Neuropsychologia 48 (2010) 13–25

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Delays in neural processing during working memory encoding in normal aging

Theodore P. Zanto, Brian Toy, Adam Gazzaley*

Departments of Neurology & Physiology, W.M. Keck Foundation Center for Integrative Neuroscience, University of California San Francisco, San Francisco, CA 94158, USA

ARTICLE INFO

Article history:
Received 19 March 2009
Received in revised form 1 August 2009
Accepted 4 August 2009
Available online 8 August 2009

Keywords:
Working memory
Selective attention
Aging
EEG
Processing speed delay

ABSTRACT

Declines in neural processing speed have been proposed to underlie a broad range of cognitive deficits in older adults. However, the impact of delays in neural processing during stimulus encoding on working memory (WM) performance is not well understood. In the current study, we assessed the influence of aging on the relationship between neural measures of processing speed and WM performance during a selective delayed-recognition task for color and motion stimuli, while electroencephalography (EEG) was recorded in young and older adults. A latency delay was observed for the selection negativity (SN) and alpha band activity (measures of attentional allocation) in older adults during WM encoding of both motion and color stimuli, with the latency and magnitude of the SN predicting subsequent recognition performance. Furthermore, an age-related delay in the N1 latency occurred specifically during the encoding of color stimuli. These results suggest that the presence of both generalized feature-based and feature-specific deficits in the speed of selective encoding of information contributes to WM performance deficits in older adults.

Published by Elsevier Ltd.

1. Introduction

A large body of research has documented performance deficits in the cognitive abilities of older adults. Typically affected are working memory (WM), episodic memory and attention (Craik & Salthouse, 2000; Greenwood, 2000). Within the WM domain, age-related deficits in performance have been reported for numerous stimuli, including letters, words, digits, spatial position, pattern discrimination and complex stimuli (for review, see Salthouse, 1994). In an attempt to generate an underlying account of such diverse deficits, the findings of many behavioral studies on older adults have given rise to the processing speed hypothesis of cognitive aging (Salthouse, 1996). This hypothesis attributes age-related cognitive decline to a general slowing of information processes, and is based on the premise that if less computational processing is completed in a set amount of time, then less information is available to higher-level functions. For example, time-accuracy functions indicate that older adults require a longer stimulus presentation time during encoding in order to achieve recognition accuracies comparable to younger adults (e.g. Kliegl, Mayr, & Krampe, 1994). The majority of evidence supporting this hypothesis is derived from meta-analysis studies that have revealed the statistical control of response time measurements reduces age-cognition correlations (Salthouse, 1996). Although such behavioral research and statistical analysis has provided many important insights to the field of cognitive aging, they are intrinsically limited in their ability to directly address the neural underpinnings of age-related decline. Thus, the neural correlates of changes in processing speed during memory encoding and its influence on recognition performance have yet to be established.

Research on experimental animals has generated data to support a neural basis for the processing speed hypothesis. It has revealed that age-related cognitive decline in non-human primates is not due to loss of significant numbers of neurons (Peters, 2002a,b), but rather is associated with axonal myelin integrity, thus providing anatomical evidence suggestive of diminished information transfer in the aging brain (Peters et al., 1996). Related to this, in humans, processing speed was shown to be closely related to the structural integrity of white matter tracts (Rabbitt et al., 2007a; Turken et al., 2008). Additionally, carotid and basilar artery blood flow and age-associated losses of brain volume have been correlated with white matter lesions as well as information processing speed (Rabbitt et al., 2007b).

Electrophysiological studies in humans are a direct manner in which to address neural correlates of the processing speed deficit hypothesis and its impact on cognition. Electroencephalography (EEG) allows us to measure electrical correlates of neural activity during a behavioral task with high temporal resolution (i.e., milliseconds), and is thus an ideal tool to explore neural processing speed delays with aging. Most neural data supporting the processing speed hypothesis has focused on changes in the peak latency of the P300 component of the event-related potential (ERP). The P300 is a positive deflection that occurs 300–600 ms post-stimulus

* Corresponding author at: UCSF – MC2240, 600 16th St, Room N472J, San Francisco, CA 94158, USA.
E-mail address: adam.gazzaley@ucsf.edu (A. Gazzaley).

0028-3932/$ – see front matter. Published by Elsevier Ltd.
doi:10.1016/j.neuropsychologia.2009.08.003

onset, and is thought to reflect processing involved in attention and memory operations; it is typically evoked by infrequent, random targets (i.e., oddballs; Sutton, Braren, Zubin, & John, 1965) and an increased memory load results in an increased latency (for review, see Kok, 1997). There is extensive evidence that the P300 latency is delayed in older adults, thereby providing evidence of neural slowing during cognitive operations (for reviews, see Kok, 2000; Kugler, Taghavy, & Platt, 1993; Polich, 1996). EEG studies have also shown that earlier ERP markers of visual processing exhibit slowing in older adults. In a cued, two-choice discrimination task, Curran, Hills, Patterson, and Strauss (2001) examined neural correlates of selective attention in aging and reported slowing of the P1 and N1 components of the visual ERP in older adults. The P1 is a positive deflection in the ERP, peaking around 100 ms post-stimulus onset, whereas the N1 is a negative deflection peaking approximately 170 ms after stimulus onset. Comparably, Gazzaley et al. (2008) reported that during a face/scene WM task, older adults exhibited a delayed N1 suppression index and a delayed P300 peak latency while encoding face stimuli. However, to our knowledge, the relationship between the latency of neural measures to lower-level encoded stimuli and WM recognition has not yet been assessed in an aging study. The advantage of utilizing lower-level stimuli, such as simple feature detection, is that individual perceptual differences can be controlled for. This is important when evaluating the nature of changes in processing speed on WM, since it has been suggested that discriminability differences may account for visual WM deficits in older adults (Sara & Faubert, 2000).

The current study aimed to identify age-related changes in neural measures of processing speed during the selective encoding of lower-level visual features (i.e., color hue and motion direction) and assess its influence on WM performance. To achieve this, younger (18–35 years old) and older (60–80 years old) adults performed delayed-recognition WM tasks that required selective attention while 64-channel EEG was recorded. Prior to the main experiment all participants went through visual acuity correction, as well as a thresholding procedure to adjust for feature discriminability differences between individuals in color and motion perception. Furthermore, the perception of brightness for all stimuli was equated for each participant. By minimizing these influences, we can interpret neural delays as being the result of changes in endogenous influences such as WM encoding or selective attention. Based on the processing speed hypothesis, we hypothesized that delays in neural processing during encoding would be associated with declines in WM performance.

The neural measures analyzed for age-related differences include the P1 and N1 of the ERP, the selection negativity and time-frequency (spectral) measures to cue stimuli. The P1 and the N1, which reflect early stages of visual processing for stimulus representation generated in extrastriate cortex (for review, see Herrmann & Knight, 2001) and are modulated by attention (Gazzaley et al., 2008; Hillyard, Vogel, & Luck, 1998; Rugg, Milner, Lines, & Phalp, 1987; Valdes-Sosa, Bobes, Rodriguez, & Pinilla, 1998). The selection negativity (SN), which is calculated from the ERP difference wave between attended and ignored stimuli, begins between 140 and 180 ms post-stimulus onset and may persist for more than 200 ms (Harter & Aine, 1984). The SN has been shown to reflect the timing of feature selections and is influenced by attention (AnlloVento & Hillyard, 1996; Kenemans, Smulders, & Kok, 1995). Further exploration of age-related neural changes during stimulus encoding focused on spectral activity between 4 and 50 Hz, as attentional allocation has been linked to modulation in the theta (Jensen & Tesche, 2002; Schacter, 1977), alpha (Muller & Keil, 2004) and gamma bands (Gruber, Muller, Keil, & Elbert, 1999).

Table 1
Neuropsychological scores averaged over all participants. Each participant scored within 2 standard deviations of their age-matched normative value.

Neuropsychological test	Mean	s.e.m.
Mini-mental state examination	28.9	1.2
Geriatric depression scale	2.1	2.0
CVLT: Trial 5 recall	12.5	2.9
CVLT: short delay free recall	10.8	4.1
CVLT: short delay cued recall	12.3	3.3
CVLT: long delay free recall	11.4	3.6
CVLT: long delay cued recall	12.3	3.4
Memory for modified Rey	12.3	2.7
Calculation ability (out of 5)	4.9	0.3
WAIS-R: backward digit span	5.6	1.6
WAIR-R: digit symbol	48.9	10.1
Trail making test: A	34.6 s	8.5 s
Trail making test: B	88.2 s	37.4 s
Stroop: color naming	82.9	15.3
Stroop: color-word naming	48.6	16.8
Semantic fluency	20.3	5.5
Phonemic fluency	15.8	5.2

2. Methods

2.1. Participants

Twenty-two healthy young adults (mean age 24.0 years; range 18–29 years; 8 males) and twenty-one older adults (mean age 70.1 years; range 60–83 years; 10 males) gave informed consent to participate in the study approved by the Committee on Human Research at the University of California in San Francisco. All participants had normal or corrected to normal vision and were screened to ensure they were healthy, had no history of neurological, psychiatric, or vascular disease, were not depressed, and were not taking any psychotropic or hypertensive medications. Visual acuity was checked for each participant using a Snellen chart and corrective lenses were utilized as necessary to achieve 20/40 vision or better. Additionally, all participants were required to have 12 years minimum education.

2.2. Neuropsychological testing

To ensure older adults were "normal" relative to their age-matched peers, participants in the older age group were required to score within two standard deviations of control values on 13 neuropsychological tests. The neuropsychological evaluation consisted of tests designed to assess general intellectual function (MMSE; Folstein, Folstein, & McHugh, 1975), verbal learning (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000), geriatric depression (GDS; Yesavage et al., 1982), visual-spatial function (copy of a modified Rey-Osterrieth figure), visual-episodic memory (memory for details of a modified Rey-Osterrieth figure), visual-motor sequencing (trail making test A and B; Reitan, 1958; Tombaugh, 2004), phonemic fluency (words beginning with the letter 'D'), semantic fluency (animals), calculation ability (arithmetic), executive functioning (Stroop interference test; Stroop, 1935), working memory and incidental recall (backward digit span and digit symbol, WAIS-R; Wechsler, 1981). All neuropsychological test scores are summarized in Table 1.

2.3. Stimuli

The stimuli consisted of a circular aperture of 290 dots ($0.08^\circ \times 0.08^\circ$ each) that subtended 8° of visual angle at a 75 cm viewing distance and were centered at the fovea. Two types of dots were used during the experiment: (1) gray and moving coherently at 10° per second or (2) stationary and colored along the tritan axis. All colored and gray dots were equated for brightness by minimizing heterochromatic flicker in tests carried out prior to the experiment for each participant (for details on color generation and flicker photometry, see Hardy, Delahunt, Okajima, & Werner, 2005). Stimuli were presented with a gray fixation cross in the center of the circular aperture and a black background with a luminance level of 0.32 cm/m^2. Stimuli were presented through E-Prime software (Psychology Software Tools, Inc.) run on a Dell Optiplex GX620 and a ViewSonic G220fb CRT monitor.

2.4. Thresholding

After all stimuli were equated for brightness, participants went through two thresholding tests (one for motion, one for color) in order to minimize discriminability differences. A stair-step procedure required participants to determine whether two stimuli (directions of motion or colors) were different from each other. The two stimuli were presented for 800 ms each and separated by 2000 ms. The procedure continued until a "just 100%" level of performance was reached, meaning that if the stimuli were any more similar, performance would drop below 100% as determined by 10 out of 10 correct responses. An angle of discrimination was identified as the difference between the two directions of motion at the just 100% level of perfor-