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Is descriptive writing useful in the differential diagnosis of logopenic variant of primary progressive aphasia, Alzheimer's disease and mild cognitive impairment?

Emilia J. Sitek [a,b,*], *Anna Barczak* [c], *Klaudia Kluj-Kozłowska* [a,d], *Marcin Kozłowski* [d,e], *Maria Barcikowska* [f], *Jarosław Sławek* [a,b]

[a] *Neurology Department, St. Adalbert Hospital, Copernicus Podmiot Leczniczy Sp. z o.o., Gdansk, Poland*
[b] *Department of Neurological and Psychiatric Nursing, Medical University of Gdansk, Gdansk, Poland*
[c] *Neurology Department, Central Clinical Hospital of the Ministry of Interior, Warsaw, Poland*
[d] *Speech Therapy Department, Faculty of Languages, University of Gdansk, Gdansk, Poland*
[e] *Neurological Rehabilitation Department, Specialist Hospital in Koscierzyna, Dzierzazno, Poland*
[f] *Neurodegenerative Disorders Department, Mossakowski Medical Research Center, Polish Academy of Sciences, Warsaw, Poland*

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ABSTRACT

Current classification of primary progressive aphasia (PPA) encompasses three variants: non-fluent (nfvPPA), semantic (svPPA) and logopenic (lvPPA). Previously lvPPA was regarded as aphasic form of Alzheimer's disease (AD). However, not all patients with lvPPA phenotype present with AD pathology. Despite abundant literature on differentiation of lvPPA from svPPA and nfvPPA, studies comparing lvPPA with AD and mild cognitive impairment (MCI) are scarce. This study aimed at analyzing written descriptive output in lvPPA, AD and MCI. Thirty-five patients participated in the study: 9 with lvPPA, 13 with AD and 13 with MCI. Most aspects of writing performance were comparable in three groups. However, letter insertion errors appeared in 44% patients with lvPPA, while they were absent in AD and MCI. Patients with lvPPA used more verbs than patients with AD. Writing profile may complement other neuropsychological assessment results in the differential diagnosis of lvPPA. Letter insertion errors and frequent verb use may raise a query of lvPPA.

* *Corresponding author at*: Copernicus PL Sp. z o.o., St. Adalbert Hospital, Neurology Department, Al. Jana Pawła II 50, 80-462 Gdańsk, Poland. Tel.: +48 58 768 46 61; fax: +48 58 349 92 90.
E-mail address: emiliasitek@gumed.edu.pl (E.J. Sitek).
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1. Introduction

Primary progressive aphasia (PPA) is currently regarded as a spectrum of progressive language disorders due to either frontotemporal lobar degeneration (FTLD) or Alzheimer's disease (AD). The most recent PPA subdivision encompasses its three variants: non-fluent (nfvPPA), semantic (svPPA) and logopenic (lvPPA) [1,2]. The last, logopenic variant, described formally in 2004 by Gorno-Tempini et al. [3] was previously regarded as language variant of AD [4]. Logopenic progressive aphasia is characterized by word-finding difficulties (with preserved semantic knowledge and word comprehension), impaired phonological processing and short verbal span causing deficient repetition and comprehension of long sentences [5–9].

While svPPA has a clinically distinct profile, with generalized semantic impairment and circumscribed temporal pole atrophy, the differentiation of lvPPA from nfvPPA remains challenging in the clinic [1,10–12], especially in patients with more advanced disease. In the research setting beta-amyloid imaging and cerebrospinal fluid biomarkers profile assessment are very useful for the differential diagnosis between AD and FTLD pathology [13]. However, their availability is very limited. Moreover, a subset of patients with lvPPA has negative beta-amyloid imaging [14]. Thus, the diagnosis of lvPPA is established mainly on the basis of the clinical presentation and longitudinal observation. Patients with lvPPA show rapid and wide-spread cognitive deterioration [7,15,16] and decline in the activities of daily living [17]. Several algorithms have been proposed to differentiate between three variants of PPA [18–20]. However, in the clinical practice lvPPA needs to be differentiated not only from nfvPPA and svPPA, but also from AD and mild cognitive impairment. This differentiation is important for planning patient management, as patients with lvPPA require more frequent neuropsychological follow-ups and language intervention.

Thus, neuropsychological assessment is crucial for early differential diagnosis. Magnin et al. [21] has recently shown that lvPPA (in comparison to AD and MCI) is characterized by a recent onset or aggravation of anxiety, preserved orientation to time, poor verbal span and fluency, dissociation between poor verbal memory performance and much better visual memory performance as well as very impaired mental calculation. This is to our knowledge, the only paper addressing the neuropsychological differential diagnosis of lvPPA from MCI and AD.

Agraphia in the context of AD is quite well described in the literature [22] and written output is more sensitive than spoken output to early language problems in AD [23]. In the course of AD initial lexical dysgraphia (that affects spelling of irregular words) progresses to phonological agraphia (that affects also spelling of regular words due to graphemic buffer impairment). Moreover, agraphia in AD is closely related to cognitive impairment, mainly attentional and executive deficits [22], typical for the later disease stages. Writing assessment in the context of AD spectrum differential diagnosis may also be helpful to detect parkinsonian features (more likely in nfvPPA than lvPPA) or spatial problems, suggestive of posterior cortical atrophy.

The current diagnostic criteria for PPA highlight the role of writing assessment in the diagnosis of svPPA, which is characterized by surface dysgraphia [1]. However, psycholinguistic assessment of spelling in patients with nfvPPA, lvPPA, svPPA and unclassified PPA showed that spelling errors lack variant specificity and all PPA patients, regardless of the PPA variant, may present with impaired access to lexical or lexical-semantic representations, impaired sublexical phonology-to-ortography conversion and graphemic buffer impairment [24]. Most commonly, patients with lvPPA have lexical or surface dysgraphia, but there are also reports of graphemic buffer disorder [25].

Our study aimed at establishing the value of written picture description in the differentiation of lvPPA from AD and MCI. It was hypothesized that lexical content will be most impoverished in lvPPA, due to prominent word-finding difficulties. Similarly, it was expected that spelling errors will be more common in lvPPA than in AD and MCI, because of primary phonological deficit in lvPPA.

2. Materials and methods

2.1. *Participants*

Thirty-five patients participated in the study: nine (seven women, two men) with the clinical diagnosis of lvPPA according to Gorno-Tempini et al. criteria [1], 13 with mild AD (seven women, six men) diagnosed according to the criteria by McKhann [26], scoring 1 on Clinical Dementia Rating (CDR) [27] and 13 patients with MCI (CDR = 0.5) (11 women, 2 men) according to the criteria by Petersen [28]. Within the MCI group eight patients had amnestic MCI and five multiple-domain MCI (amnestic with attentional deficits). The patients were diagnosed in two centers specializing in the differential diagnosis of neurodegenerative disorders. The groups were matched in terms of years of education (see Table 1), sex ($p = 0.196$) and time since onset ($p = 0.320$). The lvPPA group did not significantly differ in age either from MCI or AD group. The MCI group was significantly younger than the AD group. The median time since symptom onset was 2 years in both lvPPA and AD and it ranged from 1 to 10 years in lvPPA and from 1 to 6 years in AD. None of the patients reported the history of developmental language problems (e.g. dyslexia or dysgraphia). All participants volunteered for this study and provided informed consent to participate. The study procedures were approved by local Bioethics Committee.

2.2. *Methods*

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 [29], picture from Frenchay Aphasia Screening test [30] or A beach scene by Prof. EK Warrington [31]. The choice of two 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 neuropsychologist (EJS or