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Research Report

Age-related decline in differentiated neural responses to rare target versus frequent standard stimuli

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ABSTRACT

One mechanism hypothesized to contribute to cognitive aging is the failure to recruit specialized neural modules and generate differentiated neural responses to various classes of stimuli. Here, ERPs were used to examine the extent to which target and standard stimulus types were processed differently by well-matched adults ages 19–99. Subjects responded to designated visual target letters under low and high load conditions. Temporospatial PCA was used to parse the P3b component, an index of categorization/memory updating. The P3b amplitude difference between targets and standards decreased substantially as a function of age. Dedifferentiation began in middle age, and continued into old-old age. The reduced differentiation of neural responses was driven by an age-related decline in the size of the P3b to targets and an age-related increase in the P3b to standards. Larger P3b amplitude to standards among older subjects was associated with higher executive capacity and better task performance. In summary, dedifferentiation begins relatively early in adulthood and progresses in a linear fashion throughout the lifespan. The age-related augmentation of the P3b to standards appears to reflect a compensatory mechanism that helps maintain task performance.

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1. Introduction

As individuals grow older, there appears to be a decrease in the specificity of activation of neural modules in response to different kinds of stimuli, such as target vs. non-target letters or numbers,

images of faces vs. non-faces, and cued vs. non-cued locations (Curran et al., 2001; Hahn et al., 2011; Kenemans et al., 1995; Looren de Jong, 1988; Lorenzo-Lopez et al., 2007; Park et al., 2012). This age-related loss of neural specialization has been indexed by comparing neural responses to different stimulus types and by

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measuring changes in the distribution of neural activity recruited to carry out task demands (Cabeza et al., 2002; Lorenzo-Lopez et al., 2007).

Several functional neuroimaging techniques, including functional magnetic resonance imaging (fMRI), positron emission tomography (PET), and event-related potentials (ERPs) have been leveraged to demonstrate a loss of neural specialization with age. For example, in a recent fMRI study, Park et al. (2012) showed images of faces and houses to adult subjects while measuring activity in two brain regions: the fusiform face area and the extended face network. In young adults, these two brain regions were preferentially activated in response to faces. Relative to young subjects, old subjects exhibited greater activation of the fusiform face area in response to non-faces (houses) and less activation in the extended face network in response to faces. These results suggest that observed reductions in specialization may be the combined result of decreased specificity in some regions and diminished sensitivity in others.

Cabeza et al. (2002) used PET in a verbal source memory task to examine changes in hemispheric asymmetry with age. They compared young adults to old adults who were divided into high- and low-performing groups based on standardized memory test scores. Young adults and low-performing old adults recruited a similar region of the right prefrontal cortex, whereas high-performing old adults exhibited bilateral prefrontal activity. The authors suggest that the recruitment of bilateral frontal areas served as compensatory activity, allowing those subjects to maintain performance more like their younger counterparts. This interpretation supports the compensation hypothesis of cognitive aging, which posits that the recruitment of additional brain regions to carry out the task reflects an advantageous compensatory mechanism to counter a decline in neurophysiologic processing (Cabeza et al., 2002, 2004). In contrast, Li and Lindenberger (1999) have argued that the aging process leads to a deterioration in the brain's ability to recruit specialized neural mechanisms to carry out a task, reducing the signal-to-noise ratio in cognitive operations and decreasing processing efficiency. The dedifferentiation hypothesis, as this has been labeled, emphasizes the deleterious nature of these age-related changes.

ERPs, specifically the P3b component, have been used to study age-related changes in the generation of differentiated neural activity. The P3b component is a posteriorly-distributed component peaking between ~400 and 600 ms that reflects the categorization of an event in accordance with task demands, the updating of working memory once an event has been categorized, or the bridge between stimulus evaluation and response selection (Daffner et al., 2011a; Donchin, 1981; Donchin and Coles, 1988; Knight and Scabini, 1998; Kok, 2001; Verleger, 2008; Verleger et al., 2005). In young adults, repetitive standard events elicit minimal or no P3b response. By contrast, young adults produce a robust P3b component in response to rare target events (Dien, 2012; Dien et al., 2004; Spencer et al., 1999, 2001). The generation of highly differentiated P3b responses to targets vs. standards in young adults provides the context for examining the extent to which this pattern of processing changes in older adults.

In previous work, we compared P3b responses to letter stimuli under attend and ignore conditions that were based on

a non-spatial feature (color) (Alperin et al., 2013). We found that young adults generated a robust P3b in response to designated target letters in the attended but not ignored color, demonstrating a clearly differentiated neural response between conditions. In contrast, older subjects generated a P3b of similar magnitude to target letter forms under both conditions, i.e., no differentiation. Hahn et al. (2011) used the P3b to examine age-associated changes in stimulus processing in attend vs. ignore conditions that were defined by spatial location. They used a spatial attention paradigm that required subjects to respond to designated target letters, but only when they appeared in a cued location. Young subjects generated a much larger P3b to target letters in cued than non-cued locations, indicating a differentiated neural response to stimulus types that were supposed to be attended vs. ignored. Older subjects generated a P3b component with the same amplitude in response to target letter forms in both cued and non-cued locations. Results from these studies suggest an age-related loss of differentiation in P3b responses to stimuli under attend vs. ignore conditions across tasks that manipulate either spatial or non-spatial attention.

Several outstanding issues in research on dedifferentiation remain. First, many ERP studies that have examined age-related dedifferentiation, including our own, compared responses to the same class of stimuli under attend vs. ignore conditions (Alperin et al., 2013; Hahn et al., 2011; Lorenzo-Lopez et al., 2007), but have not investigated responses to different classes of stimuli under an attend condition only. Second, almost all prior reports have limited their investigation to young adults in their 20s and young-old adults in their 60s and 70s (Alperin et al., 2013; Cabeza et al., 2002; Curran et al., 2001; Hahn et al., 2011; Looren de Jong et al., 1988; Lorenzo-Lopez et al., 2007; Vallesi et al., 2009), leaving open questions about when in the lifespan dedifferentiation begins and whether it continues to progress in old-old age. Third, most prior studies have not explicitly tried to match different age groups in terms of cognitive capacity or performance on the experimental task (Curran et al., 2001; Hahn et al., 2011; Looren de Jong et al., 1988), making it problematic to interpret whether differences in neural activity between groups were due to age or other factors such as executive capacity, perceived task difficulty, or task performance. Fourth, most previous studies have included tasks with only one level of difficulty (Curran et al., 2001; Hahn et al., 2011; Looren de Jong et al., 1988; Lorenzo-Lopez et al., 2007), which does not provide the opportunity to address the issue of whether an age-related reduction in differentiated neural responses is a function of task demand.

The current study addressed these limitations. The P3b was used to examine age-related differences in the specificity of neural response to two different attended stimulus types, presented sequentially, that varied in task salience: infrequent target letters and frequent standard letters. To expand the age-range investigated beyond those used in previous studies, Middle-aged (40–60) and Old-Old (80+) participants were included in addition to Young (18–32) and Young-Old (65–79) subjects. Groups were matched in terms of cognitive capacity by inclusion criteria limiting participants to individuals whose neuropsychological test performance was in the top third relative to age-appropriate norms. Level of difficulty was manipulated by incorporating a low demand task (one target stimulus) and a high demand task (multiple target

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