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One of the most well-established age-related changes in neural activity disappears after controlling for visual acuity

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A B S T R A C T

Numerous studies using a variety of imaging techniques have reported age-related differences in neural activity while subjects carry out cognitive tasks. Surprisingly little attention has been paid to the potential impact of age-associated changes in sensory acuity on these findings. Studies in the visual modality frequently report that their subjects had "normal or corrected- to-normal vision." However, in most cases, there is no indication that visual acuity was actually measured, and it is likely that the investigators relied largely on self-reported visual status of subjects, which is often inaccurate. We investigated whether differences in visual acuity influence one of the most commonly observed findings in the event-related potentials literature on cognitive aging, a reduction in posterior P3b amplitude, which is an index of cognitive decision-making/updating. Well-matched young ($n = 26$) and old adults ($n = 29$) participated in a visual oddball task. Measured visual acuity with corrective lenses was worse in old than young adults. Results demonstrated that the robust age-related decline in P3b amplitude to visual targets disappeared after controlling for visual acuity, but was unaffected by accounting for auditory acuity. Path analysis confirmed that the relationship between age and diminished P3b to visual targets was mediated by visual acuity, suggesting that conveyance of suboptimal sensory data due to peripheral, rather than central, deficits may undermine subsequent neural processing. We conclude that until the relationship between age-associated differences in visual acuity and neural activity during experimental tasks is clearly established, investigators should exercise caution attributing results to differences in cognitive processing.

Introduction

Numerous studies have reported age-related differences in neural activity while subjects carry out cognitive tasks, using fMRI, PET, and ERPs as dependent variables (Cabeza et al., 2002; van Dinteren et al., 2014; Gazzaley et al., 2008; Madden et al., 1999, 2002, 2004; Miller et al., 2008; Reuter-Lorenz et al., 2000; Rossini et al., 2007; Rypma and D'Esposito, 2000; De Santi et al., 1995; Stern et al., 2005). Reports of task-related studies in the visual modality frequently indicate that their subjects had "normal or corrected-to-normal vision". However, in most cases, there is no indication that visual acuity (VA) was actually measured, and it is likely that the investigators relied largely on subjects' self-reported visual status. This approach is problematic for two major reasons: first, self-reports of VA are often inaccurate (Daffner et al., 2013; Friedman et al., 1999), and second, aging is associated with an increased likelihood of reduced VA, most frequently related to outdated prescriptions for corrective lenses (Skeel et al., 2003; Tielsch et al., 1990) or other peripheral, not central, problems (Kanthan et al., 2008; Klaver et al., 1998). These observations raise questions about the extent to which undetected differences in VA across age groups may contribute to the frequently reported age-related changes in neural activity during visual tasks, which are typically attributed to alterations in cognitive operations.

Here, we focused on one of the most commonly observed findings in the ERP literature on cognitive aging: reduction of the amplitude of the posterior P3b component in response to target visual stimuli, a result that has been published innumerable times over the last few decades, reflecting experiments conducted in either the visual or auditory modality (Alperin et al., 2014; Anderer et al., 1998; van Dinteren et al., 2014; Fabiani and Friedman, 1995; Fabiani et al., 1998; Kok, 2000; Li et al., 2013; Mullis et al., 1985; O'Connell et al., 2012a; Polich, 1997). Age-associated decline in P3b amplitude has not been attributed to degraded sensory information that is delivered to neural systems

Abbreviations: AMNART, American National Adult Reading Test; DSM-IV, Diagnostic and statistical Manual of Mental Disorders, 4th ed.; ERPs, event-related potentials; LIP, lateral intraparietal area; MHL, mean hearing loss; MMSE, Mini Mental State Exam; PCA, principal component analyses; RT, reaction time; VA, visual acuity.

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involved in decision-making. Rather, based on well-established research regarding the cognitive and functional significance of the P3b component, its diminished size among older adults has been interpreted as an attenuation of the categorization process or the reduced ability to update working memory after a target has been categorized (Daffner et al., 2011; Donchin, 1981; Donchin and Coles, 1988). Within the framework of information processing theory, the age-associated decline in P3b amplitude reflects diminished transfer of information and greater remaining uncertainty about an event and its implications for the generation of expectations about future ones (Johnson, 1986; Picton, 1992). Recently, O'Connell and colleagues have suggested that the P3b[1] may represent a theoretical decision variable involved in the accumulation and temporal integration of sensory evidence, that determines behavior once it crosses a threshold or boundary criterion (O'Connell et al., 2012b). These investigators found that in young adults this component is very sensitive to systematic perturbation of physical evidence during decision formation, which suggested a tight, dynamic coupling between perceptual and decision processes in the human brain. In keeping with this perspective, even subtle age-associated reductions in sensory fidelity might undermine the decision process, be associated with greater residual uncertainty, and manifest as a smaller P3b.

There is a large body of research on the relationship between age-related impairments in sensory and cognitive processing (most often measured in terms of cognitive test performance), which has led to an ongoing debate between interpretations offered by the Common Cause (Baltes and Lindenberger, 1997; Christensen et al., 2001; Lindenberger and Baltes, 1994; Salthouse et al., 1996) vs. the Sensory Deficit (Gilmore et al., 2006; Scialfa, 2002) hypotheses. Surprisingly, despite this literature, the issues at stake have received little attention in research investigating age-associated differences in underlying neural activity. To address this issue, the current study aimed to establish whether age-related deficits in VA mediate the decline in the P3b amplitude to target visual stimuli. To accomplish this objective, ERP data from a visual oddball task were analyzed before and after controlling for VA, as measured in young and old subjects. To test the modality specificity of the relationship between VA and the P3b to target visual stimuli, we determined whether the predicted age-related decline in P3b to visual targets would remain significant after controlling for measured auditory acuity in subjects. We chose to investigate young adults (late teens and early 20s) and older adults (mid 60s and 70s) to replicate the approach most typically found in the literature (Alperin et al., 2014; Anderer et al., 1998; van Dinteren et al., 2014; Fabiani and Friedman, 1995; Fabiani et al., 1998; Kok, 2000; Li et al., 2013; Mullis et al., 1985; O'Connell et al., 2012a; Polich, 1997).

Material and methods

Participants

Subjects were recruited through community announcements in the Boston metropolitan area and underwent informed consent approved by the Partners Human Research Committee. Participants were between 18 and 32 years in the young group or between 65 and 79 years, in the old group (see Alperin et al., 2014 for a more detailed account of the methods employed). Subjects underwent an initial telephone screen in which they were asked about vision, hearing, and medical history. To be included in this study subjects had to report that they had normal vision or corrected-to-normal vision with glasses or contact lenses. In addition, inclusion criteria required that subjects be English-speaking and have 12 or more years of education, a Mini Mental State Exam (MMSE) score (Folstein et al., 1973) of ≥26, and an estimated Intelligence Quotient (IQ) on the American National Adult Reading Test (AMNART) (Ryan and Paolo, 1992) of ≥100. Subjects were excluded if their mean performance on a battery of neuropsychological tests (Table 1) was <33rd percentile (which was done to reduce the likelihood of including older subjects with mild cognitive impairment or early dementia), had a history of CNS diseases or major psychiatric disorders based on Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV) criteria (American Psychiatric Association, 1994), a history of clinically significant medical diseases, mean hearing loss (MHL) (see below) of >40 dB, or >20 dB difference between ears at any tested frequency, were unable to distinguish between the color red and blue, had a Beck Depression Inventory (Beck et al., 1988) (for young subjects) or a Geriatric Depression Scale (Yesavage et al., 1982) (for old subjects) score of ≥10, or had focal abnormalities on neurological examination consistent with a central nervous system lesion. Subjects were paid for their time.

Binocular VA was measured in all subjects with a Snellen 10 ft model wall chart, and recorded as a decimal representation of 20/x, such that 20/20 = 1.0 and represents "normal" visual acuity. Worse than normal vision was represented with a visual acuity value of less than 1.0 (e.g., 20/40 = 0.5). Vision better than 20/20 was represented with a visual acuity value greater than 1.0.

Subjects also had a formal audiological examination in which hearing thresholds were tested at 6 frequencies: 250, 500, 1000, 2000, 4000, and 8000 Hz. Hearing acuity was determined by the decibel threshold for detecting sounds at each of the frequencies. Hearing loss was calculated as the difference between the measured dB level at threshold and 20 dB (Friedman et al., 1998). MHL was the average hearing loss across the 6 frequencies tested. Zero or negative values represents no hearing loss; positive values indicate some degree of hearing loss.

Two age groups were studied. The young subject group included 26 subjects with a mean age of 22.5 (2.2), and the old subject group included 29 subjects with a mean age of 72.8 (3.8). An additional 3 young and 5 old subjects completed the experiment, but were excluded due to excessively noisy ERP data. Table 1 provides a summary of information about subject characteristics.

Table 1
Subject characteristics (mean (SD)).

Variable	Young	Old
Number of subjects	26	29
Gender (male/female)	12/14	14/15
Age (years)[a]	22.5 (2.2)	72.8 (3.8)
Executive capacity (percentile)	67.3 (16.7)	68.6 (7.54)
Years of education	15.1 (1.5)	16.1 (3.1)
AMNART (estimated IQ)	116.7 (6.6)	118.3 (9.7)
MMSE[b]	29.8 (.3)	29.4 (.8)
Mean hearing loss[c]	-9.8 (4.9)	13.5 (10.5)
Visual acuity[d]	1.02 (0.1)[#]	0.74 (0.1)[*]
20/12.5	1	–
20/16	7	1
20/20	16	2
20/25	–	11
20/30	1	12
20/35	–	--
20/40	1	3

Executive capacity = average (composite) percentile performance on the following tests: Digit Span Backward, Controlled Oral Word Association Test, Letter–Number Sequencing, Trail Making Test Parts A and B, and Digit–Symbol Coding.
AMNART = American National Adult Reading Test.
MMSE = Mini Mental State Exam.
[a] p < .001 (young < old).
[b] p = .01 (young > old).
[c] p < 0.001.
[d] p < 0.001.
[#] ≈20/20.
[*] ≈20/25.

[1] A component that the investigators labeled as the centro-parietal positivity, which they suggested shares all of the characteristics of the P3b.