errors).

Discussion

Although the above studies have provided ample evidence for verb processing in PD patients, their results are quite inconsistent and future work is required.

First, it needs to be clarified whether PD patients only have deficits in verb generation as compared with healthy controls. Most studies involving a well-matched control group have reported a main effect for group (i.e. a significant difference between PD patients and healthy controls) in their data analysis [7-10,13,14,20]. The main effect of group suggests that PD patients generally have worse language production performance than healthy controls. But it is should be noted that the PD patients in different studies are varied in their length of disease and the severity of motor disorders. Thus, even though the control group and the PD group in each study were well matched on age, education, and MMSE scores, the disease severity can be various across studies.

To test if PD only affects verb production, a more specific analysis is required. Some studies reported that when analyses were separately conducted for nouns and verbs, PD patients only had worse performance in verb generation as compared with the control group [8,10]. The authors claim that PD patients have no global difficulty in generating words. However, this effect pattern is not consistent. For instance, Cotelli et al. (2007) and Silveri et al. (2012) showed that in two separate analyses, PD patients showed worse performance in both noun generation and verb generation. An interesting fact is that in Crescentini et al. (2008) and Peran et al. (2003) that did not show noun deficits in PD patients, the noun generation was based on word stimuli. In Cotelli et al. (2007) and Silveri et al. (2012) that showed noun deficits in PD patients, noun generation was based on picture stimuli. It is possible that differences in these stimuli cause inconsistent results. Picture stimuli provide conceptual-level information, and noun generation task based on such stimuli requires lexical retrieval and executing the phonological plans [21]. Word stimuli, on the other hand, provide lexical information, and participants in the noun generation tasks in Crescentini et al. (2008) and Peran et al. (2003) needed to access related conceptual information, retrieve related lexical information, and execute phonological plans. Thus, task demands on semantic retrieval, semantic selection and inhibition are different due to the stimuli information. The stimuli difference may modulate the task performance in PD patients and control group.

Second, even though PD patients have specific deficits in verb generation, whether the deficits reflect the role of the motor system in the semantic processing of action concepts is still unclear. At least three possibilities exist (as mentioned in the Introduction part), including the semantic view (i.e. motor theory), i.e. basal ganglia and frontal regions affected by PD contribute to the semantic processing of verbs; grammatical view, i.e. basal ganglia and frontal regions affected by PD contribute to grammatical processing that is more complex in verb generation, and executive control view, i.e. basal ganglia and frontal regions affected by PD contribute to executive control that are more complex in verb generation.

Several studies have tested the semantic view by manipulating the motor semantic features of verbs during comprehension, but their findings are inconsistent.

In Herrera et al. (2012), the authors found that PD patients had worse performance in verbs with high motor content than in verbs with lower motor content, and in Herrera and Cuetos (2012), the authors found that PD patients with off dopamine had worse generation performance in verbs with high motor content. These results indicate that PD affects the processing of motor semantic features, and this supports the semantic view. However, in Cottelli et al. (2007), no significant difference was found in the generation performance between verbs with high degree of manipulation and verbs with low degree of manipulation. The evidence from neuro imaging research does not provide clear evidence for the semantic view. For instance, Peran et al. (2009) found that PD patients had similar brain activations in verb generation when the verbs have different biological features (i.e. either man-made objects or biological objects). One factor that might cause the inconsistent effects is the motor semantic features manipulated in these studies. For example, “motor content” [12,20], “degree of manipulation” [7], and biological features of verbs can be different in the requirement of motor simulation (the enactment of action planning and execution), and thus may involve the motor system at different levels.

Third, it is always predicted that PD only affects one of the three aspects of verb production: semantic process, grammatical process, or executive control process. But there are possibilities that PD can influence more than one aspect. For example, the finding from Crescentini et al. (2008) clearly showed that PD patients only had deficits in verb generation, and that the deficits related to the degree of association between the produced verbs and the presented nouns. No such effect was found in noun-noun production. This suggests that PD may affect grammatical processing or semantic processing that require executive control functions (e.g., semantic selection or inhibition, or grammatical-related control functions).

Taken together, although current research has provided evidence about verb generation in PD patients, the findings are still inconsistent. Future research is required to address three issues: (1) whether PD only affects verb generation, (2) whether the PD affects the semantic processing during verb generation, and (3) whether PD can affect more than one aspects of verb generation. Future research should also examine the influence of other factors that might influence verb generation in PD patients, e.g., stimuli used in production tasks. In addition, future studies should consider more elaborate experimental designs that can examine a certain aspect of

verb generation while controlling other aspects. For neuro imaging research, the recruitment of a control group is necessary.

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