Distinctive Verbal Fluency Patterns in Atypical Parkinsonian Syndromes

K. Matuzevičius*

A. Rotomskis**

A. Germanavičius***

A. Žimkus**

S. Kinderytė****

G. Kaubrys*****

**Vilnius University,
Faculty of Medicine*

***Vilnius University,
Faculty of Philosophy*

****Vilnius University,
Faculty of Medicine,
Clinic of Psychiatry*

*****Lithuanian University of
Educational Sciences,
Faculty of Education*

******Clinic of Neurology and
Neurosurgery, Vilnius University
Faculty of Medicine, Vilnius*

Summary. *Background.* The verbal fluency test is a brief and accurate examination of the patients cognitive and executive functions. It is very sensitive to frontal and temporal lobe disorders which are often reported in atypical parkinsonian syndromes, namely progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), and multiple system atrophy (MSA). The verbal fluency test has been included in Addenbrooke's Cognitive Examination, primarily used for screening of various types of dementia. In this study we sought to evaluate how we could differentiate between PSP, CBD and MSA using the verbal fluency test adapted to the Lithuanian – speaking population.

Patients and Methods. 8 patients with PSP, 5 patients with CBD, and 7 patients with MSA were recruited to participate in our study. The verbal fluency test consisting of two tasks adapted to the Lithuanian – speaking population was administered to each patient and total words generated for each task were evaluated. We compared the results between each patient group. Mean values with 95% Confidence Intervals and a one – way ANOVA with a post – hoc Bonferroni was used for statistical analysis.

Results. Mean values of total words generated with a 95% CI for each group respectively were: PSP – 4.87 (4.18; 5.57), CBD – 6.20 (5.64; 6.75) and MSA – 9.28 (8.26; 10.31) for phonemic fluency; and PSP – 7.00 (6.22; 7.77), CBD – 8.40 (7.71; 9.08) and MSA – 12.86 (12.03; 13.69) for semantic fluency. Statistically significant differences were noticed between and within groups in both phonemic (F=48.422, p<0.01) and semantic (F=94.991, p<0.01) fluency. Post – hoc Bonferroni analysis revealed that significant differences were in PSP group compared to MSA (p<0.01) and MSA group compared to CBD (p<0.01) for phonemic (letter) fluency and PSP group compared to MSA (p<0.01), MSA group compared to CBD (p<0.01) for semantic (category) fluency.

Conclussions. The MSA group had significantly better results in both phonemic and semantic fluency than the CBD and PSP groups and should be differentiated accordingly. Even though the fluency comparison between CBD and PSP groups held no statistical value, the score of total words generated for phonemic and semantic fluency was lower in the PSP group, which may be helpful in differentiating between these conditions. We also determined, that phonemic (letter) fluency impairement was greater in all three patient groups than the semantic (category) fluency impairement.

Keywords: verbal fluency, atypical parkinsonian syndromes, progressive supranuclear palsy, corticobasal degeneration, multiple system atrophy, cognitive assessment.

INTRODUCTION

Verbal fluency is defined as the ability to form and express words compatible with the required criteria. While a normal level of verbal fluency is necessary for optimal com-

Adresas:

Kostas Matuzevičius
Vilniaus universiteto Medicinos fakultetas
M. K. Čiurlionio g. 21, LT-03101 Vilnius
Tel. 863747754, el. paštas kostas.mt@gmail.com

munication, the verbal fluency test can be a good diagnostic tool of particular changes in the brain that might cause a disruption in normal social functioning. The test consists of two tasks – phonemic or letter fluency and semantic or category fluency. The individual is given a 60 second time interval to produce as many unique words as possible beginning with a particular letter (e.g. F, A, S) for the phonemic fluency task and a 60 second time interval to produce as many unique words as possible belonging to a specific category (e.g. animals, things you can find in a supermarket) for the semantic fluency task [1]. The test evaluates the

individual's ability to retrieve specific information, generate a response and voice it out correctly to the tester within restricted search parameters [2]. During the test, executive control processes, such as focusing on the task, selecting the words that meet the testing criteria, avoiding repetition are evaluated [3]. Broca's region and dorsolateral prefrontal cortex of the left hemisphere are active during the performace of this test. The inferior part of the left prefrontal cortex is activated during the letter (phonemic) test and the anteroinferior part of the prefrontal cortex is activated during the category (semantic) test. Poor results of the verbal fluency test can indicate disfunction of the frontal lobe, temporal cortex, and prefrontal cortex of the left hemisphere [1]. The verbal fluency test can be used to support the diagnosis of neurodegenerative diseases which cause cognitive and executive impairement, such as Alzheimer's disease or Parkinson's disease [3].

Using the verbal fluency test we sought to assess types of dementias called atypical parkinsonian syndromes: progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), and multiple system atrophy (MSA). These dementias all exibit symptomes called "Parkinsonian features" which are rarely seen in cortical dementians, such as Alzheimer's disease. Even though every one of these diseases have their own specific symptoms (even thought of as pathognomonic) there is no single symptom which can be used to make a definite diagnosis. For example – prominent tremor is most oftenly observed in Parkinson's disease, apraxia in corticobasal degeneration but both of them are seen, even though rarely and not as extensive, in progressive supranuclear palsy [4]. Patients with MSA usually exibit subcortical symptoms (e.g. parkinsonism and ataxia) and pathological changes are limited to subcortical structures. Patients with PSP have the most pronounced pathological changes in the subthalamic nucleus, zona compacta, superior colliculi, and internal pallidum. In CBD both cortical and subcortical changes have been registered. Substantia nigra (most often), striatum, thalamus colliculi, red and dentate nuclei, and inferior olive may be affected. As for the cortical pathology, direct involvement of the frontal lobes and parietal lobes had been reported [5].

The verbal fluency test is extremely useful and pratical when dealing with or suspecting such diseases because it is very easily administered and clinically meaningful in testing frontal and temporal function of the patient. In former studies it was shown that the verbal fluency test reflects the difficulty in generation of actions which is the most important feature of parkinsonian syndromes. Impaired verbal fluency was also noticed in all atypical parkinsonian syndromes but more extensive in progressive supranuclear palsy in which it is one of the earliest exibited symptom even preceding motor abnormalities. Because of such findings the verbal fluency test has been included in multiple cognitive batteries such as Dementia Rating Scale (DRS) and Adenbrooke's Cognitive Examination (ACE) [4]. We hypothesise that because of specific changes caused by PSP, CBD and MSA in the brain, the verbal fluency test may be useful in differentiating between these conditions.

AIM

Our study sought to investigate how various types of atypical parkinsonian syndromes can be differentiated with phonemic and semantic fluency tests in the Lithuanian-speaking population.

OBJECTIVES

1. To calculate the average of total words produced with 95% CI for phonemic and semantic fluency in each group.
2. To analyze the results using a one-way ANOVA and determine the significance of our findings for each patient group.

METHODS

Patients

Consecutive referrals to the Neurology Department of the Vilnius University Hospital Santariskiu Clinics were screened for possible inclusion into the study. All patients in the PSP group fulfilled clinical research criteria for the diagnosis of progressive supranuclear palsy (Steele-Richardson-Olszewski syndrome) NINDS-SPSP International Workshop [6]. All patients in the MSA group fulfilled the diagnostic criteria of the second consensus statement on the diagnosis of multiple system atrophy [7] and all patients in the CBD group fulfilled the criteria for the diagnosis of corticobasal degeneration [8]. For our testing, we recruited 20 patients with diagnosed atypical parkinsonian syndromes from the Lithuanian speaking population: 8 patients with progressive supranuclear palsy (PSP) (mean age 71, SD 5.5, education 12 years, SD 3), 5 patients with corticobasal degeneration (CBD) (mean age 73.8, SD 4.2, education 12.8 years, SD 2.9) and 7 patients with multiple system atrophy (MSA) (mean age 71, SD 4, education 13.5 years, SD 1.9). All patients had sufficient knowledge of the Lithuanian language to participate in the study. All study participants were able to perform all tasks in the test. No patients had severe hearing impairements.

Testing

The verbal fluency test adapted to the Lithuanian speaking population was administered to each patient from every group. The patients were asked to carry out two tasks: name as many words as they could think of starting with the letter P for the first task (letter fluency) and name as many animal names as they could think of for the second task (category fluency). A 60 second time period was given for the completion of each task. Proper nouns, numbers and multiple root forms of the same words were not permit-

ted. The test was carried out in the Lithuanian language. The score calculated was the total number of words generated for each task.

Data analysis

SPSS for windows was used for data analysis. We calculated the mean of total words generated with 95% CI for both phonemic and semantic fluency in each patient group. For group comparison, a one – way ANOVA with a post-hoc Bonferroni was performed to compare the mean differences of total words generated between groups and to determine whether those differences where statistically significant. The mean difference significance level was set at 0.05.

RESULTS

Mean values of total words generated with 95% confidence intervals

We calculated the mean values of total words generated with 95% CI for both phonemic and semantic fluency in each group.

The mean words generated with 95% CI for phonemic (letter) fluency (Fig. 1):
    1. PSP – 4.87 (4.18; 5.57)
    2. CBD – 6.20 (5.64; 6.75)
    3. MSA – 9.28 (8.26; 10.31)
The mean words generated with 95% CI for semantic (category) fluency (Fig. 2):
    1. PSP – 7.00 (6.22; 7.77)
    2. CBD – 8.40 (7.71; 9.08)
    3. MSA – 12.86 (12.03; 13.69)

Analysis of Variance

A one – way ANOVA with a post – hoc Bonferroni was carried out to scan for statistically significant differences in mean values of total words generated between each group. We determined that there were statistically significant differences between groups and within groups in both phonemic (F=48.422, p<0.01) and semantic (F=94.991, p<0.01) fluency. The post – hoc Bonferroni analysis revealed that significant differences were between the following groups: PSP compared to MSA (p<0.01) and MSA compared to CBD (p<0.01) for phonemic (letter) fluency and PSP compared to MSA (p<0.01), MSA compared to CBD (p<0.01) for semantic (category) fluency. The PSP (mean difference = -4.41) and CBD (mean difference = -3.09) groups showed significant impairement in phonemic fluency compared only to the MSA group. When comparing phonemic fluency values between CBD and PSP patients they held no statistical significance (p=0.051). Similar results were found in the semantic fluency group as well. PSP (mean difference = -5.86) and CBD (mean difference = -4.46) groups showed significant semantic fluency impairement compared to the MSA group. Comparison of semantic fluency values between PSP and CBD patients held no statistical significance (p=0.029).

DISCUSSION

The only definite conclusion we can make is that the MSA group had significantly better results in both phonemic and semantic fluency than the CBD and PSP groups and should be differentiated accordingly. Even though the fluency comparison between CBD and PSP groups held no statistical value, the score of total words generated for phonemic and semantic fluency was lower in the PSP group, which may be helpful in differentiating between these conditions. We also determined that phonemic (letter) fluency impairment was greater in all three patient groups than the semantic (category) fluency impairement. Similar findings were published by T. H. Bak et al (2005), stating that the cognitive impairement was not as extensive in the MSA patients compared to CBD and PSP patients. In fact, the cognitive impairement in MSA is so unpronounced, that most pa-
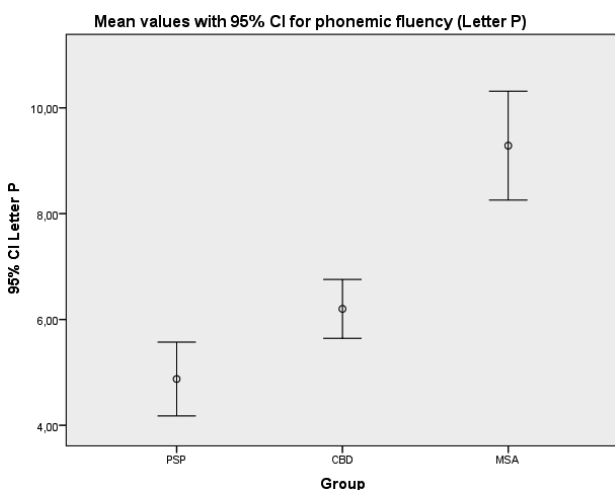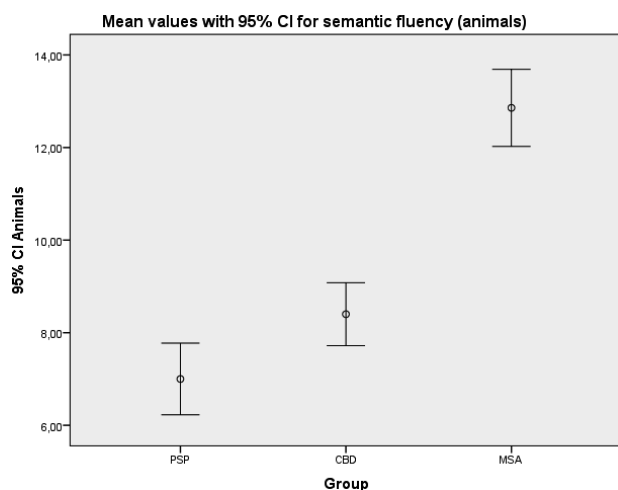

Fig. 1. **Phonemic fluency**

Fig. 2. **Semantic fluency**

tients do well on cognitive screening tests, except for verbal fluency and free recall [5, 9]. Rosser and Hodges (1994) and T. H. Bak et al (2005) demonstrated that letter fluency is more impaired in PSP than category fluency and our research supports this claim [5, 10]. Such findings would support our current understanding of the pathological changes in atypical parkinsonian syndromes: basal ganglia pathology reflected by the subcortical deficit, shared in all three diseases as well as the frontal and fronto-parietal involvement in PSP and CBD [5].

The drawback of our study was a low number of patients in each group. The results would have been more reliable if it was possible to include more patients in the study.

The verbal fluency test does not evaluate all the changes usually found in atypical parkinsonian syndromes, which is why we recommend to asses patients with the full ACE test for a definite diagnosis. However, the fluency test is useful because it it brief, easy to administer and can be performed at the patient's bedside while being sensitive to executive and cognitive abnormalities in atypical parkinsonian syndromes [5]. We recommend the verbal fluency test to be carried out for every patient with an atypical parkinsonian syndrome.

References

1. Wysokiński A, Zboralski K, Orzechowska A, Gałecki P, Florkowski A, Talarowska M. Normalization of the Verbal Fluency Test on the basis of results for healthy subjects, patients with schizophrenia, patients with organic lesions of the chronic nervous system and patients with type 1 and 2 diabetes. Arch Med Sci 2010; 6(3): 438–46.

2. Patterson J. Verbal fluency. In: Kreutzer JS, DeLuca J, Caplan B, eds. Encyclopedia of clinical neuropsychology [Internet]. Springer New York, 2011 [cited 2015 Apr 19]; 2603-6. Available at: link.springer.com/referenceworkentry/10.1007/978-0-387-79948-3_1423

3. Shao Z, Janse E, Visser K, Meyer AS. What do verbal fluency tasks measure? Predictors of verbal fluency performance in older adults. Front Psychol 2014; 5: 772.

4. Bak T. Cognitive profiles of Parkinsonian syndrome. Adv Clin Neurosci Rehabil 2006; 12–4.

5. Bak TH, Crawford LM, Hearn VC, Mathuranath PS, Hodges JR. Subcortical dementia revisited: Similarities and differences in cognitive function between progressive supranuclear palsy (PSP), corticobasal degeneration (CBD) and multiple system atrophy (MSA). Neurocase 2005; 11(4): 268–73.

6. Litvan I, Agid Y, Calne D, Campbell G, Dubois B, Duvoisin RC, et al. Clinical research criteria for the diagnosis of progressive supranuclear palsy (Steele-Richardson-Olszewski syndrome) Report of the NINDS-SPSP International Workshop. Neurology 1996; 47(1): 1–9.

7. Gilman S, Wenning GK, Low PA, Brooks DJ, Mathias CJ, Trojanowski JQ, et al. Second consensus statement on the diagnosis of multiple system atrophy. Neurology 2008; 71(9): 670–6.

8. Armstrong MJ, Litvan I, Lang AE, Bak TH, Bhatia KP, Borroni B, et al. Criteria for the diagnosis of corticobasal degeneration. Neurology 2013; 80(5): 496–503.

9. Bak TH, Rogers TT, Crawford LM, Hearn VC, Mathuranath PS, Hodges JR. Cognitive bedside assessment in atypical parkinsonian syndromes. J Neurol Neurosurg Psychiatry 2005; 76(3): 420–2.

10. Rosser A, Hodges JR. Initial letter and semantic category fluency in Alzheimer's disease, Huntington's disease, and progressive supranuclear palsy. J Neurol Neurosurg Psychiatry 1994; 57(11): 1389–94.

K. Matuzevičius, A. Rotomskis, A. Germanavičius, A. Žimkus, S. Kinderytė, G. Kaubrys

ŽODINIO SKLANDUMO YPATUMAI, SERGANT ATIPINIAIS PARKINSONIZMO SINDROMAIS

Santrauka

Įžanga. Žodinio sklandumo testas yra naudojamas greitai ir tiksliai paciento kognityvinėms funkcijoms įvertinti. Jis yra patikimas ir jautrus įrankis frontalinių ir temporalinių sričių pažeidimams atpažinti, kurie dažnai pasitaiko sergant atipiniais parkinsonizmo sindromais, tokiais kaip progresyvus supranuklearinis paralyžius (PSP), kortikobazalinė degeneracija (CBD) ir dauginė sistemų atrofija (MSA). Žodinio sklandumo testas įtrauktas į Adenbruko testų bateriją (angl. *Adenbrooke's Cognitive Examination*), naudojamą ankstyvai demencijų diagnostikai. Savo tyrime norėjome įvertinti, ar galima diferencijuoti tarp PSP, CBD ir MSA sindromų pagal žodinio sklandumo testą, pritaikytą lietuviškai kalbančiai populiacijai.

Pacientai ir metodai. Į mūsų tyrimą buvo įtraukti 8 pacientai, sergantys PSP, 5 pacientai, sergantys CBD, ir 7 pacientai, sergantys MSA. Kiekvienas pacientas atliko žodinio sklandumo testą, sudarytą iš dviejų užduočių ir pritaikytą lietuviškai kalbančiai populiacijai, buvo suskaičiuoti visi pacientų sugeneruoti žodžiai kiekvienoje testo dalyje. Atlikę vienfaktorinę dispersinę analizę (angl. *One - way ANOVA*) ir suskaičiavę sugeneruotų žodžių vidurkius su 95 % pasikliautiniais intervalais, palyginome rezultatus tarp visų pacientų grupių.

Rezultatai. Sugeneruotų žodžių vidurkiai su 95 % pasikliautiniais intervalais PSP, CBD, ir MSA grupėms atitinkamai buvo 4,87 (4,18; 5,57), 6,20 (5,64; 6,75) ir 9,28 (8,26; 10,31) foneminiam sklandumui ir 7,00 (6,22; 7,77), 8,40 (7,71; 9,08) ir 12,86 (12,03; 13,69) – semantiniam sklandumui. Vienfaktorinė dispersinė analizė parodė, kad tarp grupių buvo aptikti statistiškai reikšmingi ir foneminio sklandumo (F = 48,422, p < 0,01), ir semantinio sklandumo (F = 94,991, p < 0,01) skirtumai. Post-hoc Bonferonni analizės metu aptikta šių reikšmingų skirtumų: foneminio sklandumo, lyginant PSP su MSA (p < 0,01) ir MSA su CBD (p < 0,01), bei semantinio sklandumo, lyginant PSP su MSA (p < 0,01) ir MSA su CBD (p < 0,01).

Išvados. MSA grupės pacientai daug geriau atliko ir foneminio, ir semantinio sklandumo užduotis, lyginant su PSP ir CBD grupėmis. Nors rezultatų skirtumas tarp PSP ir CBD grupių nebuvo statistiškai reikšmingas, tačiau bendras sugeneruotų žodžių kiekis abiejose užduotyse buvo visada mažesnis PSP grupėje nei CBD grupėje ir galėtų padėti diferencijuojant šiuos sindromus. Mūsų tyrimas parodė, kad foneminio sklandumo pažeidimas buvo ryškesnis nei semantinio sklandumo pažeidimas visose trijose pacientų grupėse.

Raktažodžiai: žodinis sklandumas, atipiniai parkinsonizmo sindromai, progresuojantis supranuklearinis paralyžius, kortikobazalinė degeneracija, dauginė sistemų atrofija, kognityvinių funkcijų įvertinimas.