

## DETERIORATION OF VISUAL-PERCEPTUAL ORGANIZATION ABILITY IN ALZHEIMER'S DISEASE

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### ABSTRACT

Although deterioration of higher-order visual information processing abilities occurs in Alzheimer's disease (AD), few cross-sectional or longitudinal studies have systematically examined this deficit. The performance of 135 patients with probable AD and 97 matched normal control (NC) participants were compared on a structured test of perceptual organization ability, the Hooper Visual Organization Test (VOT). Both the standard VOT score and a derived score that corrected for anomia were significantly lower for AD patients than for NC participants, but neither score was particularly effective at distinguishing between the groups. The derived VOT score proved to be a more effective measure of visuospatial functioning than the standard VOT score as it loaded with other visuospatial tests in a principal components analysis while the standard score loaded with language tests. The VOT was sensitive to severity of dementia in the AD patients. Longitudinal assessment of 37 of the AD patients and 46 NC participants revealed significant decline over one year in the VOT scores of AD patients, but not in those of NC participants. These results indicate that higher-order visual information processing is impaired in patients with AD and gradually deteriorates with disease progression. This deficit may not be a particularly salient early marker of the disease, but it may be useful in tracking disease course.

Key words: visual cognition, Hooper Visual Organization Test, Alzheimer's disease, dementia

A number of studies have shown that higher-order visual information processing abilities are impaired in patients with Alzheimer's disease (AD). At a point when basic visual functions such as visual acuity, contrast sensitivity, flicker fusion, and simple motion perception are retained (Mendola et al., 1995), patients with AD are impaired in the ability to draw or copy complex geometric designs (Becker et al., 1988; Brouwers et al., 1984; Guerin et al., 2002; Mohr et al., 1990; Padovani et al., 1995; Rouleau et al., 1996; Villardita, 1993; Mendez et al., 1990) or to assemble two-dimensional or three-dimensional objects (Mohr et al., 1990; Storandt et al., 2002; Salmon et al., 2002; Padovani et al., 1995; Becker et al., 1988; Villardita, 1993; Kurylo et al., 1994). They are also often impaired on visual-perceptual tasks such as visual object recognition (Done and Hajilou, 2005; Kurylo et al., 1996), judgment of line orientation (Ska et al., 1990; Ricker et al., 1994), figure/ground discrimination (Kurylo et al., 1994), or perceptual organization (Kurylo et al., 2003; Locascio et al., 1995; Mendez et al., 1990). These results have led some investigators to propose that visual information processing deficits are a prominent feature of AD that can be used for differential diagnosis (e.g., between AD and fronto-temporal dementia; Rascovsky et al., 2002) and for tracking the progression of disease (Rouleau et al., 1996; Rizzo et al., 2000).

In order to determine if visual information processing deficits are clinically useful for detecting and monitoring the course of AD, it is necessary to know whether or not a particular task to be used for this purpose can discretely assess the target ability (i.e., has construct validity) while remaining sensitive to dementia and its progression. Many of the tasks used to assess visual information processing abilities are multi-factorial, and it may be the case that AD initially affects attention, language, or executive functions that are engaged by a particular task rather than visual information processing abilities per se. Before it can be concluded that a visual information processing task is sensitive to the presence and progression of AD, these potential confounding factors need to be identified and controlled.

A widely-used visual information processing task that might be particularly sensitive to the presence and progression of AD is the Hooper Visual Organization Test (VOT; Hooper, 1983). The VOT requires the perceptual and conceptual reorganization of the parts of a dissected visual object into a coherent whole so that the object can be identified and named. In its standard form, the VOT requires the integration of spatial and object identity information separately processed by dorsal and ventral visual neural circuits or "streams" that analyze different aspects of the visual scene

(Lennie, 1998; Livingstone and Hubel, 1988; Merigan and Maunsell, 1993; Ungerleider and Mishkin, 1982). Thus, the VOT might be especially sensitive to AD because the disease adversely affects both dorsal and ventral stream information processing (Rizzo et al., 2000) and interferes with the integration of visual information separately processed in each neural stream (Festa et al., 2005). Consistent with this possibility, a number of studies have shown that mildly demented patients with AD are impaired on the VOT (Mendez et al., 1990; Padovani et al., 1995; Ricker et al., 1994; Villardita, 1993).

Previous demonstrations of impaired performance on the VOT by patients with AD, however, may not be a true reflection of an early visual information processing deficit. While the VOT does not appear to place heavy demands upon attention or executive functions, and does not involve construction or motor manipulation common to many visuospatial tasks, it does require confrontation naming ability that may be compromised in patients with AD (Bayles and Tomoeda, 1983; Hodges et al., 1991; Huff et al., 1986). It is possible that patients with AD can effectively perform the perceptual integration aspect of the task, but score poorly because they are unable to correctly name the perceived objects.

Evidence for an important role of confrontation naming in VOT performance is mixed. Several studies have shown that the VOT performance of normal individuals (Paolo et al., 1996; Paul et al., 2001; Ricker and Axelrod, 1995) or patients with a variety of neurological disorders (Merten, 2005) is more strongly related to performance on visuospatial or visual-perceptual tasks than on tests of confrontation naming. It should be noted, however, that the VOT comprises common, easily-named objects and the impact of naming might only be observed in individuals with some degree of anomia. This possibility is supported by a study of stroke patients with anomia that showed they were impaired on the standard version of the VOT, but significantly improved their performance on a multiple choice version that did not require naming (Schultheis et al., 2000). Further evidence for a role of naming in VOT performance is provided by a recent functional magnetic resonance imaging (fMRI) study in normal individuals (Moritz et al., 2004). When performing a version of the VOT that did not require overt naming, task-related activation was evident in cortical regions involved in visuospatial processing (i.e., bilateral superior occipital and posterior superior parietal cortex), object identification and semantic retrieval (i.e., lateral occipital and posterior inferomedial temporal cortex), and covert naming (i.e., left inferior/middle prefrontal gyrus). These latter studies indicate that semantic processes contribute to VOT performance, and suggest that performance on the standard version of the test needs to be corrected for anomia

when used as a measure of higher-order visual information processing in patients with AD.

The present study was designed to evaluate the utility of the VOT in assessing visual-perceptual information processing in patients with AD. While other tests or test batteries such as the Visual Object and Space Perception Battery (VOSP; Warrington and James, 1991), Cortical Vision Screening Test (CORVIST; James et al., 2001), or Birmingham Object Recognition Battery (BORB; Riddoch and Humphreys, 1993) may be more specific than the VOT in measuring visual and spatial perceptual functioning, the VOT was chosen for study because it is one of the most widely-used clinical measures of perceptual abilities in patients with AD, it is quickly and easily-administered to demented patients, and it has been validated against measures of brain function (Moritz et al., 2004). Although it is known that patients with AD are often impaired on the VOT, little is known about how effective this measure of visual-perceptual ability might be in detecting AD and tracking the progression of the disease. Furthermore, the impact of the language deficit associated with AD on the clinical efficacy of the test remains unknown. Therefore, the present study had four primary goals: (1) to confirm previous studies demonstrating that the visual-perceptual organization abilities tapped by the VOT are impaired in patients with AD; (2) to identify the relationship between VOT performance and deficits in language and other cognitive abilities in patients with AD; (3) to determine the accuracy with which the VOT can differentiate between patients with AD and healthy, non-demented individuals; and (4) to determine the degree to which visual-perceptual organization abilities measured by the VOT deteriorate with the progression of AD.

## METHODS

### *Participants*

Two hundred and thirty two individuals participated in this study: 135 patients with probable AD (76 females, 59 males) and 97 elderly normal control (NC) participants (44 females, 53 males). All participants were recruited from a longitudinal study of dementia and aging at the University of California, San Diego (UCSD) Alzheimer's Disease Research Center (ADRC) through which they received annual neuropsychological, neurological, and medical evaluations. Written informed consent was obtained from all participants (or their conservator) after the study procedures had been fully explained to them.

The clinical diagnosis of AD was made by two senior staff neurologists at the ADRC on the basis of criteria developed by the National Institute of Neurological and Communicative Disorders and

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