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A behavioral study of the nature of verb production deficits in Alzheimer's disease

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ABSTRACT

Patients with Alzheimer's disease (AD) may experience greater difficulty with verb production than with noun production. In this study, we sought to assess the nature of verb production deficits in AD by using verb fluency and verb naming tasks. We designed two hypotheses for this verb deficit: (1) executive impairment drives the deficit; (2) semantic impairment drives the deficit. Thirty-five patients with AD and 35 matched healthy controls participated in the study. Both groups performed a verb naming task composed of 45 pictures (low-, medium-, and high-frequency subsets) and a verb fluency task (scored for total correct words and for mean word frequency). Patients with AD were equally impaired in verb naming and verb fluency, with an effect of disease severity on verb naming. Word frequency influenced verb naming, but not verb fluency, performance. Our results indicate that verb production deficits in AD seem to be driven more by semantic than by executive impairment.

1. Introduction

Studies focusing on the evaluation of the processing of different grammatical classes have already been performed using picture naming and verbal fluency tasks. Some of these studies show evidence of a double dissociation between verb and noun production in neurological disorders. Neurological disorders characterized by a predominance of frontal-lobe (or frontal-circuitry) impairment are associated with deficits in verb production, such as in the behavioral variant of frontotemporal dementia (bvFTD) (Cotelli et al., 2006; Davis et al., 2010), the nonfluent variant of primary progressive aphasia (nfvPPA) (Cotelli et al., 2006; Davis et al., 2010; Hillis, Oh, & Ken, 2004; Thompson, Lukic, King, Mesulam, & Weintraub, 2012), Parkinson's disease (PD) (Cotelli et al., 2007; Herrera, Rodríguez-Ferreiro, & Cuetos, 2012; Piatt, Fields, Paolo, Koller, & Tröster, 1999a; Rodríguez-Ferreiro, Cuetos, Herrera, Menéndez, & Ribacoba, 2010; Rodríguez-Ferreiro, Menéndez, Ribacoba, & Cuetos, 2009; Signorini & Volpato, 2006), agrammatical post-stroke aphasia (Luzzatti et al., 2002), progressive supranuclear palsy (PSP) (Cotelli et al., 2006), corticobasal syndrome (CBS) (Cotelli et al., 2006), amyotrophic lateral sclerosis (ALS) (Hillis et al., 2004), HIV-1 infection (Woods, Carey, Tröster, Grant, & HIV Neurobehavioral Research Center (HNRC) Group, 2005a), and schizophrenia (Badcock, Dragović, Garrett, & Jablensky, 2011; Woods, Weinborn, Posada, & O'Grady, 2007). On the other hand, conditions which predominantly involve temporal lobe impairments are associated with difficulties in noun production, as in the case of the semantic variant of PPA (Thompson et al., 2012) and Wernicke's aphasia (Luzzatti et al., 2002).

Based on this evidence, it has been assumed that verb processing (i.e., semantic knowledge for actions) relies on frontal brain circuits, while noun processing (i.e., semantic knowledge for nouns) relies on temporal and more posterior circuits in the brain (Vigliocco, Vinson, Druks, Barber, & Cappa, 2011).

If this assumption were true, one would expect patients with Alzheimer's disease (AD) to experience greater difficulty with noun production than with verb production, due to the predominance of temporal atrophy and relative sparing of frontal areas, at least in the early stages of the disease.

The most recent, well-controlled studies about verb and noun naming in AD (Druks et al., 2006; Kim & Thompson, 2004) demonstrated that AD patients name object pictures faster and with fewer errors than action pictures.

AD patients perform significantly worse than healthy controls on verb fluency tasks. However, when AD patients have been compared to people with other neurological disorders, such as PD or FTD, patients with the latter conditions presented more significant impairments than those with AD (Davis et al., 2010; McDowd et al., 2011). Another study showed that verb fluency impairment in AD may be associated with temporal lobe dysfunction, since it was

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predicted by a temporal hypoperfusion factor obtained by single-photon emission computed tomography (SPECT) (Ostberg et al., 2007). The authors believe that such impairment is a consequence of entorhinal cortex lesions, since this brain structure has connections with the frontal motor cortex and subcortical projections to the basal ganglia, basal forebrain, and amygdala.

This evidence shows that, even though patients with AD have no frontal brain atrophy, they do experience difficulty in naming and fluency tasks involving verbs. However, the driving factor behind the impairment in verb production observed in AD patients is still poorly understood. It is known that verb processing is more complex than noun processing and seems to rely on a more dispersed network of brain connections. Hence, difficulty in producing verbs can be a result of disruptions in many different parts of the brain network involved in this process. We believe that, in the specific case of AD, impairments in verb naming or verb fluency can be due either to a failure in the integration of information, which relies on executive function, or to a difficulty in recognizing or accessing semantic knowledge related to actions.

To understand how verbs are processed in the brain, we believe that one should not only consider comparisons between verb and noun productions, but also analyze how verbs are produced in response to different demands. One possible method for doing so is to compare verb production between verb fluency and verb naming, obtaining models of verb production from a predominantly executive demand and from a predominantly semantic demand, respectively. This paradigm may allow us to understand which cognitive aspect is driving verb impairment in AD.

Another aspect to consider in studies involving fluency and naming tasks is that words have many lexical attributes, which can influence the process of word production. One important attribute of any word is its frequency in the language (Johnson, Paivio, & Clark, 1996). Studies have suggested that word frequency is an attribute of lexical and semantic organization in the brain (Graham, Patterson, & Hodges, 2000; Jefferies, Hoffman, Jones, & Ralph, 2008; Segui, Mehler, Frauenfelder, & Morton, 1982).

Thus, the aim of this study was to investigate the nature of verb impairment in patients with mild and moderate AD by using the paradigm of comparing verb fluency and verb naming task performance between patients with AD and healthy subjects. In addition, to further investigate verb impairment, we decided to analyze the lexical factor word frequency in the studied tasks.

We designed two competing hypotheses for this study. The first was that impairment in verb production in AD would be mainly a consequence of executive impairment, resulting from a rupture in connections between the temporal lobe and frontal areas. Consequently, patients with AD might exhibit a more expressive impairment in verb fluency than in verb naming; word frequency would not influence task performance (since word frequency is an attribute of lexical and semantic organization, which are not the cause of the verb deficits in this hypothesis). The second hypothesis was that impairment in verb production in AD would be mainly a consequence of semantic memory impairment, as a result of the involvement of the temporal region and connections with occipitoparietal areas, which are important for semantic memory and integration of sensory information. In this hypothesis, word frequency might influence task performance.

2. Methods

2.1. Participants

Thirty-five patients with probable AD, diagnosed according to the DSM-IV and NINCDS-ADRDA criteria (McKhann et al., 1984), all at least 65 years of age and native speakers of Brazilian Portuguese, participated in the study. Patients with associated comorbidities, overt uncorrected hearing or visual impairment, or severe AD were excluded. Depressive symptoms were evaluated using the Geriatric Depression Scale (GDS) as exclusion criteria (Almeida & Almeida, 1999; Yesavage et al., 1982). All patients were recruited from the Dementia Clinic of *Hospital de Clínicas de Porto Alegre* (HCPA).

The neuropsychological and clinical status of the AD group was assessed using the Mini-Mental Status Examination (MMSE) (Kochhann, Varela, de Macedo Lisboa, & Chaves, 2010), the Hachinski Ischemic Score (Hachinski et al., 1975), the Consortium to Establish a Registry for Alzheimer's disease (CERAD) fixation, recall, and recognition word lists (Bertolucci et al., 2001), the immediate logical memory and digit span subtest (forward) of the WAIS III (Nascimento, 2007); clock drawing test (Silva, 2013), phonemic verbal fluency (FAS) (Machado et al., 2009), and semantic verbal fluency (animals) (Brucki & Rocha, 2004). Dementia severity was assessed using Clinical Dementia Rating (CDR) global scores (mild = CDR 1; moderate = CDR 2) (Hughes, Berg, Danziger, Coben, & Martin, 1982) The CDR Sum of Boxes score was also assessed.

The control group was composed of individuals recruited from social groups from the local community and matched to the patients for age, sex, and education. A brief interview was conducted to verify the health condition and functional independence of potential controls. Only native speakers of Brazilian Portuguese without significant health problems and with normal MMSE scores were included in the study. The exclusion criteria were history of neurological or psychiatric disorders; alcohol, drug, or benzodiazepine use; and overt, uncorrected visual or hearing impairment. The demographic and clinical profile of all participants is shown in Table 1.

This study was approved by the HCPA Research Ethics Committee (registration number 11-0178) and all participants gave written informed consent.

2.2. Stimuli

The study used a set of 45 action pictures, taken from the Object and Action Naming Battery (Druks & Masterson, 2000) for the verb naming task. We obtained name agreement and ratings (on a scale

Table 1
Demographic profile of the Alzheimer's disease (AD) and control groups.

Variable	AD group (n = 35)	Control group (n = 35)	p-Value
Sex, female (%)	22 (62.9%)	22 (62.9%)	1000
Age	77.74 (±5.93)	73.14 (±4.82)	0.001*
Education (years)	4.37 (±3.83)	5.66 (±3.56)	0.150
Right-handedness, n (%)	31 (88.6%)	30 (85.7%)	0.721
MMSE	16.60 (±4.88)	26.51 (±2.11)	<0.000*
CDR (Sum of Boxes)	7.61 (±2.73)	–	–
CDR (Global)			
CDR 1, n (%)	19 (54.3%)	–	–
CDR 2, n (%)	16 (45.7%)	–	–
Hachinski Ischemic Score	1.79 (±1.28)	–	–
Word Span	3.00 (±1.18)	–	–
Immediate Logical Memory	1.21 (±0.97)	–	–
CERAD		–	–
Word List – Fixation	7.19 (±4.50)	–	–
Word List – Recall	1.41 (±1.91)	–	–
Word List – Recognition	4.35 (±2.74)	–	–
Clock Drawing Test – Free	1.75 (±1.65)	–	–
Clock Drawing Test – Copy	2.39 (±1.79)	–	–
Phonemic Verbal Fluency – FAS	12.65 (±8.70)	–	–
Semantic Verbal Fluency – Animals	7.03 (±4.08)	–	–

Data expressed as mean (±SD) or n (%), * $p < 0.05$ (t-test), ** $p < 0.05$ (chi-square test).