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Commentary

Cortical motion blindness in visuospatial AD

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AD's behavioral complexity and generalized end-stage pathology sheltered it from twentieth century cortical localizationism. But fundamental principles of brain organization cannot be avoided forever. Cummings [3] has developed a comprehensive case for recognizing the relevance of cortical localization to a twenty-first century understanding of AD. Our work supports this proposal by suggesting that visuospatial disorientation in AD reflects disordered visual motion processing in specific parts of visual association cortex.

Visual association cortex contributes to spatial orientation by processing optic flow, the patterned visual motion seen during observer self-movement. Optic flow supports spatial orientation by registering self-movement to create an internal representation of the path between locations [5]. Our neurophysiological studies of monkey cerebral cortex show that the medial superior temporal area (MST) is devoted to optic flow analysis during self-movement [4]. Our psychophysical studies in humans show that optic flow perception is selectively impaired in visuospatial AD, suggesting dysfunction in the homologous cortical systems [16].

We measure visual perception by presenting motion coherence stimuli in a two-alternative forced-choice paradigm. In motion coherence stimuli, dots moving in a coherent pattern are combined with different numbers of randomly moving dots in a two second animated sequence projected on a large video screen. Subjects respond by indicating which of two possible coherent patterns is present in a given stimulus. A subject's motion coherence threshold is the minimum percentage of dots that must be in the coherent pattern for that subject to respond correctly on 75% of the trials.

We use motion coherence stimuli containing horizontal motion patterns with either leftward or rightward movement (Figure 1A, left), and motion coherence stimuli containing radial optic flow patterns with either leftward or rightward simulated directions of self-movement (Fig. 1A, right). Young normal (YN), elderly normal (EN), and Alzheimer's disease (AD) subjects were first screened to control for basic visual function (Snellen acuity, visual fields, and contract sensitivity) and then tested to determine their thresholds for horizontal motion and radial optic flow stimuli. All protocols were approved by the University of Rochester Medical Center's Human Research Subjects Review Board.

YN subjects show similarly low motion coherence thresholds for horizontal motion and for radial optic flow and EN subjects show small elevations in both measures. However, AD subjects show somewhat higher horizontal motion thresholds and greatly elevated radial optic flow thresholds. The AD subjects were readily divisible into two groups based-on the relative horizontal motion and radial optic flow thresholds: About half of the AD subjects show thresholds that are similar to those seen in EN subjects, whereas the other half of the AD subjects (55%, 6/11) show much higher radial optic flow thresholds then horizontal motion thresholds. Thus, some AD subjects have a substantial and selective impairment of radial optic flow perception. (Figure 1B).

A battery of neuropsychological studies revealed no major differences between AD subjects with and without optic flow perceptual impairments. We assessed open-field navigational capacity by questioning subjects about the path traveled from the hospital lobby to the visual laboratory. Scores on this test yielded a statistically significant difference across the three groups (ANOVA $F_{2,18} = 10.38$, $p < .01$). Furthermore, in the AD group there was a significant correlation between navigation test score and optic flow threshold ($r = -.66$, $p < .05$). This suggests a link between selectively elevated radial optic flow thresholds and visuospatial impairments in AD.

These observations confirm the recognition of visual motion processing deficits in AD [6,11,17] and demonstrate a selective impairment in radial optic flow perception that is linked to navigational deficits. This syndrome may be linked to the impaired use of visual motion for object

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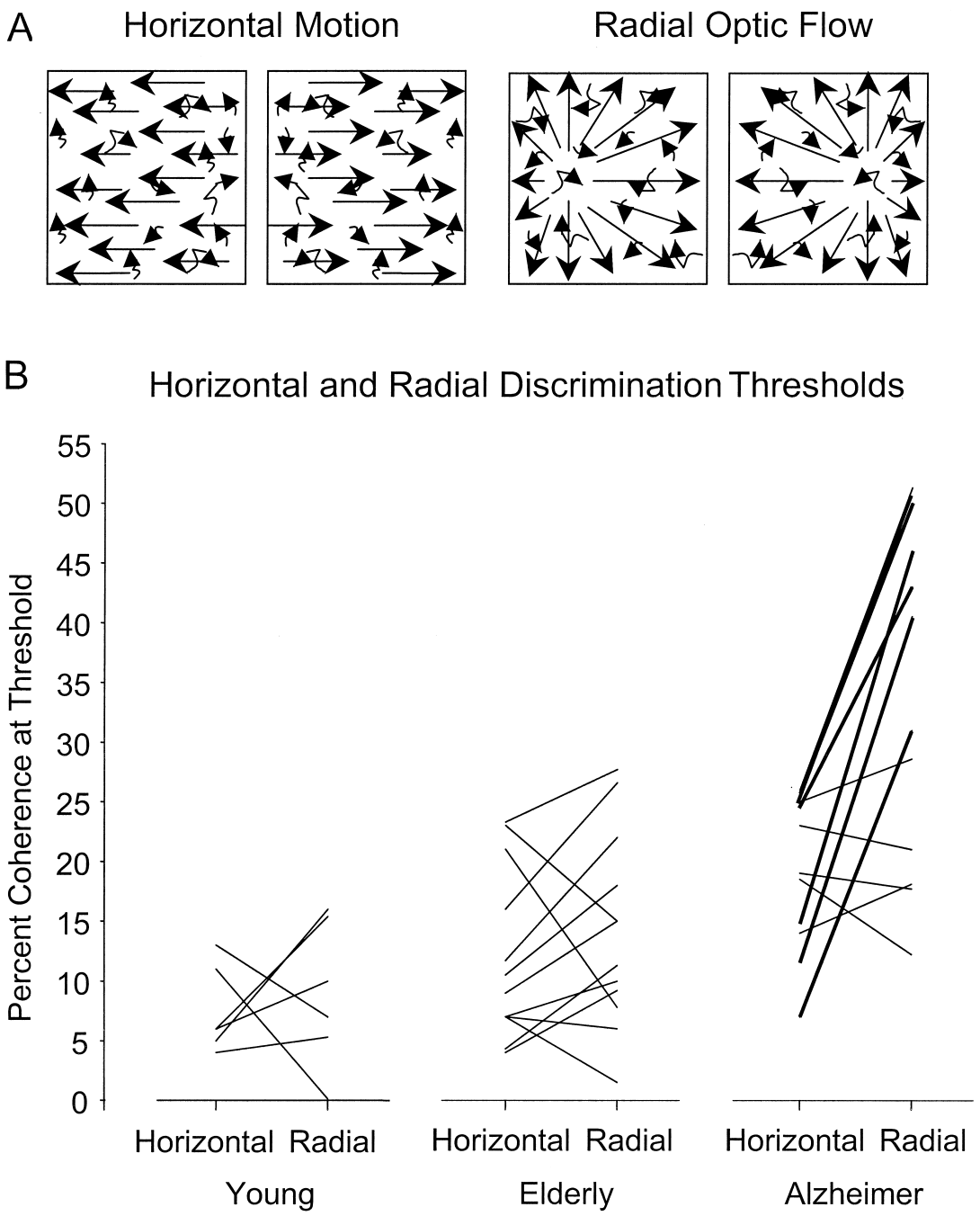

Fig. 1. A. Visual motion stimuli used in this study. Each stimulus consisted of a coherent pattern of moving white dots on a black background (straight arrows) with the remaining dots moving randomly. Horizontal motion stimuli (left) contained either leftward or rightward moving dots superimposed on randomly moving dots. Radial optic flow stimuli (right) consisted of an outward radial pattern with a focus of expansion 15° to the left or right of center with superimposed randomly moving dots. B. Graph of the motion coherence thresholds (ordinate) for the three subject groups test with horizontal and radial motion stimuli (abscissa). Each line represents the thresholds for one subject, the bold lines on the far right represent the thresholds for AD subjects having selectively elevated radial optic flow thresholds. YN subjects ($n = 6$) show motion coherence thresholds (mean ± s.e.) of 7.5 ± 1.5 for horizontal motion and 9.0 ± 2.5 for radial optic flow. EN ($n = 12$) subjects show small elevations in both measures: 12.0 ± 2.0 for horizontal motion and 14.2 ± 2.3 for radial optic flow. AD subjects ($n = 11$) show horizontal motion thresholds that are somewhat higher (19.0 ± 1.9) but their radial optic flow thresholds are greatly elevated (32.7 ± 4.3). Thus, AD is associated with large, selective elevations of radial optic flow perceptual thresholds.

identification [13] and other aspects of visuospatial misperception [1] in AD. These deficits do not seem to reflect impairments in basic visual function but rather reflect visual association cortical dysfunction [2,14,15].

Visual association cortex involvement is consistent with evidence that visuospatial AD is linked to focal posterior cortical hypometabolism [9,12] and neuropathology [8]. Clinical and experimental analysis of these brain regions provides a theoretical context for understanding these observations: visual association cortex contains both a dorsal "where" pathway for spatially-oriented function and a ventral "what" pathway for object-oriented function [7,10,18].

The visuospatial variant of AD illustrates that we should adhere to the basic principles of cortical neurology in our analysis of AD. Cummings [3] encapsulates the reasons why we must identify both the what and the where of AD to understand and control this disease.

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