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REVIEW ARTICLE

Is semantic impairment a predictive sign for Alzheimer disease?

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KEYWORDS
Semantic impairment;
Alzheimer's disease;
Mild cognitive impairment;
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Visual confrontation naming

Abstract This review describes the performance of persons with Alzheimer disease and mild cognitive impairment in some semantic tasks reported in the literature due to their diagnostic and prognostic values. Most of the studies reviewed included visual confrontation naming and verbal fluency tasks. There is a controversy about whether naming deficits are due to a degradation of semantic contents, difficulties in accessing contents, and an inability to access to word form, or whether they are due to failed connections between the semantic system and phonological and lexical representations. It is necessary to explore in detail the process of the linguistic system and its relationship with other biological and cognitive markers during predementia phases and progression to dementia, as well as to evaluate new treatment options, in order to decrease cognitive deterioration and prevent or delay progression to dementia. Semantic verbal fluency tasks and event-related potentials (N400 and P600 components) might be useful in the search for therapeutic possibilities.

PALABRAS CLAVE
Deterioro semántico;
Enfermedad de Alzheimer;
Deterioro cognitivo leve;
Fluidez verbal;
Denominación por confrontación visual

¿Es el deterioro semántico un signo predictor de la enfermedad de Alzheimer?

Resumen La presente revisión describe el desempeño de sujetos con enfermedad de Alzheimer y deterioro cognitivo leve en algunas tareas de naturaleza semántica reportadas por la literatura por su valor pronóstico y de diagnóstico. La mayoría de los estudios revisados incluyen pruebas de denominación por confrontación visual y fluidez verbal. Existe controversia en cuanto a si el origen los déficits en denominación es dado por una degradación de los contenidos a nivel semántico, dificultades en el acceso a ellos, imposibilidad de acceder a la forma de la palabra o por fallos en las conexiones entre el sistema semántico y las representaciones léxicas o fonológicas. Se destaca la necesidad de explorar detalladamente los procesos del sistema lingüístico y su relación con otros marcadores biológicos y cognitivos desde fases predemenciales y durante la progresión a demencia, así como la exploración de nuevas posibilidades terapéuticas que permitan disminuir el deterioro cognitivo y evitar o prolongar su posible evolución a demencia. La tarea de fluidez verbal semántica y los potenciales

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relacionados con eventos (componentes N400 y P600), pueden ser útiles en la búsqueda de posibilidades terapéuticas.

Introduction

Dementia is a syndrome that could be caused by a number of progressive alterations, affecting cognitive functions (including language), behavior, and the capability of doing activities of daily living (Ardila & Ostrosky, 2012; Organización mundial de la salud [OMS], 2007).

According to the international report about Alzheimer, it is calculated that more than 35.6 millions of people live with this syndrome and it generated a total cost of more than 600 billion dollars in 2010 (Alzheimer's Disease International [ADI], 2010). AD is the most common type of dementia, representing between 50 and 56% of the cases identified by autopsies and clinical semiology (Querfurth & Frank, 2010). The main risk factor is person's age since its incidence is doubled every 5 years after an age of 65; thus, 1275 new cases are reported every year per 100,000 people older than 65 (Hirtz, Thurman, Gwinn-Hardy, Chaudhuri, & Zalutsky, 2007).

In a strict way AD is not an illness but a progressive anatomic-clinic syndrome that is pathologically characterized by neuronal loss on the entorhinal and transentorhinal regions and on the hippocampus; this neuronal loss will be posteriorly extended onto the neocortex (Kowalewski & Murphy, 2012). The principal histopathological findings include accumulation of brain plaques charged of β-amiloide (Aβ) peptide and prominent neurofibrillary tangles in the medial part of the temporal lobe (Querfurth & Frank, 2010). These findings have been associated with synaptic dysfunctions and neural degeneration that entails cognitive impairment (Weiner et al., 2012).

Currently, it does not exist a cure for AD, neither a treatment that slow down the progression of this disorder (Weiner et al., 2012); one of the main obstacles in the development of therapeutic treatments is that AD's diagnosis is performed at advanced stages, when both behavior and central nervous system (CNS) are already affected (Lara et al., 2006). This has led to many investigations to focus on identifying markers at early phases of the disease (Frisoni et al., 2009).

AD could start 10 years before clinical manifestations are presented (Barandiaran, 2011). In fact, the term ''mild cognitive impairment'' (MCI) is used to differentiate the boundary between non-pathological aging and dementia (Rodríguez, Juncos-Rabadán, & Facal, 2008). MCI represents a diagnostic entity that is applied to people who have cognitive difficulties above the expectancy for their age, even though this does not interfere with their daily life activities. At this stage, progression of AD is about 15% per year, whereas 1.2% is reported for the general population, and impairments could be detected at cognitive or biological level (Taler & Phillips, 2008). Regarding the first one, memory, executive functions, perceptual speed, visuospatial skills, attention and the domain of language could be affected (Sabbagh et al., 2007).

During the process of non-pathologic aging, language is one of the latest cognitive functions that are affected; instead, language impairment is considered as one of the most usual manifestations in AD (Subirana, Bruna, Puyuelo, & Virgili, 2009). Thereby, it could be obvious at early stages, even before noticing any clinical manifestation that characterize the beginning of the most evident deterioration (Cullell, Bruna, & Puyuelo, 2006). In fact people with MCI, who have multiple affections including language, have a higher risk of progressing to an AD than those who have an isolated memory alteration (amnesic SCI), (Rey Pérez and Lleó Bisa, 2010; Taler & Phillips, 2008). This confirms the importance of evaluating language when AD is suspected.

First signs of deterioration are evident in the semantic component of language (Juncos-Rabadán, Pereiro, Facal, & Rodríguez, 2010). A detailed examination of linguistic difficulties indicates that conceptual and lexical organizations are the main alterations (Garrard, Lambon Ralph, Patterson, Pratt, & Hodges, 2005). This is specially reflected on the difficulty to find words (Fisher, Rourke, & Bieliauskas, 1999) and on the verbal disfluency (Henry, Crawford, & Phillips, 2004).

This literature review aims to describe the performance of people with AD and MCI at some semantic tasks reported by the literature due to their diagnostic and prognostic value.

Search strategy to identify the selected studies

PubMed (MedLine), LILACS, y EBSCO HOST were the databases used in this study. The articles included encompassed dates from 1993 to February 2013. The key words used were ''Alzheimer'', ''semantics'' and ''mild cognitive impairment''; ''OR'' and ''AND'' were connecting words also used. This electronic searching was complemented by eligible original studies reviewed at the bibliographic resources of the National University of Colombia. Furthermore, experts on the field were contacted in order to seek for information about potential studies that had not been identified through the strategies previously described.

375 articles were found and 40 of them were included in this literature review. Studies had to have a task that evaluated semantic processing in AD and/or MCI. Observational studies were included in order to help evaluating the prognostic value and the diagnosis of semantic processing. Some other inclusion criteria were: studies had to be published in a thesis or a journal; they had to include mean and standard deviation and; data had to be compared by age range and level of schooling. In some cases semantic processing tasks were part of a neuropsychological test. Single case studies were excluded since they present very partial aspects on the

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