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Neurobiology of Aging 33 (2012) 2551–2560

NEUROBIOLOGY OF AGING

www.elsevier.com/locate/neuaging

Early Alzheimer's disease blocks responses to accelerating self-movement

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Received 15 June 2011; received in revised form 6 December 2011; accepted 28 December 2011

Abstract

We assessed the cortical processing of self-movement stimuli in aging and Alzheimer's disease (AD). Our goal was to identify distinguishing effects on neural mechanisms related to driving and navigation. Young (YNC) and older (ONC) normal controls, and early AD patients (EAD) viewed real-world videos and dot motion stimuli simulating self-movement scenes. We recorded visual motion event related potentials (VMERPs) to stimulus motion coherence and speed. Aging delays motion evoked N200s, whereas AD diminishes response amplitudes. Early Alzheimer's disease patients respond to increments in motion coherence, but they are uniquely unresponsive to increments in motion speed that simulate accelerating self-movement. AD-related impairments of self-movement processing may have grave consequences for driving safety and navigational independence.

Keywords: Aging; Alzheimer's disease; Vision; Motion; Event related potentials

1. Introduction

Navigational impairments limit the quality of life in aging and Alzheimer's disease (AD). These impairments limit way-finding, even in familiar environments, leading to the withdrawal from driving and independent living.

Autonomous navigation greatly relies on the visual processing of optic flow, the patterned visual motion that accompanies self-movement (Gibson, 1950). We previously found that AD patients, and a subset of neuropsychologically intact older adults, have selectively increased perceptual thresholds for optic flow (O'Brien et al., 2001). The critical role of optic flow processing in the navigational impairments of aging and AD has been supported by combining the psychophysical analysis of optic flow perception with behavioral assessments of real-world navigation (Mapstone et al., 2003; Monacelli et al., 2003). Those studies suggest that navigational impairments in aging and AD reflect cortical deficits of optic flow processing that block access to the visual cues about self-movement heading and speed.

Visual motion processing has been previously studied by using event related potentials (ERPs) evoked by horizontally moving dot patterns or gratings in normal subjects (Kubová et al., 1990; Bach and Ullrich, 1994). Such stimuli evoke a negative wave peaking at around 200 ms after motion onset (N200 response). We later modified these techniques by using random dot stimuli that simulate the radial pattern of optic flow and were able to evoke posterior N200s in older adults and AD patients, and relate them to navigational deficits in AD (Kavcic et al., 2006). Furthermore, linking these deficits to responses evoked by the sudden presentation of a stationary dot pattern revealed cortical hyperresponsiveness in our most mildly impaired patients, raising the possibility that early hyperresponsiveness might be a precursor to more profound deficits (Fernandez et al., 2007).

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10.1016/j.neurobiolaging.2011.12.031

To better understand the neural mechanisms and behavioral implications of navigational impairments in aging and AD we varied the motion coherence and speed in real-world video clips of optic flow. Those pilot studies are followed by detailed analysis of responsiveness to simulated optic flow. We find that coherence and speed have different effects on motion responses highlighting behaviorally important distinctions between aging and early AD.

2. Methods

2.1. Subject groups

We studied young normal control subjects (YNC), older normal control subjects (ONC), and patients with early Alzheimer's disease (EAD) with normal, or corrected to normal, vision: YNCs were local undergraduates. ONCs were from programs for healthy elderly or patient's spouses. EADs were from the University of Rochester's clinical programs and met NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association) criteria for probable AD (McKhann et al., 1984) with functionally significant memory impairment by history and testing (Table 1), and aphasia, agnosia, apraxia, inattention, or executive incapacity. Informed consent was obtained from all subjects before enrollment. All procedures were approved by the University's Research Subjects Review Board.

Table 1
Demographic and neuropsychological characteristics of older normal control subjects (ONC) and early Alzheimer's disease patients (EAD) enrolled in the dot motion dynamics neurophysiological studies

	Older adults (n = 16)	Alzheimer's disease (n = 15)
Age, y	76.2 ± 10	78.6 ± 8
Education, y	16.6 ± 4	14.7 ± 3
OS visual acuity (20/x)	31.8 ± 20.1	33.5 ± 20.6
OD visual acuity (20/x)	27.0 ± 7.7	28.9 ± 7.8
Contrast sensitivity (20/x)*	29.7 ± 14.7	34.7 ± 19.3
MMSE (maximum 30)**	28.9 ± 1.1	25.2 ± 2.5
Money Road Map (maximum 32)*	29.4 ± 3.0	25.8 ± 3.6
Figural Memory (maximum 10)**	7.1 ± 1.4	5.2 ± 1.5
Verbal Fluency (normal > 12)**	17.6 ± 3.3	10.8 ± 4.9
Delayed Recall (maximum 8)**	6.8 ± 1.2	3.6 ± 1.8
Categorical Naming**	20.6 ± 6.0	12.6 ± 3.3
Line Orientation (maximum 30)	23.8 ± 3.9	21.6 ± 7.1
Facial Recognition (maximum 54)	46.7 ± 3.5	45.2 ± 6.1

The ages of subjects in these groups were not significantly different. Their neuropsychological characteristics are consistent with group assignment. Data are mean ± SD.
* $p < 0.05$.
** $p < 0.005$.

2.2. Neurophysiological experiments

Visual neurophysiological studies were controlled by the REX (real-time experimental) system (Hays et al., 1982) running on RTOS-QNX for PCs to control stimuli, displays, monitor eye position, and create data files. Subjects sat facing a rear-projection tangent screen's 60° × 40° image while they maintained centered fixation (± 10°) on a spot at the center of the screen under eye and head position monitored using infrared oculometry (ASL, Inc.). Subjects used their left and right index fingers to press 2 buttons.

2.2.1. Real-world video stimuli

Video sequences were recorded from a vehicle moving at 20 mph using a 30 frame per second digital video camera and edited with Final Cut Express (Apple, Inc.) and presented using QuickTime (Apple, Inc.). Each stimulus transition was marked by the white squares on the upper left corner, outside the subject's field of view, and detected by photocells and sent to NeuroScan (Compumedics, Inc.) as event markers.

All movies began with 1 second of a gray screen with centered red fixation spot which was followed by alternating cycles of 400 ms stationary images and 400 ms motion stimuli. After the last motion stimulus an additional stationary image was presented which switched to gray scale in a randomly selected 50% of the trials to prompt the subject's button press response to maintain the subject's sustained attention. Trials were separated by a 3-second blank screen as a fixation break.

To study real-world visual motion effects we created 2 types of video stimuli like those seen in the random dot simulations: pattern coherence and motion speed. The motion coherence paradigm (Fig. 1A) consisted of trials in which the self-movement video was presented over a period of 11 seconds with increasing image coherence. The coherence changes were created by importing each video frame into Image Ready (Adobe, Inc.) and dividing the frames in to a selected number of equal sized rectangular segments which were then randomly repositioned in the image. The same segmental repositioning was applied to all 12 frames in a 400-ms movement stimulus to maintain motion direction in each segment. A series of 8 segmentation levels were presented in each trial: 192, 96, 48, 36, 16, 8, 4, and 1 (full screen).

The motion speed paradigm (Fig. 1B) consisted of trials in which the self-movement video was presented over a period of 10 seconds with increasing image speed. The speed changes were created in FinalCut Express (Apple Inc.) by adding or subtracting individual frames to the original video sequence, thus creating a change in the apparent rate of self-movement. The resulting motion stimuli were each 500 ms in duration. Seven levels were presented having average motion speeds of: 2.5°, 5°, 10°, 20°, 40°, 80°, or 160° per second.