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The Usage of Verbal Fluency Tests in the Research of Parkinson's Disease and the Potential Implications for Diagnosis: Systematic Literature Review

Literature review

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Abstract

Parkinson's disease (PD) is a neurodegenerative disorder that primarily impacts motor system. However, it also influences language system, and verbal fluency tests can greatly help in the research of PD in this field. 17 papers were chosen with the primary eligibility criteria being the presence of verbal fluency testing in PD population and potential implications for diagnosis. Several conclusions were drawn. (1) Verbal fluency testing has been used for a long time and continues to be of importance. (2) When it comes to the procedure, most verbal fluency tests are used similarly. (3) Verbal fluency tests have downsides (e.g., difficulties with differentiating language testing and executive function). (4) The points of possible improvement are standardizing the categories in the tests and exploring less common types of tests (e.g., action fluency testing) further.

Keywords: Parkinson's disease, verbal fluency, diagnosis, literature review

1. Introduction

Parkinson's disease (PD) is a neurodegenerative disorder of the central nervous system, with its main symptoms being the ones related to the motor system. According to DeMaagd & Philip (2015), the main pathological sign is the death of dopaminergic neurons in the part of the brain called basal ganglia. Most prominent signs of PD

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include tremor, rigidity and slowness of movement. Currently, there is no definite cure for PD, and treatment involves mitigating symptoms. Moreover, anxiety and depression are prevalent in persons with PD. Other issues are also frequent, for example, problems with one's senses and sleep. These changes may appear even before the onset of motor decline (DeMaagd & Philip, 2015).Treatment for PD may include using drugs like levodopa at first. Levodopa helps with increasing dopamine concentrations in the brain as it is able to cross the blood-brain barrier which is resistant to dopamine itself. As PD progresses, medication can become less effective, so subthalamic nucleus deep brain stimulation (STN-DBS) can be considered. DBS is a neurosurgical procedure which involves microelectrodes placed under the skull to send signals to specific brain areas. DBS can reduce the symptoms of PD and facilitate the decrease in medications such as levodopa (Beitz, 2014).

PD is usually diagnosed via the assessment of motor functions, even though according to some scholars, speech of persons with PD can also be used in diagnosis as it has features that are not present in the speech of people without PD (Hireš et al., 2022). In general, the speech in PD is characterized by slurring of words, stuttering and mumbling. Persons with PD may experience issues with expressing emotions and having the right pitch and volume of the voice. Dysphagia (problems with swallowing) and aspiration are also the issues that persons with PD struggle with. Speech therapy can help with these problems (Parkinson's Foundation, n.d.). There are pieces of advice that can help – for example, using short phrases, communicating in non-noisy spaces, and planning the periods of vocal rest. Unfortunately, as with the treatment of PD overall, there is no immediate cure or definite solution to speech problems (Parkinson's Foundation, n.d.). Therefore, research is being conducted to counteract speech problems in PD.

In addition, both motor-speech and language-cognition characteristics can alter throughout the course of the disease. The latter is often studied with the help of verbal fluency tests as deficits in verbal fluency are considered existent in PD. Verbal fluency in PD may be impacted by many factors, for example, the presence of dementia, the age of the patient, the number of years since the onset of PD, etc. (Smith & Caplan, 2018). Verbal fluency testing has been described extensively in the literature, but it is still under development. The verbal fluency tests that are most commonly used are the phonemic (or letter) fluency and semantic fluency tests. Phonemic fluency involves participants naming as many words as they can that start with a specific letter within a prespecified amount of time. This type of fluency is thought to rely more on the frontal areas of the brain. Semantic fluency involves naming words from the same semantic category. Unlike phonemic fluency, semantic fluency uses neural networks in the temporal regions (Henry & Crawford, 2004).

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Other fluency tests include alternating verbal fluency, alternating phonemic fluency and alternating semantic fluency. The first one is a test which consists of switching between a semantic category and a letter (e.g., *animals* and *T*). Alternating phonemic fluency involves switching between two letters during the naming process (e.g., *B* and *F*). Finally, alternating semantic fluency is a task where a participant switches between two semantic categories (e.g., *animals* and *professions*). Both the ability to switch from one category to another one effectively and the ability to generate items in the same category (so-called cluster size) are areas of increasing interest in the research of speech in PD. These two abilities in patients with PD may have differences when compared to the typical population (Smith & Caplan, 2018). Additionally, it may be the case that there are also differences in patients on or off STN-DBS and with or without dementia.

In summary, verbal fluency testing has been explored in the literature, and various directions have been taken. The aim of this literature review is to find the tests that are the most relevant for possible implications in diagnosis.

2. Research Questions

Four research questions are presented that this systematic literature review strives to provide answers to.

RQ 1: What is the current state of using verbal fluency tests in patients with Parkinson's disease?

RQ 2: How are different types of verbal fluency tests used?

RQ 3: What are the main conclusions regarding Parkinson's disease that are made thanks to verbal fluency tests?

RQ 4: What can be improved in testing of verbal fluency?

3. Methods

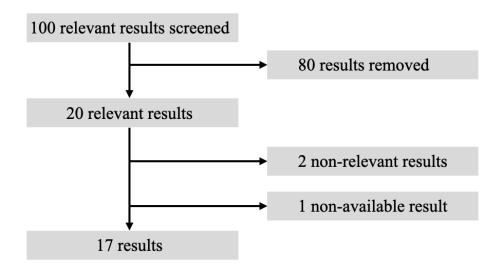
3.1 Search strategy and eligibility criteria

The main stage of searching for the papers involved conducting a search with the help of *Web of Science* (Web of Science, n.d.) which is a research tool to look for relevant

research literature. The key concepts in searching were (1) Parkinson's disease (PD), (2) fluency, and (3) language or speech. The following two inquiries were used: (1) ALL=(("parkinson's disease" OR pd) AND fluency AND (language OR speech)) which produced 321 results, and (2) ALL=(("parkinson's disease" OR pd) AND "verbal fluency" AND (language OR speech)) which produced 186 results. The second search query appeared more convenient as it was more refined and produced a smaller number of results, however, there was a chance that some papers could have been missed with this search. Therefore, the first inquiry was chosen as the main one. The main eligibility criteria are described below (Table 1). In the end, 17 papers were chosen. They cover the field of verbal fluency testing with the implications for the diagnosis well and can lead to significant conclusions. Out of the first 100 results of the search ALL=(("parkinson's disease" OR pd) AND fluency AND (language OR speech)) which produced 321 results, the reasons for the papers not meeting the criteria were that they: (1) were not concerned with verbal fluency at all (n=36), (2) were not considered to have major possible implications for diagnosis (n=24), (3) described fluency of speech or other types of fluency (e.g., reading fluency) without testing (usually with analysing recordings and speech samples) (n=19), (4) described PD as in phonological disorder instead of Parkinson's disease (n=1). The list of the papers can be found in the Supplementary Materials.¹

Figure 1

Summary of the Search Process to Select the Studies (Related to the First 100 Results Screened)



¹ Supplementary materials are accessible at <u>https://www.rutsjournal.nl</u>.

Table 1

	Inclusion Criteria	Exclusion Criteria
Aim	Testing verbal fluency in PD with possible implications for diagnosis	Other aims
Methods	Using verbal fluency tests	Testing fluency but not using verbal fluency tests (e.g., automatic speech, fluency of speech, etc.)
Publication Type	Empirical research papers	Book chapters, reviews, manuals, etc.
Publication Language	English	Any other languages

Inclusion and Exclusion Criteria

4. Results

4.1 Overview of Main Themes

The main condition for a paper to be eligible for this systematic literature review was to have the contents that revolve around verbal fluency tasks, hence the main theme in these papers is studying verbal fluency in the population of persons with PD. However, there are more narrow themes discussed in these papers that are relevant for this literature review.

Several papers focused on cognitive deficits and different stages of PD. These include not only dementia (Azuma et al., 1997; Koerts et al., 2013; Piatt et al., 1999; Signorini & Volpato, 2006; Suhr & Jones, 1998) but also mild cognitive impairment (MCI) (Hamada et al., 2021; Yang et al., 2022) which can indicate a future decline to dementia. Verbal fluency is important when studying cognitive decline as the results of the tests might point at the stages of deterioration (e.g., Hamada et al., 2021).

Other papers concerned the relationship between PD and different aspects that are relative for patients with PD. Considering executive function and its connection to verbal fluency is a prominent direction of research when it comes to several papers (Barbosa et al., 2017; Hedman et al., 2022). Differentiating the deficits of executive function from the deficits of language can be difficult, and this is why research in this direction is of significance. Medication (Herrera et al., 2012) and DBS (Romann et al., 2017) are other factors potentially influencing verbal fluency in PD. Persons with PD on and off dopamine medication have different outcomes in verbal fluency tests, therefore, describing these differences is essential. As for STN-DBS, there have been multiple studies on its impact on patients' wellbeing and the rate of cognitive deterioration. However, the relationship between DBS and verbal fluency still requires a lot of research (Beitz, 2014).

A few papers were primarily concerned with action fluency (Bayram & Akbostanci, 2018; Rodrigues et al., 2015; Signorini & Volpato, 2006). The tendency to look closely at testing verbs can also be observed in other fields of studying language in clinical populations. For instance, action naming has become more common in preoperative and intraoperative language mapping during awake brain surgery in order to diminish the possible aphasia outcomes (Rofes & Miceli, 2014). More attention is paid to verbs and action language when it comes to studying clinical populations, and understandably, persons with PD should also be looked at closely.

In several papers, neuroscientific methods were used to study verbal fluency. Functional imaging helps to learn more about verbal fluency abilities of patients with PD on a neuroimaging level (Ellfolk et al., 2014; Hamada et al., 2021). This can be a major strand for future research as neuroscientific methods can uncover the areas of brain involved in different processes relating to verbal fluency.

4.2 Employed methods

In this part of the literature review, the methods used in the chosen papers are presented.

4.2.1 Types of tests

The tests that were used in the papers selected for this systematic literature review most often were semantic and phonemic (letter) fluency tests. Semantic fluency testing was present in 16 out of 17 papers, and phonemic fluency was in 14 out of 17 papers. When semantic fluency is tested, the most frequently used semantic category is *animals*. It is considered standard and has many benefits, for instance, examining clustering and switching between subcategories can be achieved quite easily for this category. When phonemic fluency is tested, the most frequently used letters are *F*, *A* and *S* which are also considered standard for English. In some papers, only one semantic category or letter was tested but often two or more groups in both fluency

tests are used.

There are verbal fluency tests that are less common than phonemic and semantic fluency tests but are employed nonetheless. Name fluency is a rather uncommon task which involves generating names starting with a specific letter. It is a task with an additional constraint that is used in the study by Azuma (1997). In an initial-letter-specific name fluency task the participants produce names beginning with a letter M (e.g. Mila, Mary, etc.). This task is used to understand how PD patients perform in tasks that are more effortful than semantic or phonemic fluency tests.

Action fluency is a test that is gaining popularity in the 2020s. The task for the participants is to name as many verbs as they can. The verbs should be infinitives and the same word forms should not be named (e.g., *go, gone, going*). It is interesting that action naming in verbal fluency testing is becoming more common now, as there is also a tendency to use it more often in language testing during awake brain surgery (Rofes & Miceli, 2014).

Regarding semantic fluency, in the experiment by Azuma (1997), the tasks were divided into sets, and the semantic categories were animals and fruits (Set A), and vegetables and colours (Set B). Before the main part of the task participants were given a category to practice with. For the practice session for semantic category, transportation was chosen. Both sets were given to all participants. In the other studies, when one category was tested, it was usually the *animals* category (Barbosa et al., 2017; Bayram & Akbostanci, 2018). When there were multiple categories in an experiment, there was a wider range of categories, for example, categories like *fish*, *flowers*, *weapons*, fruits, birds, clothing, insects, sports (Gurd, 2000). It can be noticed that the animals category is not used here but it is rather separated into subcategories (fish, birds, *insects*). In one of the papers, there were three unusual semantic fluency tasks present. They had two conditions, for example, the participants had to name things that are both square-shaped and hard. This was a practice task, after which feedback on the performance was provided by the examinator. Following this, the participants had to name things that are round and flat, and then things that are long and sharp (Hedman et al., 2022). It is also important not to confuse name fluency with the boys' names category which is a semantic category also used in the studies (Yang et al., 2022; Zec et al., 1999). Suhr and Jones (1998) used double categories, for instance, *fruits/vegetables* and tools/kitchen utensils.

As for the phonemic fluency, in the experiment by Azuma (1997), where the tasks were divided into sets, the letters for the phonemic fluency were A and S (Set A), and F and D (Set B). The letter for the practice category was T. In general, the choice of the letters is dependent on the language. For instance, in a study on the Turkish language, the English letters for F, A and S, correspond to the Turkish letters K, A and

S, respectively. As a result, a slight modification was done (Bayram & Akbostanci, 2018). In Japanese, the letter system is completely different, therefore the participants had a task to generate as many words as possible, beginning with the Japanese letter that is pronounced as /ka/ (Hamada et al., 2021). In Dutch, the letters used were D, A and T (Koerts et al., 2013). In Portuguese, the letters were P, M and R. They were selected instead of more popular F, A and S as they were a better fit for Portuguese based on their orthographic transparency and the number of words in a Portuguese dictionary beginning with these letters (Rodrigues et al., 2015). However, in a study on Brazilian Portuguese by Romann et al. (2017), the letters were of the standard FAS version. Overall, the F, A and S letters are used most often (e.g., Signorini & Volpato, 2006; Yang et al., 2022; Zec et al., 1999). Another version that is also used is the CFL test which is found to be more difficult (e.g., Suhr & Jones, 1998).

As for the other types of verbal fluency tests, in the alternating semantic fluency tasks, *animals* and *furniture* were chosen as the categories by Ellfolk et al. (2014). *Fruits* and *furniture* were agreed by Yang et al. (2022), while Zec et al. (1999) picked *colours* and *occupations*, and *animals* and *states*. For alternating phonemic fluency, letters *C* and *P* were chosen (Zec et al., 1999). In the name experiment by Azuma (1997), names that participants had to say needed to start with the letters *M* and *J* (Set A), and *L* and *P* (Set B). The letter for the practice category was *B*.

4.2.2 Carrying out testing

The standard time of testing is one minute. However, it is not the case in every study. In older papers, the time could be longer, for instance, five minutes for the phonemic fluency task and four minutes for the semantic fluency task (Flowers et al., 1995). However, in their study, Hedman et al. (2022) opted for the longer time for the tasks as well. The semantic fluency task had two constraints, and since it was a more difficult task than a regular semantic fluency task, two minutes were allotted.

The instructions for participants need to be clear in order to be understandable. This is how Flowers et al. (1995, p. 35) describe the instructions given in the experiment: "Tell me as many words as you can think of beginning with the letter S; keep going until I tell you to stop". In the next task (for semantic fluency), it was indicated to the participants that they no longer had to rely on the letter S and only the semantic category of words was relevant.

When giving scores to the participants, different strategies were used in different studies. Usually, one point was given for each correct example of a word. The points were not given when, for instance, in the semantic fluency task, participants named general category exemplars (like *birds* for the *animals* category, even though the *birds* group has many other exemplars inside it), or when they named words that

began with the same phoneme but a different letter (*cement* for a condition of letter *S*) in the phonemic fluency task. When it came to the name fluency, a name reference book and the researchers' common knowledge were taken into account (Azuma et al., 1997). Repeated words were counted only once, and derived words were not counted (Barbosa et al., 2017). Additionally, in some studies some metrics were calculated. The percentage of intrusion (words that did not suffice the condition of the task) and repetition (any repeated word that was already given as a response before) errors were calculated in an experiment by Suhr and Jones (1998). Multiple measures were calculated by Koerts et al. (2013, p. 404–405): (1) the number of correct exemplars for a category, (2) the number of clusters (for semantic fluency – groups of at least two words in the same subcategory; for phonemic fluency – words beginning with the same two letters, rhymes, etc.), (3) the size of the largest observed cluster, (4) the number of extra-dimensional shifts (that is the shifts between different clusters, like from *pets* to *insects*), (5) the number of intra-dimensional shifts (that is the shifts within one cluster, like *European foreign animals* and *Asian foreign animals*).

In most papers, it was described or presumed that testing was conducted in a quiet and calm setting with the researchers both writing down and recording the responses given. All errors and repetitions were written down as well.

5. Discussion

In this systematic literature review, the papers that focused on verbal fluency as a method and that could give a new outlook on applying verbal fluency tests for diagnosis were summarized. The review provides a brief summary of the previous research on the topic and clarifies how it can be used in the direction of diagnosis. Several research questions were stated in the introduction of the paper that this review aims to answer, and they are going to be addressed in this section.

Verbal fluency tests are commonly used in research on PD but are not prevalent enough when it comes to diagnosis, even though their diagnostic value is quite high, particularly when it comes to cognitive deterioration in PD (e.g., Hamada et al., 2021). Areas that have been developing and are continuing to develop are the ones that are associated with action fluency (Piatt et al., 1999; Signorini & Volpato, 2006; Rodrigues et al., 2015), subcategorization as a strategy in verbal fluency tasks (e.g., Azuma et al., 1997), dementia (Piatt et al., 1999; Signorini & Volpato, 2006), and MCI (Hamada et al., 2021; Yang et al., 2022).

The first research question concerned the current state of using verbal fluency tests in patients with Parkinson's disease. The systematic literature review revealed that even though these tests have been around for quite a long time, they still have a lot of potential. The first paper included in this review was published in 1995 (Flowers et al., 1995), and the most recent papers are dated 2022 (Hedman et al., 2022; Yang et al., 2022) which indicates that fluency tests are continuing to stay relevant. Phonemic and semantic fluency tests are used most often, but other tests like the alternating verbal fluency and action fluency tests are also used in research and can be used in diagnosis.

As for the second question, different types of verbal fluency tests are used in a similar manner. The examinators present them one by one, with similar instructions and usually the same time is given to the participants. In the majority of the papers described in this review, the time for verbal fluency tasks is one minute. However, sometimes it can be extended, for instance, when a task is not an ordinary semantic fluency task but a semantic fluency task with two conditions-constraints (Hedman et al., 2022). Such a task is more difficult and therefore requires more time. The instructions are not described in all papers, but typically the task is stated, and in the case of a phonemic fluency task preceding a semantic fluency task, an additional explanation can be added (as explained in the Testing section of the review). The instructions need to be specified for the alternating verbal fluency and name fluency tasks as there are additional constraints for the items that can be said by the participants. The instructions for the action fluency task are quite vague compared to the ones for the other tasks (e.g., infinitive form of verbs, "things you can do" – Herrera et al., 2012, p. 3637). Sometimes, even an example was asked from a participant before the time started and scoring began. For example, the question after the instructions could be: "...Can you give me an example of something that people do?" - then an acceptable response had to be generated by a participant to continue with an experiment, and then an examinator clearly stated that this is the right idea for this task and asked to name as many items like this as possible in one minute (Rodrigues et al., 2015, p. 521).

Thirdly, verbal fluency testing is a convenient method in PD. The downside is that it can be unclear what exactly is tested with verbal fluency tests. It can be argued that only executive functions are tested but it can also be claimed that there are more factors influencing performance at verbal fluency tasks besides executive function (e.g., Rodrigues et al., 2015).

There are several main conclusions regarding PD that can be drawn from the literature on verbal fluency tests. The first one is that the relationships of verbal fluency tasks with a variety of different phenomena can be studied. Dementia has attracted a lot of scientific interest both in the past and today, but nowadays other stages of cognitive decline such as MCI are being explored. The second conclusion is that

persons with PD tend to experience more difficulties with verbal fluency tests. Some of these difficulties can be attributed to bradykinesia, however, others are more than just motor impairments slowing down a patient. The third conclusion is that verbal fluency tests are important for neuroimaging studies. rs-fMRI analysis showed that there is significantly reduced connectivity in the MCI group in many areas compared to the control group. What is particularly interesting is that some connectivity values were observed to correlate with the number of switches in semantic fluency task (Hamada et al., 2021). Impaired verbal fluency, in particular in semantic switching, is associated with the increased activity in the right angular gyrus in PD-MCI. A follow-up analysis for imaging results in the study showed that the right angular gyrus was revealed to be upregulated in PD-MCI patients compared to the other groups. It can be stated that the more correct responses are given in each task, the less activity can be found in the right angular gyrus (Yang et al., 2022).

Finally, based on my conclusions derived from the papers, there are multiple things that could be done to improve verbal fluency testing. It would be beneficial to have standard semantic categories for semantic fluency tasks. For the phonemic fluency task, there are two versions that are used most commonly, i.e., the FAS and the CFL versions. They can get replaced in languages other than English based on the phonology of a different language, but it is beneficial to have a version to refer to in need. Using the same letters for testing can also help when the researchers would want to compare results with other studies (however, this would only work for comparison on the material of one language). This way the impact of using different letters does not have to be considered as an influencing factor. For the semantic fluency task, the animals category is often used, however, in the papers there are multiple other options, for example, boys' names, professions, etc. The animals category is standard, but it would be favorable to have other standard semantic categories for the usage in the semantic fluency task. Animals are a good fit as clustering and switching between clusters can be analyzed quite easily. A comparable category is *professions*, as used in the study by Rodrigues et al. (2015). The researchers defined nine possible clusters (healthcare, agriculture, etc.), and the analysis of these semantic categories was also rather easy. On the contrary, when it comes to *boys' names* and *states* as used in the experiment by Zec et al. (1999), studying clustering and switching would be difficult with such categories, and it was already determined in this literature review that these performance characteristics in the semantic fluency task should be explored extensively.

Furthermore, more attention needs to be paid to other types of verbal fluency tests besides phonemic and semantic fluency tests. Action fluency is being studied as was shown in this review, but semantic fluency with additional constraints and alternating verbal fluency need to be examined further. Tasks like these are more demanding and require more effort and are on the other side of the spectrum from the action fluency task (that does not have any constraints), so it might be appropriate to explore them further.

6. Conclusion

When talking about the current stage of the art of verbal fluency tests in PD, it can be pointed out that verbal fluency testing still has a lot of potential which is why it continues to be in use. Tests are generally used in a similar manner with the same number of minutes and similar instructions given to participants. Thanks to these tests important conclusions about PD are made, for instance, the ones related to the difficulties that persons with PD have when it comes to such tests and how it is connected to other disorders such as dementia. As for future improvement, standardization of existing tests and exploration of more complex and difficult versions should be done. In summary, there are limitations in the research to date that can be changed in the future direction of the field.

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