ELSEVIER

Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring ■ (2017) 1-9

Alzheimer's & Dementia

Cognitive & Behavioral Assessment

Can visuospatial measures improve the diagnosis of Alzheimer's disease?

Shirin Salimi[a], Muireann Irish[b,c], David Foxe[b], John R. Hodges[d,c], Olivier Piguet[b,c], James R. Burrell[d,c,e,*]

[a]*Faculty of Medicine, University of New South Wales, Sydney, New South Wales, Australia*
[b]*School of Psychology and Brain & Mind Centre, The University of Sydney, Sydney, New South Wales, Australia*
[c]*Australian Research Council Centre of Excellence in Cognition and its Disorders, Sydney, New South Wales, Australia*
[d]*Central Medical School, The University of Sydney, Sydney, New South Wales, Australia*
[e]*Concord Hospital, Sydney, New South Wales, Australia*

Abstract

Introduction: Overlapping and evolving symptoms lead to ambiguity in the diagnosis of dementia. Visuospatial function relies on parietal lobe function, which may be affected in the early stages of Alzheimer's disease (AD). This review evaluates visuospatial dysfunction in patients with AD, frontotemporal dementia, dementia with Lewy bodies, and vascular dementia to determine the diagnostic and prognostic potential of visuospatial tasks in AD.

Methods: A systematic search of studies (1960–2016) investigating visuospatial dysfunction in dementia was conducted.

Results: Tests measuring construction, specifically Block Design and Clock Drawing Test, and visual memory, specifically Rey-Osterrieth Complex Figure recall and topographical tasks, show the greatest diagnostic potential in dementia. The Benton visual retention, Doors and People, and topographical memory tests show potential as prognostic markers.

Discussion: Tests of visuospatial function demonstrate significant diagnostic and prognostic potential in dementia. Further studies with larger samples of pathologically confirmed cases are required to verify clinical utility.

Keywords: Alzheimer's disease; Frontotemporal dementia; Dementia with Lewy bodies; Vascular dementia; Visuospatial; Diagnosis; Prognosis; Clock Drawing Test; Visual object space perception battery; Rey-Osterrieth Complex Figure; Benton visual retention test

1. Introduction

Overlapping and evolving symptoms make existing clinical diagnostic criteria for dementia [1] difficult to apply in a considerable proportion of patients [2]. *In vivo* markers of brain pathology (e.g., cerebrospinal fluid or amyloid PET imaging) [3] are still largely confined to research settings, so dementia is still primarily diagnosed on clinical grounds [4]. A final pathological diagnosis is restricted to the very few individuals who undergo postmortem examination or those in whom a genetic cause of dementia is identified. This diagnostic ambiguity is unacceptable because it hampers efforts to develop therapies by restricting clinical trial enrollment or necessitating large clinical trials to demonstrate efficacy [4].

It is challenging to make a diagnosis of AD in the earliest stages or in undifferentiated dementia presentations. Distinct atypical AD syndromes are recognized and characterized by prominent visual symptoms (e.g., posterior cortical atrophy), progressive aphasia (e.g., logopenic progressive aphasia), or motor symptoms (e.g., corticobasal syndrome).

The authors have declared that no conflict of interest exists.

*Corresponding author. Tel.: +61-2-97675000; Fax: +61-2-82441950.
E-mail address: james.burrell@sydney.edu.au

https://doi.org/10.1016/j.dadm.2017.10.004

A proportion of AD patients will not meet the criteria for any single dementia syndrome, including the recognized atypical AD syndromes, but rather will be present with an undifferentiated mix of cognitive and behavioral symptoms and signs [2].

In vivo diagnostic markers of amyloid pathology have existed for more than 10 years but have not been deployed clinically due to issues with availability, cost, and specificity. For instance, Pittsburgh compound type B positron emission tomography presents logistical problems because of its cost and short half-life [5]. Cerebrospinal fluid analyses require an invasive procedure and demonstrate only modest specificity in undifferentiated dementia syndromes [6,7]. Meanwhile, the diagnostic utility of structural neuroimaging in early AD is controversial as atrophy may be subtle or nonspecific [8].

Before the development of amyloid biomarkers, efforts to improve AD diagnosis emphasized improving neuropsychological tests of memory [9,10]. Memory deficits are characteristic of typical AD, but similar deficits of immediate and delayed episodic memory [11–13] and autobiographical memory [14,15] have been reported in frontotemporal dementia (FTD). Separately, early language impairment, which is characteristic of language forms of FTD, can be seen in AD [16], and individuals with nonfluent aphasia due to AD remain difficult to distinguish from patients with the progressive nonfluent aphasia phenotype of FTD [17], despite refinement of diagnostic criteria [18]. Limited specificity of memory and language deficits may not be surprising because their neuroanatomical substrates (i.e., the frontal and temporal lobes) can be affected by several underlying pathologies [19–21].

Unlike memory and language, visuospatial functioning is heavily reliant on parietal lobe integrity [22,23]. Changes in medial and lateral parietal lobe function or structure occur early in AD [22,24–26]. Consequently, tests of visuospatial abilities may prove to be more accurate in differentiating AD and non-AD dementias than other cognitive tests [8,27,28]. This review evaluates studies of visuospatial dysfunction in patients with AD, FTD, and other dementias often associated with AD pathology such as dementia with Lewy bodies (DLB) and vascular dementia (VaD). First, a critical overview of the various components of visuospatial function and their neural bases is presented. Then, the diagnostic and prognostic potential of visuospatial tasks in AD and non-AD dementias is considered.

2. Methods

Studies of visuospatial dysfunction in dementia were identified using a systematic search process. A combination of keywords, including "visuospatial function," "Alzheimer's disease," "frontotemporal dementia," "dementia with Lewy bodies," "vascular dementia," and "neuropsychological test," was searched in MEDLINE, EMBASE, and PubMed, generating a total of 297 abstracts from 1960 to 2016. Duplicates, non-English articles, and case studies/series were excluded. Articles were excluded primarily because of their focus on neurological disorders, neuropsychological tests, and cognitive domains beyond the scope of this review. Preference was given to studies of pathologically confirmed dementia cohorts. Seventy-two additional records were identified through bibliographic research. These were reviewed for relevance, and 100 papers comprising review articles and experimental studies regarding visuospatial function in dementia remained for full review. If peer-reviewed original studies or review articles were not available, textbooks were consulted.

3. What is visuospatial function?

Broadly defined, visuospatial function is the ability to specify the parts and overall configuration of a percept, appreciate its position in space, integrate a coherent spatial framework, and perform mental operations on spatial concepts [22,23]. Visuospatial function is commonly conceptualized in three components: visual perception, construction, and visual memory [29].

At its most basic level, visual perception involves light perception, contrast sensitivity, stimulus orientation, visual acuity, detection of color and motion, and processes mediated primarily by the occipital cortices. Progressive integration of this visual perception involves input from the parietal, temporal, and frontal cortices. Progressive integration of visual information occurs via two major visual processing streams: the ventral "what" stream and the dorsal "where" stream [27,30,31]. The ventral stream is responsible for (1) resolving visual interference; (2) the ability to identify an object masked by an overlapping picture; and (3) the ability to make sense of fragmented or ambiguously presented objects [29]. The dorsal "where" stream is responsible for spatial orientation and relies on posterior and inferior parietal regions [29].

Visual memory consists of two main components: recall (or recognition) of visual information and topographical memory. Topographical memory involves perception and encoding of spatial orientation to navigate surroundings. Topographical orientation is characterized as being either egocentric (relative to the self) or allocentric (relative to other objects).

3.1. Incidence of visuospatial deficits in dementia

Visuospatial dysfunction is among the earliest manifestations of AD [8,32], eventually affecting 20%–43% of patients [27,32–34]. One study showed disabling visuospatial disorientation in more than one-third of AD patients [35] while almost half of patients complained of visuospatial problems when questioned directly [34]. AD patients may describe impaired discrimination of form, colors and contrast, motion detection, as well as disturbances of higher order functions such as reading, visuospatial orientation, and