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Original research article

Writing in Richardson variant of progressive supranuclear palsy in comparison to progressive non-fluent aphasia

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ABSTRACT

Background: The overlap between progressive supranuclear palsy (PSP) and progressive non-fluent aphasia (PNFA) is being increasingly recognized. In this paper descriptive writing in patients with Richardson syndrome of progressive supranuclear palsy (PSP-RS) is compared to writing samples from patients with PNFA.
Methods: Twenty-seven patients participated in the study: 17 with the clinical diagnosis of PSP-RS and 10 with PNFA. Untimed written picture description was administered during neuropsychological assessment and subsequently scored by two raters blinded to the clinical diagnosis. Lexical and syntactic content, as well as writing errors (e.g. omission and perseverative errors) were analyzed.
Results: In patients with PSP-RS both letter and diacritic mark omission errors were very frequent. Micrographia was present in 8 cases (47%) in PSP-RS group and in one case (10%) with PNFA. Perseverative errors did not differentiate between the groups.
Conclusions: As omission errors predominate in writing of patients with PSP-RS, writing seems to be compromised mainly because of oculomotor deficits, that may alter visual feedback while writing.

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1. Introduction

Richardson–Steele–Olszewski syndrome, also known as progressive supranuclear palsy (PSP), was initially described as a mainly movement disorder with early falls, gaze palsy, axial rigidity and retrocollis [1]. However, cognitive, behavioral and language problems in PSP are being increasingly recognized [2].

Writing impairment in neurodegenerative disorders may be due to linguistic, cognitive and/or motor deficits. Patients with PSP present with progressive abnormalities of (oculo) motor, cognitive and language functions [3]. Thus, their writing impairment may be compromised because of different motor and non-motor factors.

The relationship of writing errors to cognition (especially attention and executive function) is best described in the context of Alzheimer's disease [4], while the impact of hypokinesia on writing is well known from studies in Parkinson's disease (PD) [5]. Despite early observations of writing impairment in PSP [6], literature on writing in PSP remains very limited. Early report on language functions in PSP identified, in terms of writing, both degradation of graphical performance due to motor deficits and dysgraphic errors, of which letter omission was the most commonly observed error type [6].

In terms of motor features, micrographia is more common in PSP than in PD. However, in PSP, in contrast to PD patients, it is not characterized by decrement in script size while writing [7], so its pathophysiology may be also different than in PD.

Recently, the overlap between atypical Parkinsonian syndromes and spectrum of primary progressive aphasia (PPA) is being increasingly recognized [8,9]. On the one hand, in the spectrum of PSP phenotype, a specific subtype with progressive non-fluent aphasia (PSP–PNFA) is recognized [2,9]. On the other hand, Parkinsonian features are more frequently identified in patients with PNFA than in patients with logopenic variant of PPA [10].

Frequent letter omission errors that were reported in PSP [6], may be related to oculomotor impairment, apraxia of eyelid opening and retrocollis, all of which make visual control of handwriting very difficult or even impossible in some cases.

This paper aims at comparing several aspects of writing in patients with PSP-RS and PNFA. It is hypothesized that omission errors affecting both letters and diacritical marks are more common in PSP-RS. Perseveration errors are expected to appear in writing samples by patients with PSP-RS. Micrographia is hypothesized to occur both in PSP-RS and in patients with PNFA, in line with previous report on Parkinsonian features in PNFA [10].

2. Patients and methods

2.1. Participants

Twenty-seven Polish speaking patients participated in the study: 17 (9 men, 8 women) with the clinical diagnosis of PSP-RS according to Litvan et al. criteria [3] (10 probable, 7 possible) and 10 (2 men, 8 women) with PNFA, diagnosed at level I according to Gorno-Tempini et al. criteria [11] (see Table 1). The patients were diagnosed in two centers specializing in the differential diagnosis of neurodegenerative disorders. None of

Table 1 – Patients' demographic characteristics.					
	Clinical diagnosis	Sex	Age at onset	Age at testing	Years of education	MMSE score (max. 30)
1	Possible PSP	F	71	74	17	25
2	Probable PSP	F	66	69	13	24
3	Possible PSP	F	63	66	16	29
4	Possible PSP	M	84	87	15	27
5	Probable PSP	M	80	82	13	25
6	Probable PSP	F	64	69	16	23
7	Possible PSP	M	57	58	22	30
8	Probable PSP	F	68	71	13	25
9	Probable PSP	M	74	77	13	20
10	Probable PSP	M	54	59	15	29
11	Possible PSP	F	63	65	13	27
12	Probable PSP	M	74	77	14	25
13	Possible PSP	M	47	50	17	29
14	Probable PSP	F	54	55	11	23
15	Possible PSP	F	78	81	9	26
16	Probable PSP	M	68	71	10	22
17	Probable PSP	M	77	80	15	23
18	PNFA	F	70	75	12	–
19	PNFA	F	55	56	14	
20	PNFA	M	62	65	12	
21	PNFA	F	79	81	11	
22	PNFA	F	71	72	11	
23	PNFA	M	82	86	16	
24	PNFA	F	69	70	11	
25	PNFA	F	68	70	16	
26	PNFA	F	67	69	16	
27	PNFA	F	63	65	11	

the patients with PNFA fulfilled criteria for PSP-RS and vice versa in at least 12-month follow-up.

The patients' age averaged 70 ± 10 years in PSP-RS and 71 ± 8 years in PNFA group. Time since symptom onset ranged at the time of the study from 1 to 5 years both in PSP-RS and in PNFA groups. However, in the cases of both patient groups subsequent follow-up examinations (1–3 years after the baseline testing) confirmed the initial diagnosis. Thus, in each case there was at least 2-year history of PSP-RS or PNFA. The groups were matched in terms of age ($p = 0.829$) and years of education ($p = 0.275$). All participants volunteered for this study and provided informed consent to participate. The study procedures were approved by local Bioethics Committee.

2.2. Methods

Descriptive writing samples, written in Polish, were collected and analyzed. Polish language belongs to West Slavic group of the Indo-European languages, consisting of 32 letters, nine of which are differentiated with the use of diacritics. Polish, as Latin, is an inflectional language, but in contrast to English and many other European languages, does not contain articles.

To assess the patients' descriptive writing the untimed written description of one of three pictures was administered: cookie theft picture from Boston Diagnostic Aphasia Examination-3 (BDAE-3), A beach scene by Prof. EK Warrington or picture from Frenchay Aphasia Screening Test [12]. The components of BDAE were previously used in Polish patients [13,14], however as there are no Polish normative data, only raw data was analyzed.

The choice of various pictures was due to the fact that most patients were administered an oral picture description task few days before the study procedure and the use of the same picture for a written task was not considered appropriate. Written picture description was administered by a neuro-psychologist (EJS or AB). All picture descriptions were subsequently scored by two independent raters specializing in speech pathology (KKK and MK). The raters were aware of the spectrum of disorders being analyzed, but they were blinded to the clinical diagnosis in each patient. Divergent scores were discussed with the third rater (EJS) and scores reported were reached by consensus. For each assessed parameter raw scores (number of occurrences) were used in the analysis: number of words, lexical content (number of nouns and verbs), letter errors (omissions, additions, substitutions and transpositions), perseverative errors (words, phrase construction), syntactic structure parameters (number of sentences, number of complex sentences and correct sentences, max. sentence length). Raters were also asked to detect features suggestive of micrographia, the presence of omission of diacritical marks, punctuation errors and the use of mixed script (cursive and print).

Subsequently, so as to make the results independent of the variable sample length, several variables were computed as ratio or proportion of raw scores (e.g. percentage of nouns to total number of words used).

Additionally, Mini-Mental State Examination [15] was applied to patients with PSP-RS. Due to the severity of language problems in individuals with PNFA, it could not be administered to all patients. Thus, MMSE score is reported only for patients with PSP-RS.

2.3. Statistical analysis

The normality of distribution was tested with the use of Shapiro–Wilk test and the homogeneity of variance with Levene's test. For normally distributed data t-test for independent samples was used, while for non-normally distributed data Mann–Whitney U test was applied. The qualitative data was analyzed with the use of chi-square test.

3. Results

Patients with PSP-RS provided longer writing samples than individuals with PNFA. However, the lexical content, analyzed independently of writing sample length (when percentage of nouns/verbs was considered), was similar in all groups (see Table 2). Letter errors were more frequent in PSP-RS than PNFA. More specifically, letter omission errors were slightly more frequent in PSP-RS, which was not statistically significant.

Table 2 – Comparison of descriptive writing in patients with Richardson variant of progressive supranuclear palsy (PSP-RS) and patients with non-fluent progressive aphasia (PNFA).

	PSP-RS $n = 17$	PNFA $n = 10$	p[*]
General output characteristics			
Overall number of words (rs)	37 (21)[a]	15.6 (8.44)	0.005
Nouns (rs)	15.82 (7.14)	7.6 (4.72)	0.003
Verbs (rs)	6.53 (2.35)	3.4 (1.96)	0.002
Lexical content			
Percentage of nouns	46.15 (8.87)	47.81 (10.76)	0.669
Percentage of verbs	20.36 (6.96)	22.09 (7.07)	0.540
Letter errors			
Omissions (rs)	2.5 (0–8)[b]	1 (0–2)	0.053
Additions (rs)	0 (0–6)	0 (0–2)	0.551
Substitutions (rs)	2 (0–7)	1 (0–3)	0.363
Transpositions (rs)	0 (0–1)	0 (0–1)	0.938
Letter errors – sum (rs)	6.38 (5.16)	2.4 (1.90)	0.011
Perseverations			
Perseveration – word level (rs)	0	0	–
Perseveration – sentence level (rs)	0 (0–1)	0	0.824
Syntactic structure			
Max. sentence length	9 (0–22)	5.5 (4–10)	0.093
Sentences (rs)	5.24 (1.52)	2.9 (1.66)	0.001
Complex sentences[c] (rs)	5 (2–9)	0.5 (0–1)	0.170
Correct sentences[d] (rs)	4 (1.62)	2.20 (1.87)	0.014

rs-raw score.
[*] Intergroup comparisons were performed with t-test for independent sample or Mann–Whitney U test.
[a] Mean (SD).
[b] Median (range).
[c] Number of sentences containing more than one phrase composed of subject and predicate.
[d] Number of sentences without syntactic errors.

Table 3 – Comparison of script in patients with Richardson variant of progressive supranuclear palsy (PSP-RS) to patients with non-fluent progressive aphasia (PNFA).			
	PSP-RS $n = 17$	PNFA $n = 10$	p^*
n of cases/percentage			
Features of micrographia	8 (47%)	1 (10%)	0.091
Omission of diacritical marks	15 (94%)	6 (60%)	0.153
Punctuation errors	14 (82%)	6 (60%)	0.365
Mixed script: cursive/print	1 (6%)	1 (10%)	0.613
* Statistical analysis was performed with chi-square test.			

In terms of script features, half of the patients with PSP-RS had unequivocal micrographia, while only one patient with PNFA presented with this symptom (see Table 3). Also, most patients with PSP-RS were likely to omit diacritical marks. This tendency was less frequent in PNFA, but the difference was not statistically significant. No differences were noted in terms of perseverative or punctuation errors.

4. Discussion

This paper adds to the discussion about the overlap between PSP-RS and PNFA and changing classifications of frontotemporal lobar degeneration syndromes, analyzing writing performance in PSP-RS and PNFA. In our study patients with PSP-RS were found to commit more omission errors than individuals with PNFA. This is in line with the early report by Podoll et al. [6] assessing writing to dictation, in which 4 out of 6 PSP patients committed dysgraphic errors and 87% of dysgraphic responses were letter omissions. They also reported the occurrence of word omissions, letter perseverations, additions and transpositions in PSP, but much less frequently than letter omissions. Spelling errors other than omissions, such as letter additions, substitutions and transpositions were also present in our PSP-RS sample. Only in one case of PSP-RS letter addition was clearly perseverative ("mototorowa" instead of "motorowa" – in Polish). However, no word perseverations and only one phrase perseveration were observed in writing samples produced by patients with PSP-RS. As omission errors predominate in PSP-RS and other spelling errors are infrequent, oculomotor deficits may have compromised the patients' performance. While good proprioception remains the most important factor for writing [16], visual control is associated with writing speed and legibility [17]. In patients with PSP, not only vertical but also horizontal saccades are affected [18]. As vertical saccadic impairment is an early and predominant feature in PSP and – especially if associated with retrocollis and/or apraxia of eyelid opening – it may prevent the patient from looking down at his/her handwriting. However, as reading and writing require horizontal movements they may be differentially affected by the deficient horizontal saccades. Future studies should address the relationship of handwriting errors in PSP to the impairment of vertical and horizontal saccades.

The differential impact of disturbance in distinct aspects of saccadic movements on writing may be also suggested by the complexity of their cerebral correlates. Saccades are thought to be controlled at the level of brainstem structures (in terms of direction, amplitude and velocity), rostral cerebellum [19] and the cortex (frontal and supplementary eye fields being crucial for voluntary saccadic movements and smooth pursuit) [19,20]. However, recent studies, using diffusion tensor imaging MRI (DTI MRI), have shown the importance of white matter tracts microstructure integrity for visual processing, both in healthy controls [21] and PSP patients [22]. Voineskos et al. [21] evidenced that the integrity of inferior longitudinal fasciculsus (ILF), subserving a "direct short-latency pathway" of visual processing [23], is important for visuomotor dexterity and fast visual processing. Whitwell et al. [22] detected early diffusivity changes within the inferior and superior longitudinal fasciculi in PSP, the latter correlated with the degree of saccadic impairment. The dysfunction, and subsequent atrophy of these tracts [24] is likely to contribute to writing impairment in PSP.

Of note, in our study perseveration errors were very uncommon in writing samples produced by patients with PSP-RS. It may be surprising as executive dysfunction is a core feature of PSP [25] and attention and executive function strongly contribute to writing performance in patients with Alzheimer's disease [4]. However, as writing in general is a difficult task for PSP patients and obviously it requires additional conscious effort in a descriptive writing task, so that automatic perseverative reactions may be more efficiently suppressed in writing than in spontaneous speech. Palilalia (repetition of words or phrases), which is considered typical PSP feature [26], as it is observed during conversation, is also not as common in objective measurements in controlled conditions [27]. There are no data comparing the incidence of palilalia in a conversation and in oral picture description. However, both the task specificity (picture description as opposed to spontaneous speech/writing) and its difficulty may prevent perseverative tendencies.

Half of our PSP-RS group presented with micrographia, which was previously described as a common feature in PSP [7]. Interestingly, in PD micrographia is reduced when visual feedback is unavailable [28]. However, as micrographia profile is different in PSP than in PD, with no script decrement while writing [7], the positive effect of lack of visual feedback on micrographia in PSP is very doubtful.

In line with our expectations, micrographia did appear in one individual with PNFA. It is consistent with the observation of Parkinsonian features, such as bradykinesia, Parkinsonian speech/facial expression and possibly rigidity in patients with PNFA [10]. Our findings also support the relationship between PSP and PNFA that is not restricted to PSP–PNFA phenotype [9] as some symptom overlap is noted between PSP-RS and PNFA.

Our study has several shortcomings. We have not used computerized assessment of handwriting that was recently shown to better detect dysgraphia in PD than paper and pencil tasks [29]. Three different pictures were used to elicit writing samples. However, the pictures used in our study are very commonly used to assess descriptive speech [29,30] and as shown by Ash et al. the use of different stimuli (Cookie Theft vs. Frog Story) does not significantly influence the picture description outcomes [31]. The descriptive writing, that is very variable in healthy population [4], was not compared to writing to dictation. Also, small group sizes and heterogenous

pharmacological and non-pharmacological therapy options used did not allow to study the effect of medication or speech therapy on descriptive writing. Longitudinal observation of the evolution of writing impairment in PSP could possibly shed light upon its main underlying cause, progressive language impairment, working memory deficit or oculomotor dysfunction.

Our findings suggest that writing impairment in PSP-RS is compromised mainly because of oculomotor deficits, which needs confirmation in further research with oculographic assessment. Moreover, they support overlap between PSP and PPA syndromes that extends beyond PSP–PNFA phenotype.

Conflicts of interest

We have no conflicts of interests.

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Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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