Research Article

Graph Theoretical Analysis of Semantic Fluency in Patients with Parkinson’s Disease

Guanyu Zhang¹,², Jinghong Ma,³ Piu Chan,⁴ and Zheng Ye⁵

¹China Institute of Sport Science, Beijing, China
²Institute of Psychology, Chinese Academy of Sciences, Beijing, China
³Department of Neurology, Xuanwu Hospital of Capital Medical University, Beijing, China
⁴Department of Neurology and Neurobiology, National Clinical Research Center for Geriatric Disorders, Xuanwu Hospital of Capital Medical University, Beijing, China
⁵Institute of Neuroscience, Center for Excellence in Brain Science and Intelligence Technology, Chinese Academy of Sciences, Shanghai, China

Correspondence should be addressed to Guanyu Zhang; 1601466858@qq.com

Received 27 January 2022; Revised 2 April 2022; Accepted 16 April 2022; Published 23 April 2022

Academic Editor: Luigi Trojano

Copyright © 2022 Guanyu Zhang et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Semantic fluency is the ability to name items from a given category within a limited time, which relies on semantic memory, working memory, and executive function. Semantic disfluency is a common problem in Parkinson’s disease (PD) and Alzheimer’s disease (AD). We demonstrated a graph theoretical analysis of semantic fluency in patients with PD (N = 86), patients with AD (N = 40), and healthy controls (HC, N = 88). All participants completed a standard animal fluency test. Their verbal responses were recorded, transcribed, and transformed into directed speech graphs. Patients with PD generated fewer correct words than HC and more correct words than patients with AD. Patients with PD showed higher density, shorter diameter, and shorter average shortest path length than HC, but lower density, longer diameter, and longer average shortest path length than patients with AD. It suggests that patients with PD produced relatively smaller and denser speech graphs. Moreover, in PD, the densities of speech graphs correlated with the severity of non-motor symptoms, but not the severity of motor symptoms. The graph theoretical analysis revealed new features of semantic disfluency in patients with PD.

1. Introduction

Semantic fluency is the ability to name items from a given category (e.g., animals) during a given time interval, usually one minute (semantic fluency test). This task is significantly influenced by semantic memory (e.g., semantic representations to be organized), working memory (e.g., keeping the search for new satisfying words), and executive function (e.g., the ability to select and retrieve correct words and inhibit those that are not inherent with the specific category) domains. Semantic disfluency is a common problem in Parkinson’s disease (PD) and Alzheimer’s disease (AD). Patients with PD or AD generate fewer correct words than healthy adults in the semantic fluency test [1–4].

Different approaches have been developed to quantify verbal responses in semantic fluency tests. Troyer and colleagues [5] proposed a method to segment the verbal response into clusters according to the semantic relatedness between words. For example, a participant may begin with farm animals (e.g., ox, horse, and donkey) and then switch to forest animals (e.g., wolf, bear, and fox). This method generates two primary parameters: the mean cluster size, which is the average number of sequential words from the same subcategory, and the number of switches between subcategories. It is assumed that the mean cluster size reflects semantic storage in the temporal lobe and the number of switches reflects executive functions in the frontal lobe. PD patients with dementia or mild cognitive impairment often switch less than healthy adults but they do
not necessarily produce smaller clusters [6, 7]. In contrast, patients with AD switch less and produce smaller clusters than healthy adults [6].

The Troyer method relies heavily on experimenters’ subjective judgment of semantic relatedness and cluster segmentation. Farzanfar et al. compared an automated computational assessment with the traditional experimenter-based assessment of semantic fluency data from patients with PD [8]. In the computational assessment, each word was represented as a vector in a semantic space derived from corpora. Semantic relatedness between a given pair of words was defined as the cosine of the angle between the corresponding vectors (range from -1 [low relatedness] to 1 [high relatedness]). Sequential words with a semantic relatedness value higher than a predetermined threshold (0.5-0.6) were members of the same cluster. A semantic relatedness value below the threshold indicated a switch between clusters. The computational assessment was inconsistent with the experimenter-based assessment in detecting clusters: the correlation between the two assessments varied as a function of the threshold. In the experimenter-based assessment, the estimation of cluster and switch might be biased by the experimenter’s semantic knowledge.

An objective method is based on graph theory. Graph theory has been used to reveal topological changes in brain networks in various brain disorders [9–11]. Recently, Bertola and colleagues [12] used graph theory to analyze semantic fluency data of patients with AD or mild cognitive impairment. They found that speech graphs of semantic fluency become smaller and denser as general cognition decreases. In another study, Mota and colleagues [13] used a graph theory to analyze dream reports and found that speech graphs of patients with schizophrenia were less connected than those of healthy adults. The individual patients’ connectivity within speech graphs correlated with their severity of negative and cognitive symptoms. As a sensitive measurement, we hypothesize that the graph theoretical analysis can extract more semantic features, which potentially contributes to the identification of mild cognitive impairment in PD from healthy adults or AD.

In this study, we revisit the semantic disfluency of patients with PD, comparing speech graphs of patients with PD with those of healthy adults and patients with AD. All participants completed a standard animal fluency test. We transformed participants’ verbal responses into directed speech graphs, with each node representing a correct word and each arc representing a temporal link between sequential words (Figure 1). First, we wanted to detect group differences in the number of correct words, repetitions, incorrect words, metalinguistic reference, and metacognitive reference (standard analysis). Second, we sought group differences in global characteristics of speech graphs, including density, diameter, and average shortest path (graph theoretical analysis). Third, in PD, we explored whether the speech graph parameters correlated with clinical features such as the severity of motor or non-motor symptoms.

2. Materials and Methods

This study was approved by the ethics committee of the Xuanwu Hospital according to the Declaration of Helsinki. Each participant signed a written informed consent before participating in this study.

2.1. PD Patients and Clinical Assessments. We included 86 patients with idiopathic PD (Movement Disorder Society Clinical Diagnostic Criteria for Parkinson’s Disease [14]) at the Xuanwu Hospital Research and Clinical Center for Parkinson’s disease between 2017 and 2019. Inclusion criteria were (1) Hoehn and Yahr Stages 1 to 2; (2) age 40 to 80 years; (3) education ≥6 years; and (4) Mandarin Chinese speaking. Exclusion criteria were (1) a history of epilepsy, stroke, or brain injury; (2) alcohol or drug abuse; (3) possible current depression (Beck Depression Inventory–II, BDI-II≥7) or intake of anti-depressants; and (4) possible dementia (Montreal Cognitive Assessment, MoCA<21/30) or intake of anti-dementia drugs.

All patients with PD were assessed on their regular anti-Parkinsonian drugs, including levodopa (N = 48), pramipexole (N = 25), selegiline (N = 16), piribedil (N = 13), amantadine (N = 8), entacapone (N = 4), and rasagiline (N = 1). The levodopa equivalent daily dose was calculated using the equation of Tomlinson et al. [15]. The severity of motor and non-motor symptoms was evaluated with the Movement Disorder Society-sponsored revision of the Unified Parkinson’s Disease Rating Scale (MDS-UPDRS) Part III and I subscales, respectively. Table 1 shows demographic and clinical features and neuropsychological measures.

2.2. Two Control Groups. We included two control groups: 88 age- and education-matched healthy controls (HC) from local communities and 40 matched patients with AD from the DementiaBank database [16].

For the HC group, exclusion criteria were (1) a history of significant neurological or psychiatric disorders; (2) alcohol or drug abuse; (3) possible current depression; and (4) possible dementia or mild cognitive impairment (MoCA<26/30). They completed the same assessments for cognition, mood, and sleep as patients with PD.

The DementiaBank database has 139 dementia patients assessed at the University of Pittsburgh School of Medicine. We only included AD patients matched with the other two groups in sex and age (20 women, age range 50-70 years, and mean age 62.2 years). We excluded patients diagnosed with other types of dementia, including mild cognitive impairment (N = 17), vascular diseases (N = 4), and other memory problems (N = 3).

2.3. Standard and Graph Theoretical Analyses. All participants completed a standard animal fluency test. For the PD and HC groups, we recorded and transcribed their verbal responses. For the AD group, we received their audios and transcripts from the database.

For the standard analysis, we defined five parameters: (1) the number of correct words without repetitions: all types of animals were accepted, including humans, insects, and mythical creatures (e.g., dragon); (2) the number of repetitions; (3) the number of incorrect words; (4) metalinguistic reference: the number of times participants talked about their responses (e.g., “did I say horses?”); (5) metacognitive...
Figure 1: (a) Directed speech graphs of three representative participants. HC004, a healthy control subject; PD021, a patient with Parkinson’s disease; AD663, a patient with Alzheimer’s disease. (b) Graph geodesic as the shortest path (green) between two nodes (blue) in the three participants.

Table 1: Demographic and clinical features, and neuropsychological measures of PD patients and healthy controls (means, standard deviations, and group differences).

| Features/measures                                      | PD patients (N = 86) | Healthy controls (N = 88) | Group differences (p values) |
|--------------------------------------------------------|----------------------|---------------------------|------------------------------|
| Female: Male                                           | 44 : 42              | 46 : 42                   | 0.884                        |
| Age (years)                                            | 59.0 (9.5)           | 58.1 (7.0)                | 0.484                        |
| Education (years)                                      | 12.4 (3.2)           | 12.9 (2.4)                | 0.204                        |
| Montreal cognitive assessment                          | 25.6 (2.4)           | 27.9 (1.4)                | <0.001*                      |
| Levodopa equivalent daily dose (mg)                    | 243.3 (248.6)        | —                         | —                            |

Motor symptoms

| Hoehn and Yahr scale                                    | 1.4 (0.5)            | —                         | —                            |
| MDS-UPDRS III: Motor examination                       | 21.8 (12.6)          | —                         | —                            |
| Disease duration (years)                               | 1.6 (2.2)            | —                         | —                            |
| Duration of motor symptoms (years)                     | 2.8 (2.4)            | —                         | —                            |

Other non-motor functions

| MDS-UPDRS I: Non-motor experiences of daily living     | 5.3 (4.0)            | —                         | —                            |
| Beck depression inventory-II                           | 2.7 (2.0)            | 2.1 (1.7)                 | 0.039                        |
| REM sleep behavior disorder screening questionnaire     | 3.7 (2.0)            | 1.9 (1.8)                 | <0.001*                      |
| Epworth sleep scale                                    | 3.1 (3.2)            | 3.2 (2.3)                 | 0.820                        |

Note: MDS-UPDRS, the Movement Disorder Society-sponsored revision of the Unified Parkinson’s Disease Rating Scale; group differences, p values of two-sample t-tests, or Chi-square test as appropriate; asterisks (*), a significant difference (two-tailed, p < 0.007 Bonferroni correction for seven tests).
reference: the number of times participants talked about
their memory (e.g., “I really cannot think of any.”) or asked
about the time (e.g., “how much time is left?”).

For the graph theoretical analysis, we transformed par-
ticipants’ verbal responses into directed speech graphs with
Speechgraphs [12, 13]. In each directed speech graph, a node
represented a word, and an arc represented the temporal
link between an ordered pair of words (Figure 1(a)). We
computed three graph parameters, including the density,
diameter, and average shortest path length. The graph den-
sity is the ratio of arcs to the maximum possible number
of arcs. The graph geodesic is the shortest path between
two nodes (Figure 1(b)). The length of the maximum graph
geodesic is the graph diameter. The mean length of all graph
geodesics is the average shortest path length, also known as
the characteristic path length of the graph.

2.4. Statistical Analysis. Data were analyzed with IBM SPSS
Statistics 20. First, we examined group differences in the
standard and graph parameters using one-way ANOVAs
(two-tailed, \( p < 0.006 \) Bonferroni correction for eight tests).
The ANOVA had a factor group (HC, PD, and AD) and a
co-variate age. Significant group differences were followed by
pairwise comparisons (with Bonferroni correction).

Second, in PD, we examined whether the severity of
motor or non-motor symptoms (MDS-UPDRS Part III or I
subscores) correlated with the graph parameters that showed
group differences using linear regression models (stepwise,
\( p < 0.025 \) Bonferroni correction for two models).

3. Results

3.1. Group Differences in Standard Parameters. Figure 2(a)
shows standard parameters in each group. Group differences
were found in the number of correct words
\((F(2, 210) = 66.36, \ p < 0.001, \) and \( \eta^2_p = 0.39) \) and metacogni-
tive reference \((F(2, 210) = 12.37, \ p < 0.001, \) and \( \eta^2_p = 0.11) \),
but not in the number of repetitions \((F(2, 210) = 1.79, \ p =
0.169, \ \eta^2_p = 0.02) \), number of incorrect words
\((F(2, 210) = 2.03, \ p = 0.134, \) and \( \eta^2_p = 0.02) \), or metalinguistic
reference \((F < 1) \). The PD group generated fewer correct and
non-repetitive words than the HC group \((p = 0.008) \) but more
correct and non-repetitive words than the AD group
\((p < 0.001) \). The PD group talked about their memory and
time remaining more than the HC group \((p < 0.001) \). Only
the AD group generated incorrect words.

3.2. Group Differences in Graph Parameters. Figure 2(b)
shows graph parameters in each group. Group differences
were found in the density \((F(2, 210) = 51.54, \ p < 0.001, \)
and \( \eta^2_p = 0.33) \), diameter \((F(2, 210) = 38.40, \ p < 0.001, \)
and \( \eta^2_p = 0.27) \), and average shortest path \((F(2, 210) = 42.55, \ p
< 0.001, \) and \( \eta^2_p = 0.29) \). The PD group showed higher den-
sity \((p = 0.003) \), shorter diameter \((p = 0.008) \), and shorter
average shortest path length than the HC group \((p = 0.008) \).
The PD group showed lower density \((p < 0.001) \), longer
diameter \((p < 0.001) \), and longer average shortest path
length than the AD group \((p < 0.001) \). In other words,
speech graphs of the PD group were smaller and denser than
those of the HC group but larger and more sparse than those
of the AD group.

3.3. Correlations between Clinical Features and Graph
Parameters in PD. Figure 2(c) shows correlations between
graph parameters and clinical features in PD. The stepwise
regression model for the MDS-UPDRS Part I subscore
\((F(1, 83) = 7.80, \ p = 0.006, \) and \( R^2 = 0.09) \) included density
\((\beta = 29.11, \ t = 2.79, \) and \( p = 0.006) \) but removed the
diameter \((\beta = -0.14, \ t = -0.91, \) and \( p = 0.37) \) and average
shortest path \((\beta = -0.11, \ t = -0.68, \) and \( p = 0.50) \). PD
patients with more severe non-motor symptoms tended to
produce smaller and denser speech graphs.

Linear regression model did not survive at the corrected
threshold for the MDS-UPDRS Part III subscore
\((F(1, 84) = 4.24 \) and \( p = 0.043) \).

4. Discussion

In this study, we revisited the semantic disfluency in non-
demented patients with PD. We replicated previous findings
that patients with PD generated fewer correct and non-
repetitive words than healthy controls [17–19] but more
than patients with AD [20, 21]. More importantly, we exam-
ined the topology of participants’ speech graphs and found
that patients with PD produced smaller and denser speech
graphs than healthy controls but larger and more sparse
speech graphs than patients with AD. To be specific, the
speech graphs of PD patients showed higher density, shorter
diameter, and shorter average shortest path than those of
healthy controls but lower density, longer diameter, and lon-
ger average shortest path length than those of AD patients.
In PD, in addition, the density of speech graphs correlated
with the severity of non-motor symptoms. PD patients
who produced smaller and denser speech graphs exhibited
more severe non-motor symptoms in daily living.

This study suggests that the graph theoretical analysis is
more sensitive than the standard analysis to PD’s problems
in verbal fluency. For example, both approaches measured
the repetition, but only the measures of the graph theoretical
analysis (e.g., density, diameter, and average shortest path)
showed significant group differences between PD patients
and healthy controls. The repetition might reflect the
impaired selection and programming processes of semantic
fluency, which is associated with the left inferior frontal
gyrus (LIFG) and basal ganglia.

Verbal fluency tasks involve several cognitive processes:
(a) attention to search words from an abundant semantic
store, (b) selection of appropriate words to produce, (c) pro-
gramming of speech production, and (d) keeping track of
the words that have already been produced to avoid repeti-
tions. The dual stream model for language processing is a
widely accepted model that describes two large-scale streams
underlying different speech tasks [22]. The ventral stream is
comprised of bilaterally superior and middle portions of the
temporal lobes with a weak left-hemisphere bias, which sup-
ports the processing of sound-to-meaning information and
is essential for auditory comprehension and semantic

Values were demeaned. was correlated with the severity of non-motor symptoms (MDS-UPDRS I score) but not the severity of motor symptoms (MDS-UPDRS III score). Values were demeaned.

The decline of verbal fluency after pallidotomy in patients with PD may be due to surgical microlesions affecting cortical-basal ganglionic circuits involved in word generation processes [28, 29].

Semantic fluency relies on working memory and executive function, in addition to semantic knowledge. It has been described that the working memory deficits and executive dysfunction in patients with PD may result in semantic disfluency [30]. The impairments in working memory might result in the difficulty of keeping the search for new standard-compliant words and keeping track of produced words. The executive dysfunction leads to the deficits in selecting and producing appropriate words and inhibiting inappropriate words (i.e., repetitions and incorrect words). On the other hand, the difficulty of self-shifting may result in semantic disfluency. For example, Henry and Crawford (2004) [31] showed that PD patients shift from one semantic category to another with more effort than healthy adults.

Semantic disfluency has been linked to non-motor symptoms in PD in previous studies. PD patients with more severe depression or sleep disturbances tended to show worse performance in the semantic fluency tests [17, 32, 33]. In contrast, there was no correlation between PD patients’ scores of semantic fluency task and their disease durations, levodopa intakes, severities of rigidity or tremor, or Hoehn-Yahr stages [34]. From another perspective, the semantic task could distinguish patients with PD and AD. Although patients with PD were impaired in semantic fluency, they were not as severe as patients with AD. The AD patients not only generated fewer correct words, but also repeated the same word with a smaller frequency. The impairments in working memory might result in semantic disfluency. For example, Henry and Crawford (2004) [31] showed that PD patients shift from one semantic category to another with more effort than healthy adults.

Semantic disfluency has been linked to non-motor symptoms in PD in previous studies. PD patients with more severe depression or sleep disturbances tended to show worse performance in the semantic fluency tests [17, 32, 33]. In contrast, there was no correlation between PD patients’ scores of semantic fluency task and their disease durations, levodopa intakes, severities of rigidity or tremor, or Hoehn-Yahr stages [34]. From another perspective, the semantic task could distinguish patients with PD and AD. Although patients with PD were impaired in semantic fluency, they were not as severe as patients with AD. The AD patients not only generated fewer correct words, but also repeated the same word with a smaller frequency. The impairments in working memory might result in semantic disfluency. For example, Henry and Crawford (2004) [31] showed that PD patients shift from one semantic category to another with more effort than healthy adults.

Semantic disfluency has been linked to non-motor symptoms in PD in previous studies. PD patients with more severe depression or sleep disturbances tended to show worse performance in the semantic fluency tests [17, 32, 33]. In contrast, there was no correlation between PD patients’ scores of semantic fluency task and their disease durations, levodopa intakes, severities of rigidity or tremor, or Hoehn-Yahr stages [34]. From another perspective, the semantic task could distinguish patients with PD and AD. Although patients with PD were impaired in semantic fluency, they were not as severe as patients with AD. The AD patients not only generated fewer correct words, but also repeated the same word with a smaller frequency. The impairments in working memory might result in semantic disfluency. For example, Henry and Crawford (2004) [31] showed that PD patients shift from one semantic category to another with more effort than healthy adults.

Semantic disfluency has been linked to non-motor symptoms in PD in previous studies. PD patients with more severe depression or sleep disturbances tended to show worse performance in the semantic fluency tests [17, 32, 33]. In contrast, there was no correlation between PD patients’ scores of semantic fluency task and their disease durations, levodopa intakes, severities of rigidity or tremor, or Hoehn-Yahr stages [34]. From another perspective, the semantic task could distinguish patients with PD and AD. Although patients with PD were impaired in semantic fluency, they were not as severe as patients with AD. The AD patients not only generated fewer correct words, but also repeated the same word with a smaller frequency. The impairments in working memory might result in semantic disfluency. For example, Henry and Crawford (2004) [31] showed that PD patients shift from one semantic category to another with more effort than healthy adults.

Semantic disfluency has been linked to non-motor symptoms in PD in previous studies. PD patients with more severe depression or sleep disturbances tended to show worse performance in the semantic fluency tests [17, 32, 33]. In contrast, there was no correlation between PD patients’ scores of semantic fluency task and their disease durations, levodopa intakes, severities of rigidity or tremor, or Hoehn-Yahr stages [34]. From another perspective, the semantic task could distinguish patients with PD and AD. Although patients with PD were impaired in semantic fluency, they were not as severe as patients with AD. The AD patients not only generated fewer correct words, but also repeated the same word with a smaller frequency. The impairments in working memory might result in semantic disfluency. For example, Henry and Crawford (2004) [31] showed that PD patients shift from one semantic category to another with more effort than healthy adults.

Semantic disfluency has been linked to non-motor symptoms in PD in previous studies. PD patients with more severe depression or sleep disturbances tended to show worse performance in the semantic fluency tests [17, 32, 33]. In contrast, there was no correlation between PD patients’ scores of semantic fluency task and their disease durations, levodopa intakes, severities of rigidity or tremor, or Hoehn-Yahr stages [34]. From another perspective, the semantic task could distinguish patients with PD and AD. Although patients with PD were impaired in semantic fluency, they were not as severe as patients with AD. The AD patients not only generated fewer correct words, but also repeated the same word with a smaller frequency. The impairments in working memory might result in semantic disfluency. For example, Henry and Crawford (2004) [31] showed that PD patients shift from one semantic category to another with more effort than healthy adults.

Semantic disfluency has been linked to non-motor symptoms in PD in previous studies. PD patients with more severe depression or sleep disturbances tended to show worse performance in the semantic fluency tests [17, 32, 33]. In contrast, there was no correlation between PD patients’ scores of semantic fluency task and their disease durations, levodopa intakes, severities of rigidity or tremor, or Hoehn-Yahr stages [34]. From another perspective, the semantic task could distinguish patients with PD and AD. Although patients with PD were impaired in semantic fluency, they were not as severe as patients with AD. The AD patients not only generated fewer correct words, but also repeated the same word with a smaller frequency. The impairments in working memory might result in semantic disfluency. For example, Henry and Crawford (2004) [31] showed that PD patients shift from one semantic category to another with more effort than healthy adults.

Semantic disfluency has been linked to non-motor symptoms in PD in previous studies. PD patients with more severe depression or sleep disturbances tended to show worse performance in the semantic fluency tests [17, 32, 33]. In contrast, there was no correlation between PD patients’ scores of semantic fluency task and their disease durations, levodopa intakes, severities of rigidity or tremor, or Hoehn-Yahr stages [34]. From another perspective, the semantic task could distinguish patients with PD and AD. Although patients with PD were impaired in semantic fluency, they were not as severe as patients with AD. The AD patients not only generated fewer correct words, but also repeated the same word with a smaller frequency. The impairments in working memory might result in semantic disfluency. For example, Henry and Crawford (2004) [31] showed that PD patients shift from one semantic category to another with more effort than healthy adults.

Semantic disfluency has been linked to non-motor symptoms in PD in previous studies. PD patients with more severe depression or sleep disturbances tended to show worse performance in the semantic fluency tests [17, 32, 33]. In contrast, there was no correlation between PD patients’ scores of semantic fluency task and their disease durations, levodopa intakes, severities of rigidity or tremor, or Hoehn-Yahr stages [34]. From another perspective, the semantic task could distinguish patients with PD and AD. Although patients with PD were impaired in semantic fluency, they were not as severe as patients with AD. The AD patients not only generated fewer correct words, but also repeated the same word with a smaller frequency. The impairments in working memory might result in semantic disfluency. For example, Henry and Crawford (2004) [31] showed that PD patients shift from one semantic category to another with more effort than healthy adults.

Semantic disfluency has been linked to non-motor symptoms in PD in previous studies. PD patients with more severe depression or sleep disturbances tended to show worse performance in the semantic fluency tests [17, 32, 33]. In contrast, there was no correlation between PD patients’ scores of semantic fluency task and their disease durations, levodopa intakes, severities of rigidity or tremor, or Hoehn-Yahr stages [34]. From another perspective, the semantic task could distinguish patients with PD and AD. Although patients with PD were impaired in semantic fluency, they were not as severe as patients with AD. The AD patients not only generated fewer correct words, but also repeated the same word with a smaller frequency. The impairments in working memory might result in semantic disfluency. For example, Henry and Crawford (2004) [31] showed that PD patients shift from one semantic category to another with more effort than healthy adults.

Semantic disfluency has been linked to non-motor symptoms in PD in previous studies. PD patients with more severe depression or sleep disturbances tended to show worse performance in the semantic fluency tests [17, 32, 33]. In contrast, there was no correlation between PD patients’ scores of semantic fluency task and their disease durations, levodopa intakes, severities of rigidity or tremor, or Hoehn-Yahr stages [34]. From another perspective, the semantic task could distinguish patients with PD and AD. Although patients with PD were impaired in semantic fluency, they were not as severe as patients with AD. The AD patients not only generated fewer correct words, but also repeated the same word with a smaller frequency. The impairments in working memory might result in semantic disfluency. For example, Henry and Crawford (2004) [31] showed that PD patients shift from one semantic category to another with more effort than healthy adults.

Semantic disfluency has been linked to non-motor symptoms in PD in previous studies. PD patients with more severe depression or sleep disturbances tended to show worse performance in the semantic fluency tests [17, 32, 33]. In contrast, there was no correlation between PD patients’ scores of semantic fluency task and their disease durations, levodopa intakes, severities of rigidity or tremor, or Hoehn-Yahr stages [34]. From another perspective, the semantic task could distinguish patients with PD and AD. Although patients with PD were impaired in semantic fluency, they were not as severe as patients with AD. The AD patients not only generated fewer correct words, but also repeated the same word with a smaller frequency. The impairments in working memory might result in semantic disfluency. For example, Henry and Crawford (2004) [31] showed that PD patients shift from one semantic category to another with more effort than healthy adults.
5. Conclusion

In this study, we analyzed the topology of speech graphs generated in a semantic fluency test. The speech graphs of patients with PD were smaller and denser than those of healthy controls but larger and more sparse than those of patients with AD. Moreover, PD patients who produced smaller and denser speech graphs exhibited more severe non-motor symptoms.

Data Availability

Data have been uploaded to the figshare database https://figshare.com/articles/dataset/XW_data_2017-2019.xls/18393671.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

JM and ZY designed the study. GZ and JM collected the data. GZ analyzed the data. GZ and ZY wrote the original draft of the manuscript. JM and PC reviewed and edited the manuscript. All authors approved the submitted version. GZ and JM equally contributed to this work and share first authorship.

Acknowledgments

We are grateful to Sha Liu, Shaoyang Ma, and Minghong Su for their assistance in data acquisition. This work was supported by the National Natural Science Foundation of China (31961133025 to Z.Y.) and the National Key Research and Development Program of China (2018YFC1312001 to P.C.).

References

[1] A. L. R. Adlam, S. Bozeat, R. Arnold, P. Watson, and J. R. Hodges, "Semantic knowledge in mild cognitive impairment and mild Alzheimer’s disease," Cortex, vol. 42, no. 5, pp. 675–684, 2006.
[2] N. Unsworth, G. J. Spillers, and G. A. Brewer, "Variation in verbal fluency: a latent variable analysis of clustering, switching, and overall performance," Quarterly Journal of Experimental Psychology, vol. 64, no. 3, pp. 447–466, 2011.
[3] T. Azuma, K. A. Bayles, R. F. Cruz et al., "Comparing the difficulty of letter, semantic, and name fluency tasks for normal elderly and patients with Parkinson’s disease," Neuropsychology, vol. 11, no. 4, pp. 488–497, 1997.
[4] F. Pasquier, F. Lebert, L. Grymonprez, and H. Petit, "Verbal fluency in dementia of frontal lobe type and dementia of Alzheimer type," Journal of Neurology, Neurosurgery, and Psychiatry, vol. 58, no. 1, pp. 81–84, 1995.
[5] A. K. Troyer, M. Moscovitch, and G. Winocur, "Clustering and switching as two components of verbal fluency: evidence from younger and older healthy adults," Neuropsychology, vol. 11, no. 1, pp. 138–146, 1997.
[6] A. K. Troyer, M. Moscovitch, G. Winocur, L. Leach, and M. Freedman, "Clustering and switching on verbal fluency tests in Alzheimer’s and Parkinson’s disease," Journal of the International Neuropsychological Society, vol. 4, no. 2, pp. 137–143, 1998.
[7] I. Galtier, A. Nieto, J. N. Lorenzo, and J. Barroso, "Mild cognitive impairment in Parkinson’s disease: clustering and switching analyses in verbal fluency test," Journal of the International Neuropsychological Society, vol. 23, no. 6, pp. 511–520, 2017.
[8] D. Farzanfar, M. Statucka, and M. Cohn, "Automated indices of clustering and switching of semantic verbal fluency in Parkinson’s disease," Journal of the International Neuropsychological Society, vol. 24, no. 10, pp. 1047–1056, 2018.
[9] O. Sporns, "Graph theory methods: applications in brain networks," Dialogues in Clinical Neuroscience, vol. 20, no. 2, pp. 111–121, 2018.
[10] O. Sporns, D. R. Chialvo, M. Kaiser, and C. C. Hilgetag, "Organization, development and function of complex brain networks," Trends in Cognitive Sciences, vol. 8, no. 9, pp. 418–425, 2004.
[11] O. Sporns and J. D. Zwi, "The small world of the cerebral cortex," Neuroinformatics, vol. 2, no. 2, pp. 145–162, 2004.
[12] L. Bertola, N. B. Mota, M. Copelli et al., "Graph analysis of verbal fluency test discriminate between patients with Alzheimer’s disease, mild cognitive impairment and normal elderly controls," Frontiers in Aging Neuroscience, vol. 6, p. 185, 2014.
[13] M. B. Mota, R. Furtado, P. P. C. Maia, M. Copelli, and S. Ribeiro, "Graph analysis of dream reports is especially informative about psychosis," Scientific Reports, vol. 4, p. 3691, 2015.
[14] R. B. Postuma, D. Berg, M. Stern et al., "MDS clinical diagnostic criteria for Parkinson’s disease," Movement Disorders, vol. 30, no. 12, pp. 1591–1601, 2015.
[15] C. L. Tomlinson, R. Stowe, S. Patel, C. Rick, R. Gray, and C. E. Clarke, "Systematic review of levodopa dose equivalency reporting in Parkinson’s disease," Movement Disorders, vol. 25, no. 15, pp. 2649–2653, 2010.
[16] A. Lanzi, A. Lindsay, and M. Bourgeois, "Verbal fluency in dementia: changes over time," in American School Health Association Conference, Saint Louis, Missouri, USA, 2017.
[17] I. Obeso, E. Casabona, M. L. Bringas, L. Álvarez, and M. Jahanshahi, "Semantic and phonemic verbal fluency in Parkinson’s disease: influence of clinical and demographic variables," *Behavioural Neurology*, vol. 25, no. 2, pp. 111–118, 2012.

[18] O. W. Wong, A. Y. Chan, A. Wong et al., "Eye movement parameters and cognitive functions in Parkinson’s disease patients without dementia," *Parkinsonism & Related Disorders*, vol. 52, pp. 43–48, 2018.

[19] A. F. Barbosa, M. C. Voos, J. Chen et al., "Cognitive or cognitive-motor executive function tasks? Evaluating verbal fluency measures in people with Parkinson’s disease," *BioMed Research International*, vol. 2017, 7 pages, 2017.

[20] J. McDowd, L. Hoffman, E. Rozeck et al., "Understanding verbal fluency in healthy aging, Alzheimer’s disease, and Parkinson’s disease," *Neuropsychology*, vol. 25, no. 2, pp. 210–225, 2011.

[21] N. B. Araujo, M. L. Barca, K. Engedal, E. S. Coutinho, A. C. Deslandes, and J. Laks, "Verbal fluency in Alzheimer’s disease, Parkinson’s disease, and major depression," *Clinics*, vol. 66, no. 4, pp. 623–627, 2011.

[22] G. Hickok and D. Poeppel, "The cortical organization of speech processing," *Nature Reviews Neuroscience*, vol. 8, no. 5, pp. 393–402, 2007.

[23] F. Rodriguez-Porcel, J. Wilmskoetter, C. Cooper et al., "The relationship between dorsal stream connections to the caudate and verbal fluency in Parkinson disease," *Brain Imaging and Behavior*, vol. 15, no. 4, pp. 2121–2125, 2021.

[24] S. L. Thompson-Schill, M. D’Esposito, G. K. Aguirre, and M. J. Farah, "Role of left inferior prefrontal cortex in retrieval of semantic knowledge: a reevaluation," *Proceedings of the National Academy of Sciences*, vol. 94, no. 26, pp. 14792–14797, 1997.

[25] G. Robinson, T. Shallice, M. Bozzali, and L. Cipolotti, "Conceptual proposition selection and the LIFG: neuropsychological evidence from a focal frontal group," *Neuropsychologia*, vol. 48, no. 6, pp. 1652–1663, 2010.

[26] G. E. Alexander, M. R. DeLong, and P. L. Strick, "Parallel organization of functionally segregated circuits linking basal ganglia and cortex," *Annual Review of Neuroscience*, vol. 9, no. 1, pp. 357–381, 1986.

[27] S. J. Chung, H. S. Yoo, J. S. Oh et al., "Effect of striatal dopamine depletion on cognition in de novo Parkinson’s disease," *Parkinsonism & Related Disorders*, vol. 51, pp. 43–48, 2018.

[28] R. M. De Bie, P. R. Schuurman, D. A. Bosch, R. J. De Haan, B. Schmand, and J. D. Speelman, "Outcome of unilateral pallidotomy in advanced Parkinson’s disease: cohort study of 32 patients," *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 71, no. 3, pp. 375–382, 2001.

[29] A. I. Tröster, S. P. Woods, and J. A. Fields, "Verbal fluency declines after Pallidotomy: an interaction between task and lesion laterality," *Applied Neuropsychology*, vol. 10, no. 2, pp. 69–75, 2003.

[30] C. I. Higginson, D. S. King, D. Levine, V. L. Wheelock, N. O. Khampay, and K. A. Sigvardt, "The relationship between executive function and verbal memory in Parkinson’s disease," *Brain and Cognition*, vol. 52, no. 3, pp. 343–352, 2003.

[31] J. D. Henry and J. R. Crawford, "Verbal fluency deficits in Parkinson’s disease: a meta-analysis," *Journal of the International Neuropsychological Society*, vol. 10, no. 4, pp. 608–622, 2004.

[32] D. De Gaspari, C. Siri, M. Di Gioia et al., "Clinical correlates and cognitive underpinnings of verbal fluency impairment after chronic subthalamic stimulation in Parkinson’s disease," *Parkinsonism & Related Disorders*, vol. 12, no. 5, pp. 289–295, 2006.

[33] N. Kamble, R. Yadav, A. Lenka, K. Kumar, B. C. Nagaraju, and P. K. Pal, "Impaired sleep quality and cognition in patients of Parkinson’s disease with REM sleep behavior disorder: a comparative study," *Sleep Medicine*, vol. 62, pp. 1–5, 2019.

[34] S. Auriacombe, M. Grossman, S. Carvell, S. Gollomp, M. B. Stern, and H. I. Hurtig, "Verbal fluency deficits in Parkinson’s disease," *Neuropsychology*, vol. 7, no. 2, pp. 182–192, 1993.

[35] C. H. Williams-Gray, S. L. Mason, J. R. Evans et al., "The CamPaIGN study of Parkinson’s disease: 10-year outlook in an incident population-based cohort," *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 84, no. 11, pp. 1258–1264, 2013.

[36] A. St-Hilaire, C. Hudson, G. T. Vallet et al., "Normative data for phonemic and semantic verbal fluency test in the adult French-Quebec population and validation study in Alzheimer’s disease and depression," *The Clinical Neuropsychologist*, vol. 30, no. 7, pp. 1126–1150, 2016.

[37] N. Linz, J. Tröger, J. Alexandresson, M. Wolters, A. König, and P. Robert, "Predicting dementia screening and staging scores from semantic verbal fluency performance," in *2017 IEEE International Conference on Data Mining Workshops (ICDMW)*, pp. 719–728, New Orleans, LA, USA, 2017.

[38] A. M. Gotham, R. G. Brown, and C. D. Marsden, "Frontal cognitive function in patients with Parkinson’s disease ‘on’ and ‘off’ levodopa," *Brain*, vol. 111, no. 2, pp. 299–321, 1988.

[39] H. A. Hanagasi, H. Gurvit, P. Unsalan et al., "The effects of rasagiline on cognitive deficits in Parkinson’s disease patients without dementia: a randomized, double-blind, placebo-controlled, multicenter study," *Movement Disorders*, vol. 26, no. 10, pp. 1851–1858, 2011.