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Attentional dynamics and visual perception: mechanisms of spatial disorientation in Alzheimer's disease

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Summary

Visuospatial disorientation forces Alzheimer's disease patients to abandon independent activities. We found previously that limitations of ambulatory and vehicular navigation are linked to impaired visual motion processing in Alzheimer's disease. We now hypothesize that these perceptual impairments reflect temporal constraints on visual attention. We evaluated attentional, perceptual and neuropsychological capacities in 14 Alzheimer's disease patients and 12 age-matched older normal controls. The temporal dynamics of visual attention were measured using rapid serial visual presentation (RSVP) to assess the attentional blink. Visual processing for spatial orientation was assessed using perceptual thresholds for optic flow, the visual motion seen during observer self-movement. Alzheimer's disease patients show an exaggerated attentional blink during RSVP, identifying the first of two targets but missing the second target depending on the number of intervening distractors. They also show a unique form of attentional masking in which they miss the first target but identify the second, again depending on the number of intervening distractors. Both types of RSVP errors are correlated with selectively elevated optic flow thresholds in Alzheimer's disease patients. This suggests that temporal constraints on visual perception might impair optic flow analysis and contribute to spatial disorientation in Alzheimer's disease. These findings are consistent with two-stage models of visual perception, suggesting that the working memory mechanisms in the second stage provide feedback control of input to category-specific perceptual processors in the first stage.

Keywords: Alzheimer's disease; attentional blink; attentional masking; optic flow; spatial disorientation

Abbreviations: RSVP = rapid serial visual presentation; T1 = target one; T2 = target two

Introduction

Alzheimer's disease is characterized by a memory disorder accompanied by attentional and perceptual deficits (Parasuraman and Greenwood, 1998; Cummings, 2000). These perceptual deficits include impaired visual motion processing (Silverman *et al*., 1994) with greatly elevated thresholds for optic flow (Tetewsky and Duffy, 1999), the patterned visual motion seen during observer self-movement (Gibson, 1950). Elevated optic flow thresholds are correlated with deficits of ambulatory (Tetewsky and Duffy, 1999) and vehicular navigation (O'Brien *et al*., 2001), suggesting a perceptual basis of visuospatial disorientation in Alzheimer's disease (Henderson *et al*., 1989).

Attentional dynamics might constrain optic flow perception in Alzheimer's disease by limiting the rate at which visual motion signals can be integrated into a coherent representation of self-movement. Attentional constraints on visual processing have been measured using rapid serial visual presentation (RSVP) tasks (Broadbent and Broadbent, 1987) that reveal the attentional blink, a failure to perceive the second of two task-defined targets. The attentional blink occurs only when the two targets are separated by distractors presented in the interval between 100 and 500 ms after the first target stimulus (Raymond *et al*., 1992). The attentional blink is exaggerated, more prolonged and more severe after focal cortical lesions (Rizzo *et al*., 2001). The exaggeration of the attentional blink may be particularly profound with right posterior parietal cortex lesions that are associated with the syndrome of hemi-inattention (Husain *et al*., 1997).

Right posterior parietal involvement in attentional control is supported by this region's selective activation by RSVP

tasks that demand attentional processing (Marois *et al*., 2000). This region is also activated by optic flow (Morrone *et al*., 2000), with specific subregions responding to visual stimuli that simulate visual scenes during observer self-movement (Dukelow *et al*., 2001; Peuskens *et al*., 2001). Together, such findings suggest mechanistic links between attentional control and optic flow perception. Such links might help to explain classical descriptions of hemi-inattention and topographagnosia after right parietal lesions (Holmes, 1918; Critchley, 1953).

In this context, we hypothesized that attentional impairments might contribute directly to visual perceptual deficits in Alzheimer's disease. To test this hypothesis, we obtained independent measures of attentional processing and optic flow perception. Our findings reveal links between temporal constraints on attention and visual motion processing impairments. This supports two-stage models of perception (Maki *et al*., 1997) with the addition of an inhibitory feedback loop for task-dependent interactions between working memory mechanisms and perceptual processors.

Methods

Subject groups

We studied older normal control subjects and Alzheimer's disease patients without ophthalmological or other neurological disorders. All subjects had normal, or corrected to normal, visual acuity and contrast sensitivity. Alzheimer's disease subjects (mean age 78 years) were recruited from the clinical programmes of the University of Rochester Alzheimer's Disease Center with probable Alzheimer's disease by NINDS criteria (McKhann *et al*., 1984). Older normal subjects (mean age 79 years) were recruited from programmes for the healthy elderly or were the spouses of Alzheimer's disease subjects. We studied 14 Alzheimer's disease patients and 12 older normal subjects.

Informed consent was obtained from all subjects before their participation. All procedures were approved by the University of Rochester Human Subjects Review Board and complied with the Declaration of Helsinki.

Neuropsychological testing

We performed a battery of neuropsychological tests on most of the subjects: The Mini-Mental Status Examination (Folstein *et al*., 1975) was used as a measure of overall impairment in Alzheimer's disease. The Road Map test (Money, 1976) was used to assess topographic orientation in simulated route following. Two subtests from the Wechsler Memory scale (Wechsler, 1987) were used: the Verbal Paired Associates test was used to assess immediate and delayed verbal memory, and the Figural Memory test was used to assess visual memory.

RSVP

The stimulus set consisted of 22 upper case letters as targets and nine digits serving as distractors. The letters I, O, Q and Z, and the number 0 was omitted to avoid ambiguity. The stimuli were black, Arial bold font, presented on a uniform grey background (9 cd/m^2) with a visual angle of ~0.8 × ~1°. Stimuli were presented for 130 ms followed by a 50 ms blank interval to produce a 5.5 Hz stimulus rate (Husain *et al*., 1997).

RSVP testing consisted of two blocks, one each for single- and dual-target trials. Single-target blocks consisted of 70 trials that contained only one target stimulus embedded in a series of 14–23 distractors. Dual-target blocks consisted of 70 trials, 10 each with 0–6 intervening distractors between the first (T1) and second (T2) targets. Trials began with fixation of a red dot in the middle of the computer screen that was monitored by infrared oculography. Subjects pressed a mouse button and, after a 500 ms delay, the RSVP stream was presented at the centre of screen. The screen was then dark for 10 s while the subject reported their best impression of the target letter(s). Subjects responded by verbally identifying the two target letters at the end of each trial.

Testing of each subject began with 16 single-target practice trials that familiarized subjects with the apparatus and the RSVP task. If subjects scored at least 70% correct in practice trials, they continued with single-target and then dual-target testing. Four Alzheimer's disease patients did not achieve criterion RSVP performance, reporting that the stimuli were presented too quickly, and were not subjected to further testing. These four patients were not different from the rest of the Alzheimer's disease patients on any other measures.

For each subject, RSVP performance was measured for each number of intervening distractors as a conditional probability: attentional blink was measured as the conditional probability of reporting T2 given that T1 was reported correctly. Attentional masking was measured as the conditional probability of reporting T1 given that the T2 was reported correctly. Averaged conditional probabilities across 0–4 intervening distractors were used as an overall measures of RSVP performance. This time window, from 0 to 900 ms after the first target, accommodated the temporal attributes of performance of older normal and Alzheimer's disease subjects by including all intervals in which attentional blink or attentional masking errors were observed in either group.

Visual motion stimulation

Subjects sat 4 inches from an 8 × 6 inch rear-projection tangent screen maintaining centred fixation on a red LED (light-emitting diode) image as monitored by infrared oculography (ASL, Inc., Bedford, USA). They viewed a large screen computer display of visual motion coherence stimuli and pressed buttons to respond in a two-alternative forced-choice paradigm. Stimulus coherence levels were controlled by the PEST (parameter estimation by sequential

Table 1 *Results of attentional, perceptual and neuropsychological tests for older normal subjects and Alzheimer's disease patients*

Task	Participants		Statistical significance
	Older normals	Alzheimer's disease	
Neuropsychological			
MMSE	27.89 (2.03)	25.00 (1.96)	0.005
Road	30.11 (2.09)	24.67 (4.47)	0.007
Figural	7.00 (.87)	5.22 (.97)	0.001
Verbal	15.89 (4.48)	8.33 (4.06)	0.002
Delayed	6.33 (2.12)	3.33 (2.29)	0.01
Motion perception			
Horizontal	19.22 (5.63)	20.00 (8.69)	0.83
Radial	17.43 (8.89)	43.89 (32.04)	0.04
RSVP			
Single-target	92.02 (6.26)	79.43 (10.50)	0.005
Dual-target	74.17 (8.16)	48.71 (17.98)	0.001

Performance scores, means (SD) are listed with *P* values results of group-wise comparisons from independent sample *t* tests assuming unequal variances. All tests, except horizontal motion coherence thresholds, yielded significant differences between groups. MMSE = Mini-Mental Health State Examination.

testing) algorithm (Harvey, 1986) that determined psychophysical thresholds by fitting a Weibull function to find the coherence that yielded 82.5% correct responses. Trials began with an audible tone indicating that central fixation was required within 1 s. A visual stimulus was then presented for 1 s and followed by a pair of tones to prompt a push-button response. Subjects were trained on each task by presenting high coherence stimuli to test their ability to see those patterns, understand the task and respond appropriately.

Visual stimuli were generated off-line and presented by a PC driving a TV projector (Electrohome 4100) to create a $90 \times 60°$ image centred at eye height. The stimuli consisted of 500 white dots (2.69 cd/m^2) on a black background in an animated sequence of frames presented at 60 Hz. Dot positions were specified for each frame by algorithms for each type of display (O'Brien *et al*., 2001). All stimuli had the same dot density, luminance, contrast and average dot speed (see Fig. 3A).

Results

The results of attentional, perceptual and neuropsychological tests are shown in Table 1. Older normal subjects showed normal-for-age scores on all neuropsychological tests. Alzheimer's disease patients were relatively impaired on all neuropsychological tests ($P \leqslant 0.01$), consistent with their diagnosis.

RSVP testing included a block of single target trials in which subjects identified the target letter presented in a series of distractor numbers. These data established a single-letter identification rate for each group, showing significantly better performance in the older normal control group (92% correct) than the Alzheimer's disease group (79% correct) [$t(20) = 3.48$, $P = 0.0005$]. This baseline single-letter identification rate was not affected significantly by the number of distractor stimuli.

Dual-target RSVP trials included two target letters that were separated by varying numbers of distractor stimuli (Fig. 1). Subjects responded by identifying the two target letters at the end of each trial. Overall accuracy, as the rate of correctly identifying both targets, was significantly higher in the older normal group (74% correct) than in the Alzheimer's disease group (49% correct) [$t(20) = 4.41$, $P = 0.0001$].

We analysed attentional blink errors in trials where the first target was identified correctly such that only the second target might be missed. In these trials, the older normal group performed significantly better than the Alzheimer's disease group [older normal = 76% correct, Alzheimer's disease = 58% correct; $t(20) = 3.21$, $P = 0.0009$] (Fig. 2A).

Attentional blink errors showed a significant effect of the number of intervening distractors [$F(6,120) = 12.30$, $P < 0.0005$]. Both groups showed good performance with zero distractors, conventionally called lag 1 sparing. This phenomenon is viewed as the capacity to combine contiguous targets into a single perceptual item in RSVP (Raymond *et al*., 1992). With one intervening distractor, the Alzheimer's disease group showed 14% more attentional blink errors than the older normal group. The Alzheimer's disease group also performed significantly worse than the older normal group with two (25%, $P = 0.01$), three (30%, $P = 0.0003$) and four intervening distractors (11%, $P = 0.02$). Trend analysis revealed that the older normal group recovered to their single-target baseline after two intervening distractors (720 ms), whereas the Alzheimer's disease group did not recover to their single-target baseline until there were six intervening distractors (1200 ms).

Thus, the older normal group showed the same pattern of attentional blinks seen previously in young (Raymond *et al*.,

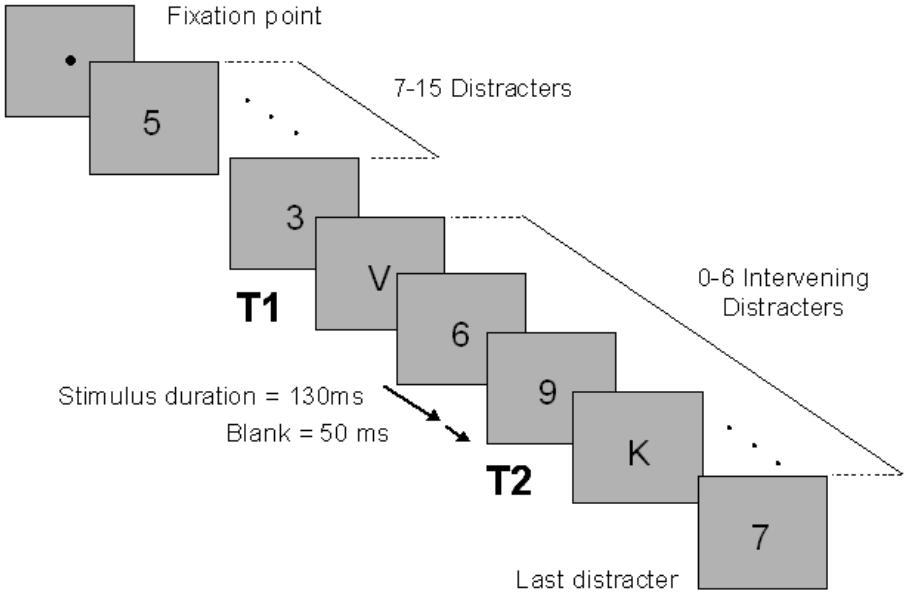

Fig. 1 RSVP test. Dual-target trials presented letter targets imbedded in a series of number distractors. Trials began with centred fixation, followed by 7–15 preceding distractors, then the two targets (T1 and T2) separated by 0–6 intervening distractors, and ending with a single distractor. Example represents dual-target trial with two intervening distractors.

1992; Chun and Potter, 1995) and older (Husain *et al*., 1997) normals, failing to report the second of two targets separated by one or two distractors (360 ms). The Alzheimer's disease group's attentional blink was more prolonged, lasting until the fifth intervening distractor (1200 ms).

Alzheimer's disease subjects also made errors in which the first target was missed and the second target was identified correctly. This resulted in significantly poorer performance in Alzheimer's disease (64% correct) than in older normal (89% correct) subjects [$t(20) = 3.81$, $P = 0.0005$] (Fig. 2B). There was a significant group × distractors interaction [$F(6,54 = 4.61$, $P = 0.001$] which *post hoc* analyses attributed to group differences with 0–4 intervening distractors. The number of intervening distractors affected the Alzheimer's disease group [$F(6,54) = 5.41$, $P < 0.003$], but not the older normal group [$F(6,66) = 1.37$, $P = 0.024$]. This suggests a qualitative distinction between the Alzheimer's disease and older normal groups. The temporal distribution of attentional masking errors resembled that of attentional blink errors except at zero intervening distractors. This suggests that attentional masking errors cannot be considered simple momentary lapses in attention, which one should expect to be distributed randomly.

The loss of the first target is not from forgetting, or from perceptual masking by the distractors. If either were the case, such errors would persist across any number of distractors rather than being limited to trials with no more than four intervening distractors (<800 ms). These errors represent category-specific attentional masking: masking because the loss of the first target is related to the arrival of the second target, and attentional because only items of the target category have the effect; a long series of five or six intervening distractors does not evoke such effects.

Thus, the Alzheimer's disease and older normal groups both showed attentional blink; Alzheimer's disease patients make more such errors and do so over a longer period. Alzheimer's disease patients, but not older normal subjects, make a unique type of error that we call attentional masking. Attentional masking errors consisted of missing the first target, but correctly identifying the second. In the Alzheimer's disease group, there is a clear correlation between attentional blink and attentional masking errors ($r = 0.081$, $P = 0.0005$). In both groups, 85% of all errors were omissions in which only one target was reported; 15% were intrusions in which a target was reported incorrectly.

We assessed horizontal motion and radial optic flow (Fig. 3A and B) perception in the older normal and Alzheimer's disease groups, finding significant task × group interaction effects [$F(1,14) = 5.24$, $P < 0.04$]. Both groups had nearly identical horizontal motion coherence discrimination thresholds (older normal controls = 20%, Alzheimer's disease = 19%). In contrast, the older normal and Alzheimer's disease groups had significantly different radial optic flow motion coherence discrimination thresholds of 17 and 44%, respectively [$t(14) = 3.36$, $P = 0.004$]. The radial thresholds revealed two subgroups of Alzheimer's disease patients: one subgroup had similar horizontal and radial motion thresholds (55%, five out of nine); while the other subgroup had selectively elevated radial motion thresholds that averaged twice the magnitude of their horizontal motion thresholds (Fig. 3C).

We compared RSVP performance and visual motion perception across all subjects. Alzheimer's disease patients, but not older normal subjects, showed a significant correlation between RSVP errors and elevated radial optic flow thresholds (attentional blink $r = –0.70$, $P = 0.004$; attentional

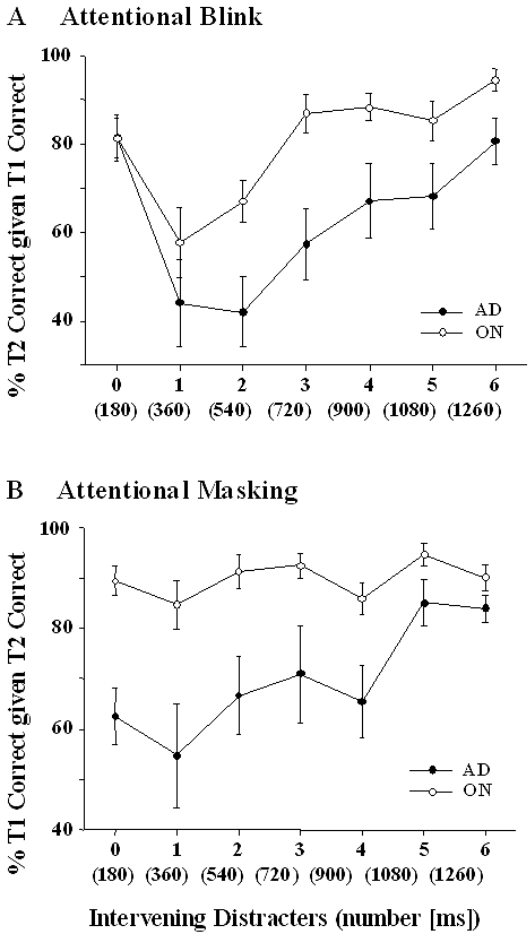

Fig. 2 RSVP errors in identifying the two targets presented in dual-target trials. (**A**) Attentional blinks: trials in which T1 was reported correctly and T2 was not. Older normal subjects showed attentional blinks with one of two intervening distractors. Alzheimer's disease patients showed a greater number of attentional blinks with up to five intervening distractors. (**B**) Attentional maskings: trials in which T2 was reported correctly and T1 was not. Older normal subjects did not show attentional maskings. Alzheimer's disease patients showed attentional maskings with up to four intervening distractors. Graphs show the frequency of errors as a percentage of trials in which both targets were identified correctly (ordinate) as a function of the number of intervening distractors (abscissa).

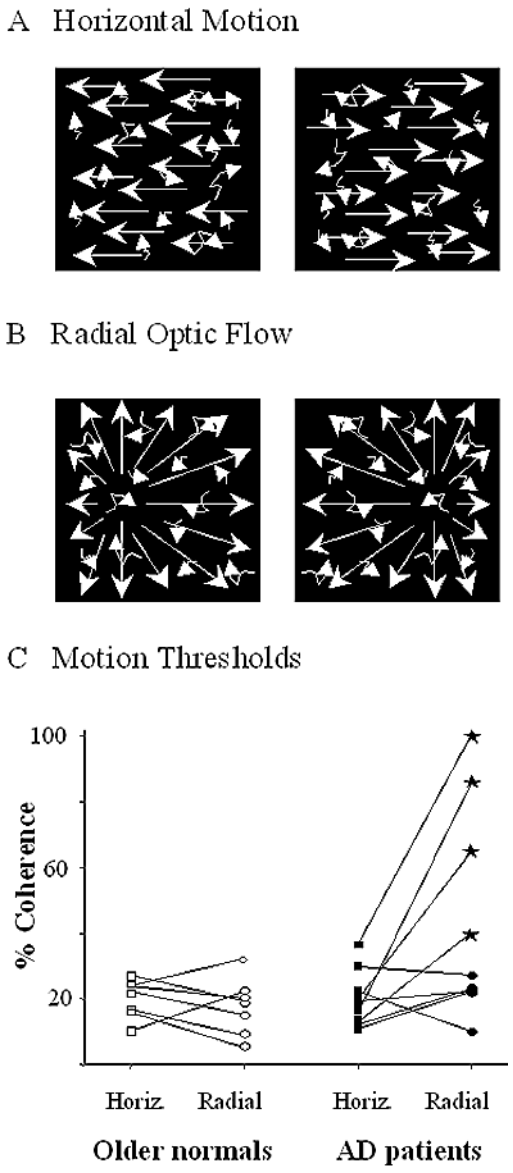

Fig. 3 Visual motion stimuli contained either horizontal movement to the left or right (**A**), or radial optic flow with a focus of expansion 30° to the left or right (**B**). Dots moving in these patterns were intermixed with randomly moving dots, with the percentage of randomly moving dots in each trial adjusted by a PEST (parameter estimation by sequential testing) algorithm (Harvey, 1986) to determine each subject's horizontal and radial motion coherence thresholds. Stimuli were presented for 1 s during oculometrically monitored central fixation. Subjects responded by pressing either a left or right hand button to indicate the corresponding pattern in the stimulus. (**C**) Horizontal motion (squares) and radial optic flow (circles) discrimination thresholds in older normal subjects (open, left) and Alzheimer's disease patients (filled, right). The Alzheimer's disease group included patients with selectively elevated radial optic flow coherence thresholds (stars, right). Older normal and Alzheimer's disease groups did not differ with respect to their horizontal motion thresholds.

masking $r = –0.71$, $P = 0.003$). The Alzheimer's disease subjects who had elevated radial optic flow thresholds showed a greater number of attentional blink and attentional masking errors. There was no correlation between RSVP performance and horizontal motion thresholds. This suggests a link between temporal constraints on the processing of a rapidly presented series of target items embedded in distractors, and the discrimination of self-movement headings simulated by optic flow stimuli.

RSVP performance was also compared with neuropsychological test scores in Alzheimer's disease patients. There was a significant negative correlation between attentional masking errors and both immediate ($r = –0.73$, $P = 0.003$) and delayed ($r = –0.66$, $P = 0.005$) verbal memory scores. Attentional blink errors were not correlated with neuropsychological test scores, although there was a non-significant

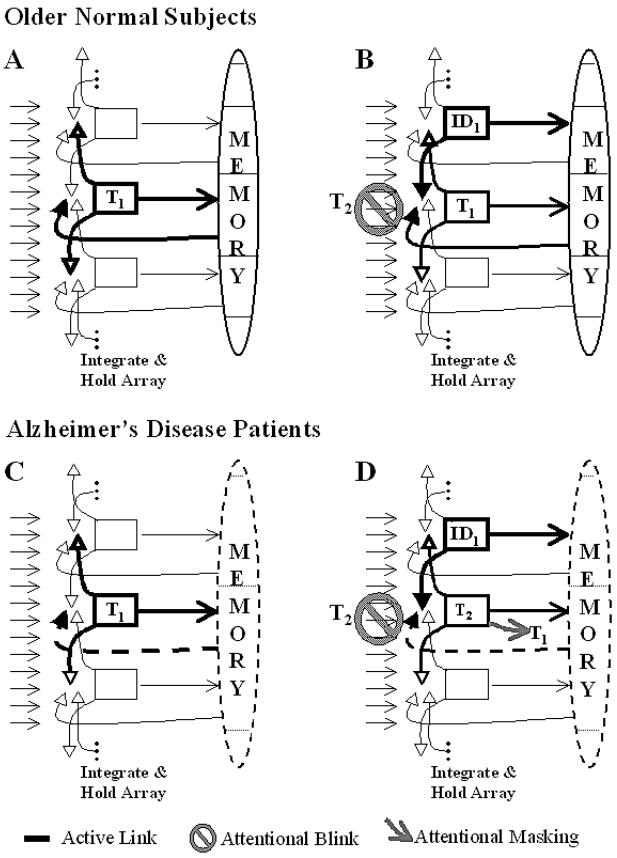

Fig. 4 A schematic diagram of the two-stage concurrent inhibition model. This model hypothesizes that visual input drives an array of perceptual integrate-and-hold modules (rectangles). Each module is tuned to respond to a specific category of visual input. Active modules inhibit input to neighbouring modules and present their content to the working memory store (oval). The working memory store provides feedback to the active categorical processor as a second source of inhibition of visual input that persists until working memory has consolidated the current content of that processor. ID_1, first intervening distractor; T1, T2, first and second target stimuli.

trend toward a negative correlation with verbal memory similar to that seen with attentional masking. Thus, RSVP performance was most impaired in Alzheimer's disease patients with milder verbal memory deficits.

Discussion

These experiments reveal an exaggerated and prolonged attentional blink in Alzheimer's disease patients with their missing the second of two targets separated by distractor stimuli. When Alzheimer's disease patients are able to report the second target, they frequently have missed the first. These errors also depend on the number of intervening distractors, prompting the analogous term attentional masking. Both types of RSVP errors are correlated with impaired optic flow perception in Alzheimer's disease. This suggests that both RSVP performance and optic flow analysis are affected by the temporal dynamics of perceptual processing which might play a significant role in the spatial disorientation in Alzheimer's disease.

The attentional blink originally was thought to reflect a perceptual gate that is closed by the first target (Raymond *et al*., 1992), but this did not accommodate the distractor's apparent access to perceptual systems. Subsequent models emphasized interference between the two target stimuli within a shared working memory mechanism (Shapiro *et al*., 1994) or between the first target and the distractors within a perceptual module that precedes working memory in a two-stage system (Chun and Potter, 1995) that may incorporate attentional filtering (Maki *et al*., 1997) or selective inhibition (Shapiro, 2001). The magnitude of the attentional blink reflects target–distractor similarity (Enns *et al*., 2001).

Alzheimer's disease patients are vulnerable to visual masking in which the second of two stimuli permanently blocks recall of the first (Schlotterer *et al*., 1984). Attentional masking in Alzheimer's disease patients resembles visual and conceptual masking (Intraub, 1999) because it obscures the preceding stimulus. Attentional masking is distinct because it only occurs with stimuli from the task-defined target category. Attentional blink and attentional masking combine to impose temporal limits on perception, restricting Alzheimer's disease patients to brief glimpses of their environment. This creates snapshot vision like that reported in motion blindness after bilateral extrastriate visual cortical lesions (Zihl *et al*., 1991).

RSVP performance and optic flow perception might be linked by the fact that both consist of sequentially presented discrete images (Raymond, 2001). The targets and distractors in RSVP stimuli are presented sequentially. Likewise, the patterned visual motion of optic flow is created by the sequential displacement of texture elements in successive video frames. Thus, RSVP performance and optic flow perception might both reflect the time course of temporal integration during sequential stimulation.

However, RSVP and optic flow performance are correlated only in Alzheimer's disease patients. This suggests an observer-oriented interpretation that might focus on the unique local motion strategy that Alzheimer's disease patients use to process optic flow. Our earlier work showed that Alzheimer's disease patients successively sample parts of the optic flow stimulus and then combine those samples to construct a perceptual mosaic of the stimulus (O'Brien *et al*., 2001). Thus, Alzheimer's disease patients process optic flow as a series of discrete images created by sequential sampling that may be subject to the same temporal constraints that limit RSVP performance. In this context, our current findings suggest that Alzheimer's disease patients suffer from a combined failure of spatial and temporal integration for visual perception.

The latter view is more consistent with preserved horizontal motion perception in our Alzheimer's disease patients. It is also consistent with Alzheimer's disease patients having difficulty shifting from local to global processing (Filoteo

et al., 1992) and having a limited spatial window for visual integration that forces them to analyse optic flow by sampling local motion in the pattern (O'Brien *et al*., 2001).

Here, we propose a modified model for RSVP processing, based on previous efforts to explain temporal dynamics of perceptual processing as measured by attentional blink (Chun and Potter, 1995). We view RSVP performance as exposing attentional constraints on perception that are consistent with a two-stage model (Maki *et al*., 1997) with gated input to category-specific integrate-and-hold perceptual processors. We speculate that this gating is a product of concurrent inhibition from two sources: lateral inhibition from distractor activation of neighbouring perceptual processors in a competitive network (Keysers and Perrett, 2002), and feedback inhibition from target activation of working memory mechanisms that remain active during mnemonic consolidation. Thus, working memory has two roles in the RSVP task: first, it maintains intermediate representation of a stimulus. Secondly, it provides inhibitory feedback when occupied with target processing. In this model, attentional blink is caused by combined lateral and feedback inhibition that blocks input to the target perceptual processor. Attentional masking is caused by impaired working memory mechanisms in Alzheimer's disease that slow consolidation and destabilize feedback inhibition of perceptual input.

In older normal subjects (Fig. 4A and B), the first target item (T1) activates an integrate-and-hold module that presents the input item to working memory (Fig. 4A). Working memory provides feedback inhibition of further input to the target integrate-and-hold module. The arrival of the first intervening distractor (ID1) activates an adjacent module that also inhibits input to the target integrate-and-hold module. Concurrent lateral and feedback inhibition blocks input to the target module to protect the contents of that module to create the attentional blink during memory consolidation. The attentional blink persists as long as both the stream of intervening distractors continues and the working memory store continues the process of consolidating T1.

In Alzheimer's disease patients, the working memory store is impaired, slowing mnemonic consolidation and destabilizing feedback inhibition of input to the target integrate-and-hold module (Fig. 4C and D). This prolongs the attentional blink and, for a similar period, can allow the second target (T2) to enter its integrate-and-hold perceptual module. In those cases, T2 over-writes T1 in the target integrate-and-hold perceptual module to create attentional masking. Attentional masking of T1 by T2 can occur until the working memory store completes the consolidation of T1.

We speculate that there may be some direct correspondence between elements of the model and functional subdivisions of the brain. Category-specific perceptual processors might reside in the functionally distinct areas of extrastriate visual cortex (Felleman and Van Essen, 1991). The dorsal extrastriate pathway (Ungerleider and Mishkin, 1982) is activated by tasks invoking visual attention (Corbetta *et al*., 1991; Coull and Nobre 1998; Yantis *et al*., 2002), motion processing (Dupont *et al*., 1994; Cheng *et al*., 1995; Tootell *et al*., 1995) and spatial cognition (Horwitz *et al*., 1992; Aguirre and D'Esposito, 1997), and, more specifically, both RSVP (Marois *et al*., 2000) and optic flow processing (Peuskens *et al*., 2001). Such inferences must be tempered by the limited correspondence between functional subdivisions of human and monkey posterior parietal and superior temporal areas (Karnath, 2001).

These areas have forward and feedback connections to hippocampal (Seltzer and Pandya, 1984; Clower *et al*., 2001) working and long-term memory mechanisms that are affected in the early stages of Alzheimer's disease (Braak and Braak, 1991) typical of our Alzheimer's disease patients. These connections might reciprocally link parietal centres for RSVP and optic flow processing with hippocampal mechanisms for stimulus sequencing (Agster *et al*., 2002; Fortin *et al*., 2002) and spatial mapping (O'Keefe and Nadel, 1978; McNaughton *et al*., 1996). Task-dependent biasing in this network might contribute to the attentional filtering of visual input (Moran and Desimone, 1985; Hopfinger *et al*., 2000) and influence the temporal dynamics of optic flow responses (Duffy and Wurtz, 1997) serving spatial orientation (Froehler and Duffy, 2002).

Our current findings suggest that optic flow perceptual impairments, linked to deficits of ambulatory (Tetewsky and Duffy, 1999) and vehicular (O'Brien *et al*., 2001) navigation in Alzheimer's disease, may reflect a failure of spatiotemporal integration in visual processing. Our previous work showed that impaired optic flow perception in Alzheimer's disease patients is partly attributable to their use of a local motion visual processing strategy. This differs from the wide spatial area of visual integration supporting the global processing of optic flow in healthy subjects. The current studies suggest that the temporal dynamics of visual integration might also be deranged in Alzheimer's disease, demanding a more prolonged period of visual stimulation to support perception. Defects in spatial and temporal integration might combine synergistically to impair vision and promote spatial disorientation in Alzheimer's disease.

These findings link two current views of dorsal extrastriate cortical areas: that they support the analysis of visual location (Ungerleider and Mishkin, 1982) and the temporal sequence of visual events (Coull and Nobre, 1998), the where and when of visual processing. This is consistent with dorsal involvement in the visual control of movement, the how of visual processing (Goodale *et al*., 1994), extending that notion from limb movements for reaching and grasping to self-movement through the visual environment.

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