Vision in Alzheimer’s Disease
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46 figures and 18 tables, 2004
Dedication

To Mark, Lucy, Olivia, and Gabriel, and in memory of my mother, Agnes Nelson Cronin (ACG)
To Esther and Jonathan (PRH)
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Introduction

Alzheimer’s disease (AD) is the most common cause of dementia in older adults. The Alzheimer’s Association estimates that 4.5 million individuals in the US currently are afflicted, and that by mid-century the prevalence in this country will be 11.3–16 million cases in the absence of a cure or prevention [1]. Understanding all behavioral, anatomical, and physiological aspects of this disease is obviously of utmost importance world-wide.

AD is viewed as a disorder primarily of memory by patients, caregivers, and most health professionals. While agreeing that the memory deficit is usually the initial sign, researchers have long known that AD is characterized by impairments in several additional domains, including visual function. In recent years, although a consensus has been reached that even lower-level visual abilities are impaired in a large number of patients with AD, these findings have not yet appeared in the diagnostic guides consulted by healthcare professionals. For example, the most recent edition of the Diagnostic and Statistical Manual of Mental Disorders states that few sensory signs occur early in AD [2]. Less recent but widely used is the report on clinical criteria for AD diagnosis developed by the NINCDS-ADRDA work group [3], in which it is stated that sensory loss or visual field deficits make the diagnosis of probable AD ‘uncertain or unlikely’. This report acknowledged that our understanding of AD was still limited and that the proposed clinical criteria should therefore be considered tentative and subject to change. The current web sites of the Alzheimer’s Association [1] and the National Institute on Aging [4], agencies that fund research on AD and promulgate information on the disease, make no mention of sensory changes.

In accordance with their own observations, and expectations, of the prominence of the memory impairment, as well as those of the clinical staffs with
whom they come into contact, patients with AD report vision problems to their physicians less frequently than do healthy elderly individuals [5]. Nevertheless, visual dysfunction is prevalent in AD [6]. The neuropathology of this disorder affects several brain areas that are devoted to processing of low-level visual functions as well as higher-order visual cognition and attention. The neuropathological changes are especially prominent in the ‘visual variant’ of AD, also known as posterior cortical atrophy, but occur as well in the more typical AD case.

Our goal in this volume is to provide information on current directions in AD vision research. While not exhaustive, the chapters represent several main foci of research including studies of structure, function, and behavior.

The first section is on aspects of structure and function. Valenti describes the state of knowledge about the anterior visual pathways through the primary visual cortex, citing work that points to AD neuropathological change at multiple levels, including the lens of the eye, the retinal nerve fiber layer and optic nerve, and hypothalamic and thalamic nuclei. Attention to the anterior system leads to the identification of interventions that may improve visual input, as she documents. Intriguingly, Valenti also raises the possibility of disruption of the circadian system at the level of the retina and other higher structures, which may provide clues to sleep-wake abnormalities common in AD patients. Von Gunten, Giannakopoulos, Bouras and Hof extend the discussion of neuropathology to the cortex, from primary to association cortices, focusing on the long corticocortical projections that are subject to significant disruption in AD. In the domain of function, Anderson and Grady provide a summary of imaging studies in normal aging and AD with an emphasis on visual areas and their prefrontal targets.

The second section introduces abnormalities in visual behavior in AD and related disorders. Cronin-Golomb supplies an overview of the prevalence of deficits in basic visual capacities in typical AD and considers the heterogeneity in the type and extent of presentations of visual signs. Mendez extends this discussion with his focus on the ‘visual variant’ of AD, or posterior cortical atrophy, including structure, function, and behavior. As described by Mendez and by von Gunten and colleagues, the characteristics of posterior cortical atrophy raise the question of whether typical AD and its visual variant fall on a neuropathological continuum or instead are distinct clinical and pathological entities. Visual hallucinations occur in some patients with AD, and Holroyd provides a careful consideration of the circumstances under which hallucinations arise and of their brain substrates, focusing on visual association cortex. As she reports, visual hallucinations are common in AD and may be the presenting symptom. Their association with more rapid cognitive decline, aggression, and premature institutionalization, as well as patient and caregiver distress, underscores the importance of research and treatment of these symptoms. Rocco points out the similarities in visual deficiencies in regard to structure, function, and behavior in Down
syndrome, a disorder in which individuals develop AD-type neuropathology by the age of 35 or 40. He makes the case that further research on Down syndrome may offer clues to the etiology of the development of changes in visual behavior in AD. The chapters constituting this section together reinforce the idea that the study of variations in pathology and behavior will likely provide insights into typical AD as well as related conditions.

The third section considers the state of visual perception and cognition in AD at a level beyond basic visual abilities. The dorsal, occipitoparietal visual pathway is the focus of work by Duffy, Cushman, and Kavcic, who describe visuospatial disorientation in AD. Part of the difficulty that patients have in spatial navigation arises from deficits in the perception of self-motion via optic flow, which contains information about heading direction and the three-dimensional structure of the visual environment. Duffy and colleagues attribute these difficulties to disruption of corticocortical pathways such as described by von Gunten and colleagues in their chapter. Gilmore, Morrison, and Groth follow with an analysis of the magnocellular hypothesis of visual dysfunction in AD, a formative theory that proposes exceptional vulnerability of functions associated with the magnocellular pathway or, in cortex, the dorsal processing stream (see also Valenti, this volume). As is clear from their review, behaviors associated with these pathways are impaired in AD, as are functions dependent more on the parvocellular pathway and the ventral, occipitotemporal processing stream. The next three chapters complement the first two through their emphasis on the ventral pathway, which is specialized for object recognition. Kurylo discusses fundamental perceptual organization, which serves to organize the visual scene in preparation for object identification. He reports extensive heterogeneity in AD patient performance on several tests of organization such as stimulus-from-noise, proximity, and alignment, and links this level to a higher level by noting that those patients with AD who performed poorly on a test of face discrimination also showed impairments on all tests of perceptual organization. Building upon this link to higher-level function, Tippett describes new findings on object recognition in AD, including apperceptive and associative agnosia, that have emerged through use of sophisticated tests drawn from the cognitive neuroscience literature. Her chapter also examines current views on the integrity of visual imagery in AD. In the last chapter of the section, Glosser and Grossman consider three cognitive models of letter-by-letter reading and alexia in AD, including impairments in lexical processing, attentional control, and general visual perception. They suggest that bottom-up effects can lead to a situation whereby a disorder early in visual processing (letter identification) can affect analysis at a later stage (orthographic lexicon). That is, a deficit in visual perception may contribute to an erroneous impression that there is a core orthographic problem in some patients.
The focus of the final section of the book is on visual attention and daily function. Vecera and Rizzo provide a summary of attentional deficits in AD and a novel interpretation of these deficits in terms of deficient visual short-term memory. Parasuraman and Greenwood further this discussion with additional studies of visual search and attentional shifting, then describe exciting new work linking attentional impairments in putatively healthy individuals to genetic risk for AD. Pulling together information from several of the preceding chapters, Mapstone and Weintraub analyze the size of the window of spatial attention in AD. Their work on driving behavior is of clear importance because of the premier role of driving in independent living, which must be balanced against the needs of society for protection against erratic drivers. The final chapter by Dunne considers the basic research reported in the previous sections on visual deficits in AD and uses it to propose modifications of the daily living environment to enhance quality of life. Dunne provides concrete suggestions for visual interventions that are designed for ease of implementation by caregivers in the home setting and by staff in long-term care facilities. She demonstrates how fairly simple changes in the visual environment can lead to increased food and liquid intake, ability to dress, and success in navigation.

In summary, this volume spans the range of topics on vision in AD and associated disorders, from structure (retinal and cortical) to function (cortical activation) to behavior (basic vision, hallucinations, perception, cognition, attention, and everyday activities). We present these multiple aspects of basic research with an eye to developing interventions that will improve the lives of patients with AD and related disorders. Far from being atypical and therefore of limited utility in understanding the common presentation of AD, the visual disorders of Alzheimer’s original case and its cousins of the 21st century have much to teach us about the changing visual system in aging and age-related neurodegenerative disease.

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References
1 http://www.alz.org/AboutAD/Statistics.htm
4 http://www.nia.nih.gov