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Perception of movement and shape in Alzheimer's disease

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Summary

Alzheimer's disease is the most prevalent cause of abnormal cognitive decline in older adults and commonly affects visual function. Recent evidence suggests that Alzheimer's disease impairs the processing of visual motion, but these conclusions are based on conflicting results in the few cases studied, and the processing of complex motion images has not been investigated. In the present study of motion processing in Alzheimer's disease we assessed visual functions in 63 adults: 41 with mild to moderate Alzheimer's disease (mean age 72.3 years) and 22 without dementia (mean age 71.7 years). Processing of motion cues was tested with computer animation sequences known as random-dot cinematograms, which resemble the stimuli used to define motion processing deficits in primates with lesions of cortical area MT. Results showed that participants with Alzheimer's disease required significantly greater thresholds for perceiving shapes defined by motion cues compared with participants without dementia ($P = 0.0005$). There were no significant differences between the two groups ($P < 0.05$) in static visual acuity, static spatial contrast sensitivity and, surprisingly, dynamic visual acuity, which was normal, and motion direction discrimination, which was relatively spared. We conclude that mild to moderate Alzheimer's disease has significant effects on the perception of structure from motion with relative sparing of motion direction discrimination. We cannot exclude a contribution by retinal pathology, but retinal dysfunction alone cannot explain the pattern of defects we observed. The complex motion image processing deficit we identified is likely to have a cerebral basis and has the potential to affect navigation and the recognition of objects in relative motion, as encountered during walking and automobile driving.

Keywords: Alzheimer's disease; area MT (V5); motion perception; structure from motion; visual cortex

Abbreviations: BLOCK = WAIS-R block design subtest (age-corrected scaled score); CFT = complex figure test (raw score); COWA = controlled oral word association (score corrected for age and education); DIGIT = WAIS-R digit span subtest (age-corrected scaled score); FRT = Benton facial recognition test (score corrected for age and education); INFO = Wechsler Adult Intelligence Scale—revised information subtest (age-corrected scaled score); MT = middle temporal; RDC = random-dot cinematogram(s); SFM = structure from motion; TMT-A, -B = trail making test, parts A and B (scaled score equivalent of raw score); TO = temporal orientation (raw score); VRT = Benton visual retention test (number correct, raw score); WAIS-R = Wechsler Adult Intelligence Scale—revised

Introduction

Alzheimer's disease is the most common aetiology of abnormal cognitive decline in older adults and is a source of visual dysfunction (e.g. Cronin-Golomb *et al.*, 1995) that is growing in prevalence due to ageing trends in the general population (Roush, 1996). Alzheimer's disease can impair reading, route-finding, object recognition (Cronin-Golomb *et al.*, 1995; Mendola *et al.*, 1995; Pantel, 1995) and shrink the useful field of view due to reduced attention and speed of processing (Ball *et al.*, 1988). This has implications for increased risk of traumatic injury from car crashes and falls (Owsley *et al.*, 1991; Dubinsky *et al.*, 1992; Ball *et al.*, 1993; Drachman and Swearer, 1993; Oleske *et al.*, 1995; Johansson, 1997). A few studies indicate that Alzheimer's disease can also impair motion perception, although there is debate about

the selectivity of the deficits, the relationship to the stage of disease, and the locus of CNS impairment, which ranges from the retina to the association cortex (e.g. Hinton *et al.*, 1986; Barton *et al.*, 1995; Sathian, 1995; Silverman and Feldon, 1995; Kurylo *et al.*, 1996). In previous studies of Alzheimer's disease ocular pursuit of moving targets or judgements of low-level movement attributes such as speed and direction have been measured (e.g. Gilmore *et al.*, 1994; Kurylo *et al.*, 1994*a*; Silverman and Feldon, 1994). Motion cues serve many purposes in human vision, allowing us to perceive direction, depth and distance and even to identify moving objects (Gibson, 1950; Wallach and O'Connell, 1953; Braunstein; 1962; Nakayama, 1985; Siegel and Anderson, 1988). During walking or automobile driving, for example, movement can impart information about the structure of the terrain, the proximity and identity of surrounding objects and time to collision, which facilitates navigation and collision avoidance (Cavallo and Laurent, 1988; Fermuller and Aloimonos, 1995; Anderson *et al.*, 1996; Rizzo *et al*., 1997). CNS lesions can disrupt these functions with debilitating effects (e.g. Zihl *et al.*, 1983; Vaina *et al.*, 1990; Barton *et al*., 1995; Rizzo *et al.*, 1995), and among those at risk are patients with Alzheimer's disease. To obtain better understanding of the effects of Alzheimer's disease on motion perception, we tested the hypothesis that Alzheimer's disease impairs the perception of motion direction, structure from motion (SFM) and moving shapes in a study involving 41 individuals with mild and moderate Alzheimer's disease and 22 control subjects without dementia. The results, which show impairments of SFM, are relevant to the understanding of the pathology of neural systems in patients with Alzheimer's disease and the progressive impact on the daily activities of affected persons.

Subjects

Forty-one volunteers with Alzheimer's disease (mean age 72.3 years, SD = 8.0 years; mean education 13.1 years, SD = 3.2 years) were recruited from the Alzheimer's Disease Research Center in the Department of Neurology, University of Iowa. The diagnosis of probable Alzheimer's disease was based on standard criteria (NINCDS-ADRDA) (McKhann *et al.*, 1984). All participants with Alzheimer's disease were living at home, able to attend to personal needs (e.g. feeding, toileting) and were either still driving or had just stopped. Twenty-two participants without dementia (controls) (mean age 71.7 years, SD = 6.7 years; mean education 14.4 years, SD = 2.7 years) were also studied. Informed consent was obtained in accordance with the standards of the Human Subjects Internal Review Board at the University of Iowa. Alcoholism, stroke and depression were exclusion criteria. Both groups participated in the same cognitive and visual tests and wore their glasses for all procedures. There were no significant differences (Wilcoxon two-sample test) between participants with Alzheimer's disease and participants without dementia in corrected static visual acuity measured for near vision using a standard Snellen card [20/26.1 (SD = 9.9) for participants with Alzheimer's disease versus 20/26.1 (SD = 8.5) for controls, $P = .84$] and for far vision using a wall chart [20/27.5 (SD = 17.0) versus 20/25.9 (SD = 10.4), $P = 0.90$] or in static spatial contrast sensitivity measured using a Pelli–Robson chart (Visitech®) (Pelli *et al.*, 1988) [1.76 (SD = 0.22) versus 1.84 (SD = 0.22), $P = 0.07$].

Method and results

Cognitive assessment

All subjects participated in a battery of standardized neuropsychological tests assessing a range of cognitive functions (Eslinger *et al.*, 1984, 1985; Tranel, 1996). All tests were administered by trained technicians who were blind to specific experimental hypotheses. In this study the following were assessed: (i) temporal orientation (TO) (Benton *et al.*, 1983); (ii) information (INFO) [WAIS-R (Wechsler Adult Intelligence Scale—revised) (Wechsler, 1981)]; (iii) controlled oral word association (COWA) (Benton and Hamsher, 1978); (iv) digit span (DIGIT); (v) Rey–Osterreith complex figure test (CFT)—copy; (vi) facial recognition test (FRT) (Benton *et al.*, 1983); (vii) visual retention test (VRT) (Benton, 1974; Benton and Van Allen, 1985; Sivan, 1992); (viii) block design (BLOCK) (WAIS-R) (Wechsler, 1981); and (ix) trail-making test (TMT), parts A and B (Reitan and Davison, 1974).

Briefly, the CFT assesses visuoconstructional ability by asking subjects to copy a complex geometrical figure; the FRT measures visuoperceptive capacity by asking subjects to discriminate between unfamiliar face pictures; the VRT assesses visuoperception, construction and memory by requiring subjects to reproduce (by drawing) 10 geometrical designs (line drawings) that are shown and then withdrawn from view; the WAIS-R block design subtest also tests visuoconstructional ability and provides a reliable measure of non-verbal intellectual capacity that is highly correlated with performance IQ (Spreen and Strauss, 1991; Lezak, 1995); and the TMT requires a subject to learn to track, simultaneously, two different types of visual information, which requires cognitive flexibility and planning.

Results

The performance of the Alzheimer's disease group was significantly worse than that of the controls on most indices and showed lower group means and greater variability (Fig. 1), as anticipated on a battery of tasks sensitive to cognitive decline. Mean scores in the Alzheimer's disease group fell in the range of mild to moderate impairment (Spreen and Strauss, 1991; Lezak, 1995). This included defective performance on tests of visual processing, including the CFT, FRT, VRT, WAIS block design and TMT.

Assessment of movement perception

Testing motion perception demands stimuli that minimize inferred movement from noticeable changes in the visual

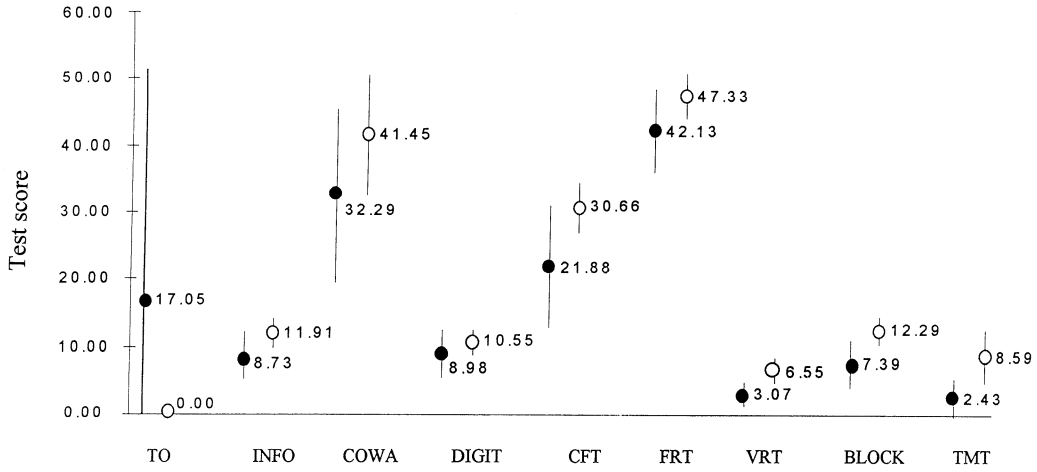

Fig. 1 Performance (mean scores) on a battery of standardized cognitive tests is shown in the group with Alzheimer's disease (closed circles) and in participants without dementia (open circles). Bars denote 1 SD above and below the mean. Participants with Alzheimer's disease had worse performance than controls on most indices and showed greater variation in performance, as expected on a battery of tasks sensitive to cognitive decline in Alzheimer's disease (see text). For parsimonious representation on a common ordinate scale, the TO score is shown as a positive (rather than the usual negative) value. Given that some tests are represented with raw scores and others with scaled scores, this graph is to be used only for comparison between groups and not for profile analyses within each group. TO = temporal orientation (raw score); INFO = WAIS-R information subtest (age-corrected scaled score); COWA = controlled oral word association (scores corrected for age and education); DIGIT = WAIS-R digit span subtest (age-corrected scaled score); CFT = complex figure test (raw score); FRT = Benton facial recognition test (scores corrected for age and education); VRT = Benton visual retention test (number correct, raw score); BLOCK = WAIS-R block design subtest (age-corrected scaled score); TMT = trail making test, part B (scaled score equivalent of raw score).

scene (the way we 'see' movement in the minute hand of a clock). Suitable stimuli are computer-generated animation sequences known as random-dot cinematograms (RDC). RDC present a motion signal amid spatially random background noise and allow variation of spatial displacement and temporal intervals at programmable exposure durations. We used RDC to test the perception of motion direction (Experiment 1) and SFM (Experiment 2). These were first-order stimuli; first-order motion refers to a change in luminance over space and time, such as when a dark object passes over a lighter surface. The associated percept relies on neural mechanisms that correlate luminance displacements over time (Watson and Ahumada, 1985; van Santen and Sperling, 1985). We also measured the effects of movement on the ability to identify 2D target shapes (Sloan acuity letters) in a test of 'dynamic acuity' not using RDC, and where form and contour cues were conspicuously available when the shapes were stationary (Experiment 3).

Experiment 1: perception of motion direction

The RDC animation sequences for this task contained 13 frames depicting 150 randomly placed small ($2' \times 2'$) black dots moving within a $4° \times 4°$ aperture upon a computer screen. Each dot was displaced a small constant distance between cinematogram frames. A proportion of the dots was displaced to give the motion signal direction (up, down, left or right). The remaining dots were given displacements from a flat distribution of directions spanning 360° to create background noise. The observer was asked to indicate the perceived direction of the motion in the stimulus. Performance was assessed by determining the ratio of signal to signal-plus-noise at the perception threshold. The higher the ratio the less able is the motion-processing mechanism to integrate local dot movement vectors into a global coherent motion flow. This task cannot be completed by scrutinizing individual dots because the dots are small, the frame and stimulus durations are brief and the assignment of dots to a signal or noise distribution varies between frames. A low dot density minimizes the possibility of accidental correspondence and prevents unreliable masking of the motion signal by the noise (Williams and Sekuler, 1984; Bravo and Watamaniuk, 1992). Thus, these first-order motion stimuli resemble those used by other investigators in monkeys and humans (Newsome and Paré, 1988; Baker and Hess, 1991; Silverman *et al.*, 1994; Mendola *et al.*, 1995).

Before the test, a group of 15 small ($24' \times 10'$) computer-generated, like-orientated arrows was presented to subjects to determine if they could report the uniform direction with the stimulus durations (195 ms) used in this task. Next, we presented RDC stimuli ranging from 90 to 100% of the signal presented to determine if subjects could perform the motion perception task. All participants were able to complete these procedures, indicating that no overt behavioural deficit was present which precluded subsequent testing of first-order motion.

To begin, subjects fixated a small cross displayed in the centre of the monochrome monitor. Displacement of each signal and noise dot by 10′ arc each 15 ms gave a stimulus velocity of ~11°/s. Stimulus duration was ~200 ms. Stimuli were presented at the point of fixation or 5° into one of the four visual quadrants. Trials were initiated by the experimenter only after the subject had fixated the small central cross. The subject then had to indicate which direction of signal motion was displayed. Responses were verbal or gestural and were recorded on the computer by the experimenter.

The ratio of signal to noise dots was varied using a method of constant stimuli, and used RDC stimuli ranging from 5 to 35% of the signal presented in a predetermined random order. Subjects completed 60 trials at each level of signal tested. Subjects who had trouble at these signal levels were tested with stimuli ranging from 20 to 80% of the signal presented. From the percentage correct performance at each signal level, the threshold (defined as 62.5% correct for a four-alternative forced-choice task) was determined using probit analysis. Normal, uncompromised motion perception requires ~12% of the signal for threshold performance in young observers (Nawrot and Rizzo, 1995) and ~40% of the signal (with stimulus duration of 495 ms) in the 'motion blind' patient L.M. (Rizzo *et al.*, 1995).

Results. Older baseline control subjects required 17.6% (median) of the signal (mean = 20.6%, SD = 8.3, range 11.7–42.0) to correctly determine the direction of signal dot movement at threshold. This is slightly higher than the thresholds we reported in older baseline subjects in another recent study (Nawrot and Rizzo, 1995). The 41 subjects with Alzheimer's disease varied widely in their abilities and as a group required 23.3% (median) of the signal (mean = 30.5%, SD = 22.3, range 10.2–100) at threshold. Distribution of these thresholds was leptokurtic (skewed and pointed) and not bimodal. Some of the subjects with Alzheimer's disease performed well and others poorly, as reflected in the high standard deviation, but as a group they were not statistically different from the baseline controls (Wilcoxon two-sample test, $P = 0.12$).

Experiment 2: Perception of 3D SFM

Perception of SFM or kinetic depth is a long-hypothesized real-world use of motion perception (Gibson, 1950; Nakayama, 1985). To quantify this ability, we used a two-AFC shape identification task in which the observer had to report the shape of the object presented in each trial. Accurate performance on this task depends on the observer's perception of the figure's shape during motion. The SFM figures were a random-dot sphere and a random-dot cube canted 45° about the x and z axes to stand on a vertex. The figures were rotated about either the horizontal or the vertical axis. Varying amounts of random-dot noise were added to a square background region surrounding the target to prevent shape identification from non-motion cues such as edges and dot density, and to index the difficulty of the task. The SFM stimuli comprised a background of 1000 small (2′ × 2′) white dots moving about randomly at 3° within an 8° square region. To this background, 'signal' dots were added which when in motion depicted a rotating SFM figure (Fig. 2). A 10% signal would mean that the SFM stimulus was depicted by 100 dots moving amongst the background dots. The two stimuli were of similar size (~2.8° of visual arc in diameter) but could be easily distinguished by the SFM cues in low-noise conditions. Initial testing showed that all participants could perceive 3D SFM in these stimuli at high signal levels (100%, i.e. 0% background noise) and make the discriminations required in this task. In the subsequent experiment, the signal-to-noise ratio of the dynamic random-dot elements comprising both the figure and background noise was varied from 5% to 35% using a method of constant stimuli. Each subject completed 24 trials at each signal level. Stimuli were presented in a predetermined random order, and in each presentation the subject viewed one complete revolution of the figure, lasting 5.4 s. From the percentage correct performance at each signal level, the threshold (defined as 75% correct for a two-AFC task) was determined using probit analysis. In cerebral akinetopsic subject LM, these thresholds (25–30% signal) are greatly elevated compared with controls (Rizzo *et al.*, 1995).

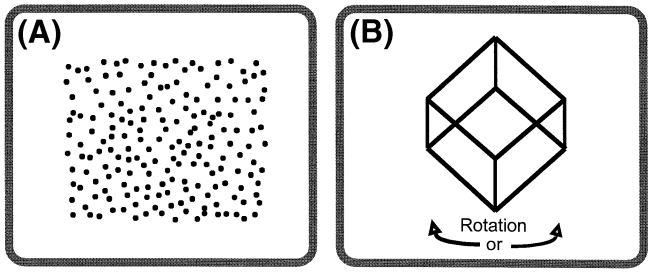

Fig. 2 Test of kinetic depth perception. (**A**) depicts the random-dot kinetic depth stimulus with the random-dot noise background that was presented to the observers. Each of the dots would actually be moving, but there is no obvious shape present in the 2D structure of the dots. (**B**) depicts what is actually perceived by observers, a 3D figure (a cube is depicted here) rotating about a vertical axis.

Results. The 41 participants with Alzheimer's disease tested with this task required a 20.4% signal at threshold (median = 13.6, SD = 20.1, range 5.0–100.0). The 21 controls tested required a 9.3% signal (median = 9.2, SD = 3.1, range 2.8–16.0). Thus, the Alzheimer's disease group required more than twice as much signal as controls at threshold. The difference was significant (Wilcoxon two-sample test, $P = 0.0005$).

Experiment 3: dynamic visual acuity

The ability to resolve detail in coherent objects in relative motion is an important ability in daily life that differs from

the ability to perceive global structure from independent local motion vectors (as in the SFM task implemented in Experiment 2). The former ability is termed dynamic visual acuity and can be measured by procedures similar to static visual acuity testing (Hulbert *et al.*, 1958; Ludvigh and Miller, 1958; Burg and Hulbert, 1961; Miller and Ludvigh, 1962; Long and Crambert, 1990). Static visual acuity is measured by presenting stationary shapes of varying size at maximum contrast, generally black letters against a white background, as on a Snellen chart. Observers are requested to identify these stationary shapes in order to obtain an index of spatial resolution ability. We implemented a dynamic version of this task on a Macintosh computer, presenting moving Sloan high-contrast (100%) letter stimuli (Sloan, 1959; Bailey and Lovie, 1976; Ferris *et al.*, 1982) viewed from a distance of 4 m. Stimulus size could range from 20/125 to 20/5 and testing started at 20/50. Letters moved across the screen from left to right and back again. The stimulus duration was 1.0 s and velocity was 5.2/°s. Subjects were seated to view the computer screen with both eyes open as in Experiments 1 and 2. As on a static acuity test, a subject had to identify five letters correctly to proceed to the next acuity level (20/45). This procedure was repeated until the subject could no longer identify five letters correctly. If a subject could not identify five letters correctly on the 20/50 line (as occurred in one person with Alzheimer's disease), the procedure was repeated at increasing letter sizes. Acuity was expressed in terms of the best level at which five letters were correctly identified (e.g. 20/25), as in Snellen testing. Group acuity scores were similarly expressed with a fixed numerator (of 20) and a variable denominator [mean (SD)].

Results. Introduction of motion into the visual acuity tasks resulted in similar performances in the two study groups. Consequently, there was no significant difference in dynamic acuity between the Alzheimer's disease group [20/33.00 (SD = 17.2)] and the control group [20/30.7 (SD = 9.8)] (Wilcoxon two-sample test, $P = 0.8044$) just as there were no differences in static acuity, as noted earlier. Had we found a defect of dynamic visual acuity, it would have been necessary to exclude a defect of smooth pursuit eye movements causing a shift of the stimulus off the fovea.

Movement processing and cognition

To gauge overall cognitive impairment, a composite score was developed. Standard *T* scores (mean = 50, SD = 10) were assigned to each of nine tests from the neuropsychological assessment battery (TO, INFO, COWA, DIGIT, CFT, FRT, VRT, BLOCK, TMT-B). Standardization of the scores allowed us to generate an equally weighted composite score due to homogeneity of variance of each test score. These nine standard scores were combined into a composite variable called ADSTAT. Lower ADSTAT scores indicate worse cognitive status. To test the hypothesis that movement-processing deficits correlate with cognitive deficits, we calculated the Pearson correlation coefficients between ADSTAT scores and movement processing scores (motion direction discrimination, SFM, dynamic acuity). Also, the contribution of the three motion tests to ADSTAT variance was modelled using stepwise regression.

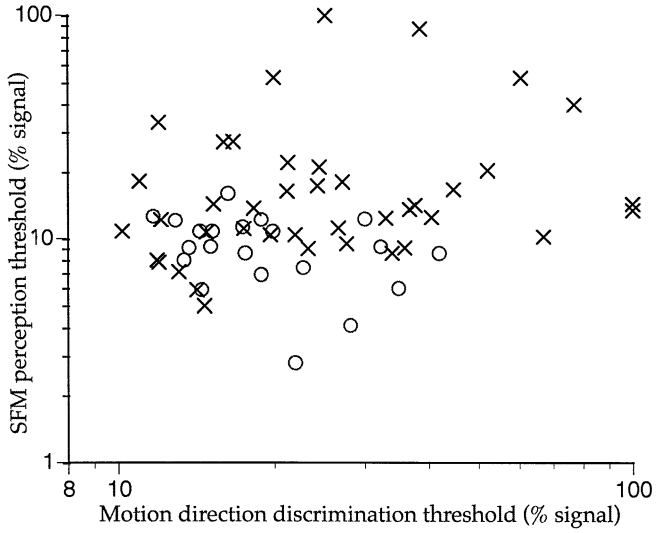

Fig. 3 Perception of motion direction and SFM in Alzheimer's disease and control subjects. The scatter diagram shows threshold performance (percent signal) of subjects with Alzheimer's disease (crosses) and control subjects (open circles) on the motion direction discrimination task (*x* axis) and SFM perception (*y* axis) task plotted on log–log axes. The Alzheimer's disease group showed higher thresholds and greater variability than controls only on the SFM task. See text.

Results

The group with Alzheimer's disease had worse ADSTAT scores than the control group, as expected ($P = 0.00005$, one-tailed). Pearson correlation coefficients ($n = 63$) showed a strong relationship between ADSTAT and SFM ($r = -0.61$), i.e. a lower overall cognitive status correlated with worse movement processing ability (higher thresholds). Also, moderate correlations were found between ADSTAT and first-order motion ($r = -0.43$) and dynamic acuity ($r = -0.41$). Similar relationships were found when the analysis was performed in the Alzheimer's disease group alone ($n = 41$). Pearson correlation coefficients showed a strong relationship between ADSTAT and SFM ($r = -0.62$), and moderate correlations between ADSTAT and first-order motion ($r = -0.35$) and dynamic acuity ($r = -0.47$). All correlations were statistically significant ($P < 0.05$).

Of note is the correlation between SFM and motion direction discrimination in the Alzheimer's disease group, which was only 0.17 (see Fig. 3 for a scatterplot). This correlation is considerably lower than the correlation between motion direction discrimination and dynamic visual acuity of $r = 0.45$. Also, in each case in the Alzheimer's disease group SFM showed a higher correlation than motion direction discrimination with tests from the cognitive battery that

required processing of complex static visual forms (–0.46 for the Alzheimer's disease group versus –0.21 for controls for CFT; –0.37 versus –0.23 for FRT; –0.51 versus –0.31 for VRT; and –0.33 versus –0.23 for BLOCK). This further underscores the differences between processing of motion direction discrimination and SFM, and suggests that SFM defects in Alzheimer's disease reflect combined effects of damage to both form-processing and motion-processing mechanisms (see Discussion).

Stepwise regression was performed to determine the relative contributions of the three motion tests to the variance of ADSTAT. SFM accounted for the most variability (R^2 = 0.39) followed by first-order motion (adding 0.10 to the overall R^2 value) and dynamic acuity (adding 0.02); the overall model accounted for 51% of the variance. Dynamic acuity contributed little once SFM was in the model (even though dynamic acuity had a higher Pearson correlation with ADSTAT in the Alzheimer's disease group than did motion direction discrimination).

It appears that movement processing worsens with progression of Alzheimer's disease. Complex motion processing is affected in persons with mild to moderate disease and may reflect early involvement of specific mechanisms. Simple motion deficits occur in more severe cases; they do not reflect 'selective' early pathology and their measurement is unlikely to facilitate the early diagnosis of Alzheimer's disease.

Discussion

We find that mild to moderate Alzheimer's disease significantly impairs the perception of SFM. This complex motion image-processing deficit has not been previously reported in Alzheimer's disease and may have real-world implications (Fermuller and Aloimonos, 1995; Anderson *et al.*, 1996; Rizzo *et al.*, 1997). Surprisingly, dynamic acuity was normal and motion direction discrimination was relatively spared. The findings were obtained using well-developed tests of proven value for detecting motion-processing deficits in humans and monkeys with CNS lesions (Newsome and Paré, 1988; Nawrot and Rizzo, 1995; Rizzo *et al.*, 1995) and are based on a sample of 41 individuals with Alzheimer's disease, which is larger than the sample sizes used in all previous studies of motion perception in Alzheimer's disease (Trick and Silverman, 1991; Gilmore *et al.*, 1994; Kurylo *et al.*, 1994*a*; Silverman *et al.*, 1994; Mendola *et al.*, 1995).

Mechanisms

Retinal

One proposed explanation for defective motion processing in Alzheimer's disease is degeneration of 'broad-band' retinal ganglion cells and drop-out of corresponding optic nerve fibres (Hinton *et al.*, 1986). These cells have large receptive fields and may contribute to a magnocellular pathway or psychophysical 'transient' channel (Kulikowski and Tolhurst, 1973) which conveys motion signals to the visual cortex via magnocellular layers 1 and 2 of the lateral geniculate body. Yet a 'broad-band' deficit would be expected to impair the processing of all motion stimuli, which is not what we found, and it would not explain the defective performance in our Alzheimer's disease group on tasks which require processing of information in stationary patterns, such as the CFT, FRT and VRT (see above). Kurylo *et al*. (1994*a*) and Mendola *et al*. (1995) described perceptual profiles in Alzheimer's disease that also failed to support a specific retinal 'broad-band' defect. While we cannot exclude a contribution by retinal pathology, retinal dysfunction alone cannot explain the pattern of defects we observed.

Cortical

Visuoperceptual deficits in Alzheimer's disease might be due to degeneration of neurons in cortical (Benson *et al.*, 1988; Hof *et al.*, 1990; Mielke *et al.*, 1995) and subcortical locations (Kuljis, 1994). A small region in the lateral visual association cortex of the monkey, area MT (V5), is thought to be important for motion perception (Allman and Kaas, 1971; Dubner and Zeki, 1971). Homologous areas are believed to occupy the dorsolateral visual association cortices in humans (Zihl *et al.*, 1983; Zeki, 1991). Area MT receives a preponderance of magnocellular pathway (broad-band) inputs from striate (area V1) and early extrastriate areas (e.g. V2) (Maunsell and Van Essen, 1983; Gross, 1991) and contains a large proportion of direction- and velocity-selective neurons (Maunsell and Van Essen, 1983; Albright, 1984; Mikami *et al.*, 1986; Lagae *et al.*, 1993). Lesions in MT impair motion perception in the contralateral visual hemifield (Newsome *et al.*, 1985; Newsome and Paré, 1988; Marcar and Cowey, 1992; Schiller, 1993; Pasternak and Merigan, 1994; Orban *et al.*, 1995*a*, *b*). Furthermore, area MT projects dorsally to the parieto-occipital cortex, which in the human brain can accumulate the signature lesions of Alzheimer's disease (neurofibrillary plaques and tangles), producing 'disconnection' (Hof *et al.*, 1990) and marked visuospatial processing deficits (Mendez *et al.*, 1990).

Lesions in the dorsolateral visual association cortices along a 'where' pathway (Ungerleider and Mishkin, 1982; Damasio, 1985) that includes area MT can also impair SFM (Vaina *et al.*, 1990; Rizzo *et al.*, 1995) and cause selective failure of visual processing of motion-defined form (Regan *et al.*, 1992). Moreover, 3D SFM is encoded by area MT neurons (Bradley *et al.*, 1998) and appears to involve the occipital and parietal cortex more than simpler types of motion discrimination. Along these lines, Orban *et al*. (1998*a*) recently used passive viewing tasks with functional MRI to show that visual motion regions (including MT/V5 and parietal regions) in humans respond more to 3D motion than to 2D motion. Participation of MT/V5 was predicted from experiments in monkeys showing that MT/V5 neurons are tuned to the direction of speed gradients corresponding to

the direction of tilt (Xiao *et al.*, 1997*a*); spatial properties of the antagonistic surround are crucial (Xiao *et al.*, 1997*b*). We hypothesize that defective processing of SFM in Alzheimer's disease is due to impairment in such mechanisms. Dorsolateral pathway lesions can also affect the processing of stationary patterns (e.g. figs 5C–F and 7 in Rizzo *et al.*, 1995), completing the pattern of deficits and helping to explain the strong correlations between SFM and static form-processing tasks (e.g. CFT, FRT, VRT) observed in our Alzheimer's disease group.

There are, however, other mechanisms to consider in Alzheimer's disease. Human and simian cortical organization may differ in the extrastriate cortex at or beyond V3A and V4 (DeYoe *et al.*, 1996; Tootell *et al.*, 1997; Van Oostende *et al.*, 1997). Recent studies of brain activity showed surprisingly little involvement of human MT/V5 in discriminations of motion direction (Cornette *et al.*, 1998) and speed (Orban *et al.*, 1998*b*). Yet parietal regions are active, as are a putative human area V3A and a ventral (lingual) area, suggesting that discrimination performance for simple motion is mediated more by occipitotemporal regions than has previously been suspected. These latter areas contribute to a 'what' or 'temporal' pathway that includes area V4 (which connects strongly with MT) and the inferior temporal area (Felleman and Van Essen, 1991). Moreover, the inferior temporal area in the macaque contains neurons that respond to shapes independently of cue types (of static texture, luminance and relative motion, i.e. cues that are processed in ventral and dorsal visual pathways) (Sáry *et al.*, 1993) and may be responsible for the cue-invariant coding of boundaries and edges (Sáry *et al.*, 1995). Damage to such a cue-invariant mechanism in humans with Alzheimer's disease could affect the perception of shapes defined by moving or static stimulus cues, and may also help explain the strong correlations between impairments of SFM and complex stationary patterns found in the current study. Motion direction discrimination would be little affected as long as the functioning of earlier motion-processing regions (such as ventral lingual and V3A) was relatively spared.

Van Oostende *et al*. (1997) used functional MRI to identify the kinetic occipital region, a motion area that differs in function and location and from other motion-processing areas and has not yet been identified in monkeys. The kinetic occipital area is located posterior to MT/V5 and is activated selectively by kinetic contours (Dupont *et al*., 1997). It may be that observers with Alzheimer's disease are normal for kinetic boundary perception, as they are for simple motion discrimination, on the grounds that the kinetic signal travels occipitotemporally to areas that are relatively unaffected in Alzheimer's disease. However, we did not use the same injected motion strategy to test 2D SFM as we did for 3D SFM; instead we used high-contrast letters (2D shapes) moving against a uniform background (the dynamic acuity task in Experiment 3). A more appropriate task for making direct comparisons between the processing of 2D SFM and 3D SFM would have been the SFM subtest used by Nawrot *et al.* (1996) to test the relative contributions of different cue types to 2D shape perception. However, we did not undertake the present study with the intention of using Alzheimer's disease as a means of elucidating the specific physiological mechanisms underlying different types of motion processing such as 2D SFM and 3D SFM. We believe that perceptual profiles in individuals with well circumscribed brain lesions in the dorsolateral and ventromesial visual association cortices and functional neuroimaging studies can better address issues of functional segregation of visual processes in humans (Rizzo and Barton, 1998).

Subcortical

Silverman *et al*. (1994) inferred disconnection of V1/V2 from MT from studies of impaired motion direction discrimination and preserved onset of optokinetic nystagmus to motion stimuli in nine individuals with Alzheimer's disease of mild severity (Mini-Mental State Examination scores of 17–25). Barton (1995) stated that this pattern could be economically explained by area MT dysfunction (manually impaired responses and impaired ocular pursuit to motion), the remaining motion-processing abilities in these Alzheimer's disease cases being explained by residual function in subcortical structures sensitive to large field motion, such as the accessory optic system and nucleus of the optic tract of the rabbit and monkey. Conversely, movement processing deficits in Alzheimer's disease may be due to lesions in subcortical structures such as the pulvinar (Kuljis, 1994), a critical site for integration of visuospatial percepts (Ogren *et al.*, 1984; Robinson and Petersen, 1992) that also contains movement-sensitive neurons (Petersen *et al.*, 1985; Robinson and Peterson, 1985), and the cerebellum, where lesions of midline structures are reported to affect the processing of motion (Nawrot and Rizzo, 1995). These subcortical areas interact with each other and contribute to cerebral circuits for processing motion that include the cortical area MT (Mohler and Wurtz, 1977; Bender, 1983; Maunsell and van Essen, 1983; Rodman *et al.*, 1990; Gross, 1991; Nawrot and Rizzo, 1995). Yet we are not aware of any study showing that lesions of the pulvinar, colliculus, cerebellum or other subcortical structures can impair SFM without significantly affecting other aspects of motion processing. Thus, lesions of subcortical structures (as of the retina) may contribute to, but alone are unlikely to explain, the pattern of deficits in our observers with Alzheimer's disease.

Separating signal from noise

Accurate perceptual judgements and decisions rely on the visual association cortex (Salzman and Newsome, 1994) and require the screening out of ubiquitous effects of noise arising from scenes, eye jitter and neurons. Lesions in the visual association cortex impair these abilities (Vaina *et al.*, 1990; Baker *et al.*, 1991; Regan *et al.*, 1992; Rizzo *et al.*, 1995) and so does Alzheimer's disease. Kurylo *et al.* (1994*b*) found

that 16 individuals with Alzheimer's disease had difficulty in identifying a square or circle defined by signal pixels amid background noise pixels (see their fig. 1) over a range of stimulus durations and signal-to-noise ratios, indicating decreased speed and increased difficulty in processing the signal in the presence of background noise for stationary patterns. Similarly, the results of the current study show that the perception of SFM in Alzheimer's disease is abnormally sensitive to background motion noise. A different explanation, i.e. 'undersampling', implies that only a portion of the available signal is processed due to loss of receptors or neurons, as hypothesized in congenital amblyopia (Hess and Anderson, 1993). However, the performance of our study participants with Alzheimer's disease is not adequately explained by a generalized 'signal-from-noise' or 'undersampling' problem. These mechanisms should affect thresholds of perception for all types of stochastic stimuli, which is incompatible with the relative sparing of motion direction discrimination for the RDC stimuli used in Experiment 1.

Comment on previous studies

Existing studies of motion perception in Alzheimer's disease are difficult to compare directly with the present study for reasons such as differing stimuli and degrees of dementia. Kurylo *et al*. (1994*a*) reported significantly impaired motion detection in 14 individuals with probable Alzheimer's disease. Stimuli comprised a small patch of dots moving upwards at 100% coherence against stationary background dots at one of four possible locations on a computer monitor. An overlapping team using the same subject pool (Mendola *et al.*, 1995) reported seemingly contradictory results in Alzheimer's disease of normal speed discrimination ($n = 11$) and global motion detection ($n = 12$). Participants fixated a cross with a target area containing dots on each side of it. In the speed discrimination task dot speed was 5°/s on one side and varied on the other, and participants judged which area contained the faster-moving dots. In the global motion detection task, coherence was 0% on one side and varied on the other; participants judged which window displayed coherent downward motion (6°/s). Mendola *et al*. (1995) contrasted their findings of normal speed discrimination in Alzheimer's disease with the abnormal findings of Trick and Silverman (1991) and Gilmore *et al.* (1994) (who studied 15 individuals with Alzheimer's disease and 15 control subjects), and argued that their test was more purely a test of motion perception and did not require additional memory and attention factors to use a joystick to respond (Trick and Silverman, 1991). However, Mendola *et al*. (1995) emphasized that the crucial factor was that Trick and Silverman (1991) and Gilmore *et al*. (1994) required motion direction discrimination whereas they did not. They argued that 'testing additional subjects with motion discrimination and motion detection tasks would clarify this issue'.

Trick and Silverman (1991) studied 20 individuals with Alzheimer's disease whose mean age (73.6 years) and dementia severity (mild, clinical dementia rating score = 1, $n = 11$; moderate, clinical dementia rating score = 0.5, $n = 9$) were comparable with those in the current study. Subjects were asked to determine the direction (up, down, right, left) of a global coherent motion signal that varied from 0 to 50% coherence, as in our Experiment 1. Compared with 29 controls (mean age 69.0 years), patients with Alzheimer's disease had significantly elevated thresholds ($P < 0.001$). However, the investigators used a stimulus in which noise was randomly plotted rather than moving in a random direction. Such noise affects both the direction and speed component in the stimuli whereas noise in the current study affected only the directional component while retaining a uniform dot speed within the stimulus. The noise stimulus used in the current study is more appropriate for a direction discrimination task (Nawrot and Rizzo, 1995). Although the gross similarities in the methods used in the two studies suggest that threshold values should lie in similar ranges, detailed comparisons between thresholds are difficult. Also, Trick and Silverman (1991) excluded nine of the 20 Alzheimer's disease subjects from the group threshold while we excluded none**.** Nevertheless, the mean threshold in our Alzheimer's disease group (30.5% signal) is similar to theirs (27.6%). Our control group, however, had higher thresholds than those observed by Trick and Silverman (1991) (20.6 versus 13.6%), perhaps because they recruited university staff (these are likely to be a highly educated and motivated group of professionals), whereas we recruited individuals from the community whose socioeconomic and educational backgrounds were probably more similar to those of participants with Alzheimer's disease. Also, Trick and Silverman (1991) presented stimuli at 16.7 cm, a close distance which can create optical blur (p. 1438 in Trick and Silverman, 1991) and actually improves motion perception thresholds at the displacements used (30′ angle) (Barton *et al.*, 1996). The 15 individuals with Alzheimer's disease studied by Gilmore *et al*. (1994) probably had worse dementia (Mini-Mental State Examination score as low as 11, severe Alzheimer's disease; mini mental status examination mean score of 15.9, moderate Alzheimer's disease) than our Alzheimer's disease group. This helps to explain why Gilmore *et al*. (1994) found large differences in contrast sensitivity and motion perception between Alzheimer's disease and controls while we did not. Gilmore's thresholds might reflect confounding effects of cognitive or behavioural deficits in Alzheimer's disease on vision scores, not visual deficits.

Conclusion

In short, we find that mild to moderate Alzheimer's disease causes marked deficits in the processing of complex motion images, as presented in an SFM task. We find no evidence that 'simple' or low-level motion attributes such as speed and direction are selectively affected or can provide a sensitive screen for early Alzheimer's disease. While visual

functions tend to deteriorate with progression of Alzheimer's disease (e.g. Cronin-Golomb *et al.*, 1995), the idea that impaired processing of low-level motion stimuli will reveal a visual system involvement in preclinical Alzheimer's disease is not supported. Poor performance was seen in some cases of mild to moderate Alzheimer's disease, but as a group they were similar to normal subjects. Impaired SFM in Alzheimer's disease is not likely to be explained on a retinal or subcortical basis alone and probably depends on lesions in the visual association cortex. Previous studies have invoked neurofibrillary tangles in the dorsolateral visual association cortex (which may contain a human homologue of primate area MT) to explain severe visuoperceptual disturbances in Alzheimer's disease. Alternatively, the co-occurring deficits in processing patterns and shapes defined by static and moving cues that were identified in the current study may also be explained by lesions of a common form-perception mechanism located in the temporo-occipital cortices. Patterns of performance in persons with focal structural lesions or functional neuroimaging are more likely to identify such a mechanism.

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