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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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Abstract

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.

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1. 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; Madden et al., 2004; Madden et al., 2002; 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., 2012; Polich, 1997). Age-associated decline in P3b amplitude has not been attributed to degraded sensory information that is delivered to neural systems 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., 2012). These investigators found that in

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

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 and Hancock, 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., 2012; Polich, 1997).

2. Material and methods

2.1 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) ≥ 26, and an estimated Intelligence Quotient (IQ) on the American National Adult Reading Test (AMNART) (Ryan and Paolo, 1992) ≥ 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 feet 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.

2.2 Experimental Procedures

A visual oddball task was administered under low and high memory load. Under both loads, half the visual stimuli were presented in the color red and half in the color blue, in randomized order. The low load task required subjects to respond by button press on a computer mouse, to one specific target letter. To help minimize group differences in performance on the high load task, demands were made easier for old subjects. For the high load task, the number of target letters chosen for each age group was based on pilot data: young subjects responded to 5 target letters and older subjects responded to 4 target letters. This was done to allow us to draw inferences about age-related differences in neural activity and not performance-related differences (Daffner et al., 2011; Riis et al., 2008). Subjects were instructed to pay attention to letters appearing in the designated color while ignoring letters appearing in the other color, and respond by button press to target letters appearing in the designated color only. Subjects were asked to respond as quickly and as accurately as possible to target letters. Practice trials preceded each set of experimental runs. Task order and the hand used for target response were counterbalanced across subjects.

Each task included 800 stimulus trials divided into 8 blocks. In both the high load and low load tasks, stimuli appeared one at a time within a fixation box that remained on the screen at all times and subtended a visual angle of ~3.5° × 3.5° at the center of a high-resolution computer monitor. The distance between the participants’ eyes and the screen was

approximately 5 feet. Thus, viewing of experimental stimuli depended on distance, not near, visual acuity. Target stimuli (7.5% in attend color; 7.5% in ignore color) were designated upper case letters and standard stimuli (70% overall; 35% in each color) were any non-target upper case letters. Novel stimuli, unusual/unfamiliar line drawings, such as impossible or fragmented objects (Kosslyn et al., 1994; Kroll and Potter,1984) (7.5% in each color), accounted for the remainder of stimuli presented. Visual stimuli subtended an angle of ~2.5° along their longest dimension and were presented for 250 ms. The inter-stimulus interval varied randomly between 815-1015 ms (mean ~ 915 ms) (Fig. 1). The current report focused on correct trials in response to target stimuli under the attend condition (target letters in the designated color) in the high memory load task[2].

2.3 Behavioral Data

Mean target accuracy and mean reaction time (RT) were measured. A response was considered a hit if it occurred between 200–1000 ms after stimulus presentation. Target stimuli correctly responded to (target hits) and stimuli incorrectly identified as targets (false alarms) were measured in order to determine an overall accuracy score (% target hits - % false alarms).

2.4 ERP recordings

An ActiveTwo electrode cap (Behavioral Brain Sciences Center, Birmingham, UK) was used to hold to a full array of 128 Ag-AgCl BioSemi (Amsterdam, The Netherlands) “active” electrodes to the scalp, at locations determined by a pre-configured montage. Electrodes were arranged in equidistant concentric circles from the International 10-20 system position Cz. In addition to the 128 electrodes on the scalp, 6 mini bio-potential electrodes were placed, over the left and right mastoid, beneath each eye, and next to the outer canthi of the eyes to capture eye blinks and vertical and horizontal eye movements. EEG activity was digitized at a sampling rate of 512 Hz.

2.5 Data analysis

EEG data were analyzed using ERPLAB (www.erpinfo.org/erplab) (Lopez-Calderon and Luck, 2014) and EEGLAB (http://sccn.ucsd.edu/eeglab) toolboxes that operate within the MATLAB framework (Delorme and Makeig, 2004). Raw EEG data were resampled to 256 Hz and referenced off-line to the algebraic average of the right and left mastoids. EEG signals were filtered using an IIR filter with a bandwidth of 0.03–40 Hz (12 dB/octave roll-off). Eye artifacts were removed through an independent component analysis. Individual bad channels were corrected with the EEGLAB interpolation function. Epochs were discarded from the analyses if they contained baseline drift or movement artifacts greater than ±90 μV.

2.6 Averaged ERP data

For the average waveform ERPs, the analysis focused on P3b amplitude in response to target visual stimuli under the attend condition, high memory load task. The amplitude of the

[2]An analysis (not included here) of the low memory load task revealed the same pattern of results as was observed in the high memory load task.

target P3b was measured as the mean value at Pz of the 100 ms interval around local peak latency between 400 and 700 ms.

2.7 Principal Component Analyses (PCA)

PCA was used to confirm the results of the averaged waveform analysis. PCA is a data-driven method that decomposes ERP waveforms into their underlying components and is particularly useful in parsing spatially and temporally overlapping components. Following the recommendations of Dien et al. (Dien et al., 2007), a two-step temporospatial procedure (Promax rotations) was conducted on all subjects' individual ERP averages, at all 134 electrode sites, using the ERP PCA toolkit 2.39 (Dien, 2010). A parallel test was used to restrict the number of factors generated for each PCA (Dien et al., 2007). Examination of the latency and topography of the PCA output led to the identification of factor corresponding to the P3b for the visual task (Fig. 3). Factor scores (amplitudes) were submitted to statistical analysis.

2.8 Statistical analysis

An ANOVA was conducted to assess whether there were differences between age groups (young vs. old) in size of the average amplitude at the electrode Pz and the PCA-derived P3b factor. Differences between groups (young vs. old) were reanalyzed after controlling for VA or MHL, using ANCOVA. Path analysis was used to confirm the hypothesis about the relationships between variables of interest.

3. Results

3.1 Visual Acuity

VA (with corrective lenses), as measured by a Snellen 10 feet model wall chart, ranged from 20/16 to 20/40 in both groups, with a mean of 1.02 (0.1) ≈ 20/20 in the young group and 0.74 (0.1) ≈ 20/25 in the old group (Table 1). Old subjects had worse VA than young subjects $F(1,53) = 42.7$, $p < 0.004$, partial $\eta^2 = 0.44$. Age inversely correlated with VA: the older the subject, the worse the visual acuity ($r = -0.67$, $p < 0.001$).

3.2 Auditory Acuity (mean hearing loss)

Hearing thresholds were determined by a formal audiological evaluation. Mean hearing loss (MHL) across 6 tested frequencies was calculated as the average difference between measured dB level at threshold and 20dB (Friedman et al, 1998), with positive values representing diminished hearing acuity. In the young group, MHL ranged from −15.4 to 0.8, with a mean of −9.8 (4.9); in the old group MHL ranged from −8.7 to 31.1, with a mean of 13.5 (10.5) (Table 1). Old subjects had greater MHL than young subjects $F(1,53) = 108.3$, $p < 0.001$, partial $\eta^2 = 0.67$. Age directly correlated with MHL: the older the subject, the greater the mean hearing loss ($r = 0.83$, $p < 0.001$).

3.3 Behavioral data

Comparison of target hits, false alarms and overall accuracy rates did not reveal differences between groups; however, the reaction time of the young group (610.7 (52) ms) was shorter

than that of the old group (644.1 (59) ms), F(1,53) = 4.72, p = 0.03, partial η2 = 0.08 (Supplementary Table 1).

3.4 ERP data

3.4.1 P3b to target visual stimuli before and after controlling for visual acuity

—Figure 2 illustrates the grand average waveforms of young and old subjects in response to target visual stimuli at the midline posterior electrode Pz, where the P3b component is most commonly measured. An ANOVA demonstrated an effect of age group, F(1,53) = 8.95, p = 0.004, partial η^2 = 0.14, which was present because young subjects generated a larger mean target P3b amplitude than old subjects. An ANCOVA revealed that after controlling for VA, there were no age-related differences in the amplitude of the target P3b, F(1,52) = 1.11, p = 0.29, partial η^2 = 0.02.

PCA revealed a factor (TF2SF2) whose temporal interval and spatial distribution was consistent with the P3b component. It had positive polarity, peaked at 503 ms and accounted for 9.22% of the total variance. Figure 3 illustrates the topography and amplitude (factor scores) of the P3b factor. An ANOVA demonstrated an effect of age (young > old), F(1,53) = 5.44, p = 0.02, partial η^2 = 0.09. An ANCOVA revealed that after controlling for VA, age-related differences in P3b amplitude did not survive, F(1,52) = 0.24, p = 0.62, partial η^2 = 0.005[3].

To further address the major question of this study, a path analysis was conducted examining the relationships between age (as a continuous variable), VA, and the PCA-derived target P3b amplitude (Figure 4a). It revealed a strong inverse correlation between age and VA, with a correlation coefficient of −.67 (p < .01). There was also a correlation between VA and P3b amplitude that remained significant after controlling for the impact of age (with a path coefficient = .36, p < .05). In contrast, after controlling for the impact of VA, there was no association between age and P3b amplitude (correlation coefficient = −.03, p > 0.8), suggesting that VA mediates the relationship between age the P3b amplitude. The same pattern of results was found when using age group as a categorical rather than age as a continuous variable. A path analysis was also conducted for the averaged ERP data at Pz and yielded results that were similar to the PCA-derived data (supplementary data Fig. 1a).

3.4.2 P3b to target visual stimuli before and after controlling for mean hearing loss

—Given the tight correlation between visual decline and aging, the causal link between VA and age-related decline in the visual target P3b remains ambiguous. As the Common Cause hypothesis suggests, a latent common factor may be responsible for age-associated deterioration in both non-cognitive (sensory) and cognitive processes (Baltes and Lindenberger, 1997; Christensen et al., 2001; Lindenberger and Baltes, 1994; Salthouse and Hancock, 1996). To address the issue of whether specific sensory input is a critical factor that mediates later neural processing of visual events, the original visual P3b data were re-

[3]ANCOVA was repeated using LogMAR (MAR = minimal angle of resolution) values for VA, which unlike Snellen values reflect a linear scale. The same pattern emerged: after controlling for VA using LogMAR values, age-related differences in P3b amplitude did not survive, F(1,52) = 0.28, p = 0.59, partial η2 = 0.005.

analyzed after controlling for both measures of auditory and visual acuity. Of note, MHL (auditory acuity) also strongly correlated with age, but theoretically should not directly influence visual processing and the amplitude of the P3b to visual targets. Finding that age-related differences in visual target P3b survive controlling for MHL, but not for VA, would be inconsistent with the Common Cause hypothesis.

Analysis of covariance indicated that after controlling for MHL, the difference between the groups (young > old) remained significant: for averaged P3b amplitude at Pz, $F(1,52) = 7.44$, $p = 0.009$, $eta^2 = 0.12$, and for the PCA P3b factor, $F(1,52) = 7.02$, $p = 0.01$, partial $\eta^2 = 0.11$.

To further validate these findings, a path analysis was used to examine the relationships between age (as a continuous variable), MHL, and the PCA-derived visual target P3b amplitude (Fig. 4b). It revealed a strong correlation between age and MHL, with a correlation coefficient of .83 ($p < .001$). There was also a correlation between age and P3b amplitude that remained significant after controlling for the impact of MHL (with a path coefficient = −0.6, $p < .01$). However, there was no reliable relationship between MHL and P3b amplitude ($p = .1$). Thus, in contrast to VA, auditory acuity did not impact the relationship between age and P3b to visual targets.

5.1 Discussion

The purpose of this study was to investigate whether unrecognized differences in VA across age groups contribute to the frequently reported age-related changes in neural activity during visual tasks. We replicated a very well-established observation in the ERP literature on cognitive aging (Alperin et al., 2014; Anderer et al., 1998; Fabiani and Friedman, 1995; Fabiani et al., 1998; Kok, 2000; Li et al., 2013; Mullis et al., 1985; O'Connell et al., 2012; Polich, 1997) by finding a robust age-associated decline in P3b amplitude to target visual stimuli. Consistent with numerous publications, all participants reported having normal or corrected-to-normal vision. However, actual measurements of VA revealed that, on average, young adults had better than, and old adults, worse than 20/20 vision, which was associated with a reliable difference in VA between groups. After controlling for VA, the age-related reduction in P3b amplitude to target visual stimuli disappeared. Path analysis confirmed that the relationship between age and diminished P3b to target visual stimuli was mediated by VA. These results are particularly striking since the age-associated impairments in VA were subtle (with an average acuity for old subjects of ~20/27, and no subject having worse than 20/40 vision), and the presented visual stimuli relatively large (subtending an angle of ~2.5°). Of note, even the relatively infrequent studies that have measured VA have not excluded subjects with very mild visual impairment, presumably reflecting the assumption that such deficits would not have an impact on the results (Alperin et al., 2014; Logan et al., 2002; Nielson et al., 2002; Park et al., 2012).

The study also demonstrated that the relationship between sensory input and the neural responses indexed by the P3b component to visual targets may be modality-specific. Controlling for differences in auditory acuity (MHL) did not eliminate the age-related decline in the P3b to targets in the visual modality, which was confirmed by path analysis.

These results suggest that accounting for differences in visual acuity (even relatively subtle ones) may influence how one interprets observed differences between young and old adults in neural activity elicited by experimental tasks in the visual modality, and provide a challenge to the status quo approach to investigating this subject.

Given the existence of a separate, large body of research highlighting the strong link between age-associated changes in sensory and cognitive processing (Baltes and Lindenberger, 1997; Gilmore et al., 2006; Lindenberger and Baltes, 1994; Salthouse and Hancock, 1996; Scialfa, 2002), it is curious that a discussion of this issue has not commonly been included in the literature addressing age-related changes in neural activity underlying cognition. The classic version of the Common Cause hypothesis (Baltes and Lindenberger, 1997; Christensen et al., 2001; Lindenberger and Baltes, 1994; Salthouse and Hancock, 1996) suggests that a common, biologically-based factor is responsible for age-related deterioration at all levels of functioning, including ones that mediate peripheral sensory operations. Within this framework, deficits in sensory fidelity among older adults would be viewed as another marker of the aging process, and not as a causally meaningful, intervening variable. In contrast, the Sensory Deficit hypothesis suggests that impaired sensory fidelity can have a direct effect on subsequent cognitive processing (Gilmore et al., 2006; Scialfa, 2002) by reducing the capacity to rapidly extract critical information upon which decisions depend. The data upon which these theories have been developed have largely involved paper and pencil tests of cognitive performance and not indices of neural activity. The results of our path analysis and the apparent modality specificity of sensory acuity on visual P3b amplitude are more consistent with the Sensory Deficit than the Common Cause hypothesis.

According to Mesulam, many aspects of cognition reflect the extensive associative elaboration and attentional modulation of sensory information (Mesulam, 1998). Downstream transmodal areas serve as critical gateways for transforming perception into recognition, and depend on the integrity of the products of earlier sensory processing. As suggested by sequential sampling models, decisions dependent on perceptual processing are mediated by higher-level brain regions like the lateral intraparietal area (LIP) that integrate output from lower-level sensory regions until a criterion amount of evidence is accumulated (Heekeren et al., 2008; Smith and Ratcliff , 2004) Consistent with these perceptual decision-making models, the conveyance of suboptimal sensory data due to diminished VA would undermine the accumulation of sensory evidence. This would disrupt subsequent categorization/decision-making processes, resulting in the transfer of less information (i.e., greater residual uncertainty), which can be indexed by a reduction in the size of the P3b (O'Connell et al., 2012). Viewed from this perspective, the age-related decline in posterior P3b need not be attributed to impairment in cognitive systems mediating decision-making or memory updating, but may be the consequence of the delivery of degraded visual information.

Several models of cognitive aging and adaptation have been developed to explain differences in the recruitment of neural resources across age groups, including the “posterior-anterior shift in aging” or PASA, the “compensation-related utilization of neural circuits hypothesis” or CRUNCH, and the “scaffolding theory of aging and cognition” or

STAC (Cabeza et al, 2002; van Dinteren et al., 2014; Gazzaley et al., 2008; Madden et al., 1999; Madden et al., 2004; Madden et al., 2002; 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). These models converge in terms of suggesting that age-related increases in anterior neural activity may be a compensatory response in older adults to inefficiencies of early stages of sensory-perceptual processing that are mediated by posterior cortical regions. Since most of these studies did not seem to measure, and none controlled for differences in VA, the extent to which apparent age-associated dysfunction of early cortical sensory processing may be due to undocumented differences in VA remains an open question. In a previous study, we reported that accounting for VA had a substantial impact on whether older and younger adults differed in the amplitude and latency of ERP indices of early visual processing, the P1 and N1 components (Daffner et al., 2013). These results challenge existing hypotheses that have attributed such age-related changes in the P1 and N1 components to degradation of posterior brain areas, alteration in parvocellular and magnocellular pathways, decline in the integrity of white matter tracts between different nodes of the visual system, or a disruption of the cortical processing indexed by these components (Daffner et al., 2013).

5.2 Limitations

Our study has several limitations. First, no formal ophthalmologic examination was performed to evaluate abnormalities of the lens, or to determine if cataracts or retinal pathology were present, which are relatively common in older individuals (Friedman et al., 1999; Kanthan et al., 2008; Klaver et al., 1998; Skeel et al., 2003; Tielsch et al., 1990). The most benign explanation for reduced VA is that the subjects had inadequate refraction and needed an updated prescription for corrective lenses, which is a common occurrence (Skeel et al., 2003; Tielsch et al., 1990). Most often, age-related decreases in VA are due to peripheral impairment. However, in rare cases, more central causes of visual impairment may have contributed. Second, although the number of subjects in the current study was as large (n = 55) as most reported in the P3 literature upon which inferences about age-related changes in cognitive operations have been made, the findings need to be replicated with a larger sample size, ideally one that includes subjects with a wider range of VA. The current study did not address whether the tight link between sensory fidelity and P3b amplitude would be found in modalities other than vision. Future research is needed to determine whether analogous results occur in experimental tasks involving the auditory, tactile, or olfactory modalities. A strategy for more directly determining if there is a causal link between visual impairment and age-related changes in neural activity would be to experimentally degrade visual acuity or stimulus signal in young adults and examine the impact on P3b amplitude. There is preliminary evidence that employing such an approach has been associated with a reduction of the size of early visual evoked potentials (Millodot, 1970) as well as the P3b to visual targets (Heinrich et al., 2010; Marhöfer et al., 2015). Moreover, some studies have suggested that degrading visual stimulus quality in young adults to simulate the contrast sensitivity loss of older adults can diminish or eliminate age and disease effects on a variety of cognitive tests (Cronin-Golomb et al., 2007; Gilmore et al., 2006; Toner et al., 2012).

6. Conclusion

In summary, the most critical message of this report is that until the relationship between age-associated differences in visual acuity and late markers of neural processing is clearly established, investigators need to be very careful when interpreting their findings. This cautionary tale applies to studies not only using ERPs, but also other functional imaging techniques. It may not make sense to utilize high-tech methods to precisely measure neural activity, while not collecting readily available, low-tech information about factors such as visual acuity. Our results suggest that it is not sufficient to simply ask subjects if they have normal or corrected-to-normal vision (Daffner et al., 2013; Friedman et al., 1999; Skeel et al., 2003). Objective tests of VA are necessary. Investigators may need to account for differences between age groups not only in typically assessed variables like socioeconomic status, education, sex, and estimated IQ, but also sensory acuity. In addition, research on neural changes associated with normal cognitive aging may be enhanced by collecting information not only on disorders that may impact neuropsychological functioning, such as dementia, cerebrovascular disease, diabetes, and depression, but also on conditions that can impair vision, such as cataracts, glaucoma, and macular degeneration. The issues raised by this report will become increasingly relevant as more studies focus on normal cognitive aging in adults over the age of 80, which is the fastest growing sector of our population, and for whom primary sensory deficits are extremely common. There is a strong need for additional research to help develop guidelines about the most appropriate ways to account for age-related differences in sensory fidelity in the study of neural markers of normal cognitive aging.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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List of 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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Highlights

- Age-related differences in task-related neural activity are very commonly reported
- Impact of group differences in sensory acuity on these findings has been neglected
- Here, we replicate a classical ERP finding: a decline in P3b amplitude with aging
- Age-associated differences in P3b disappeared after controlling for visual acuity
- Researchers should be cautious ascribing results to cognitive, not sensory processing

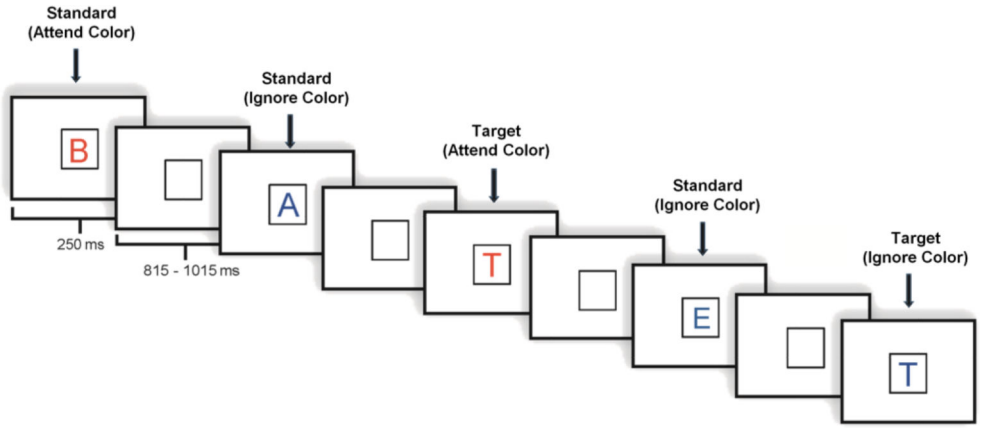

Figure 1.
Illustration of an experimental run.

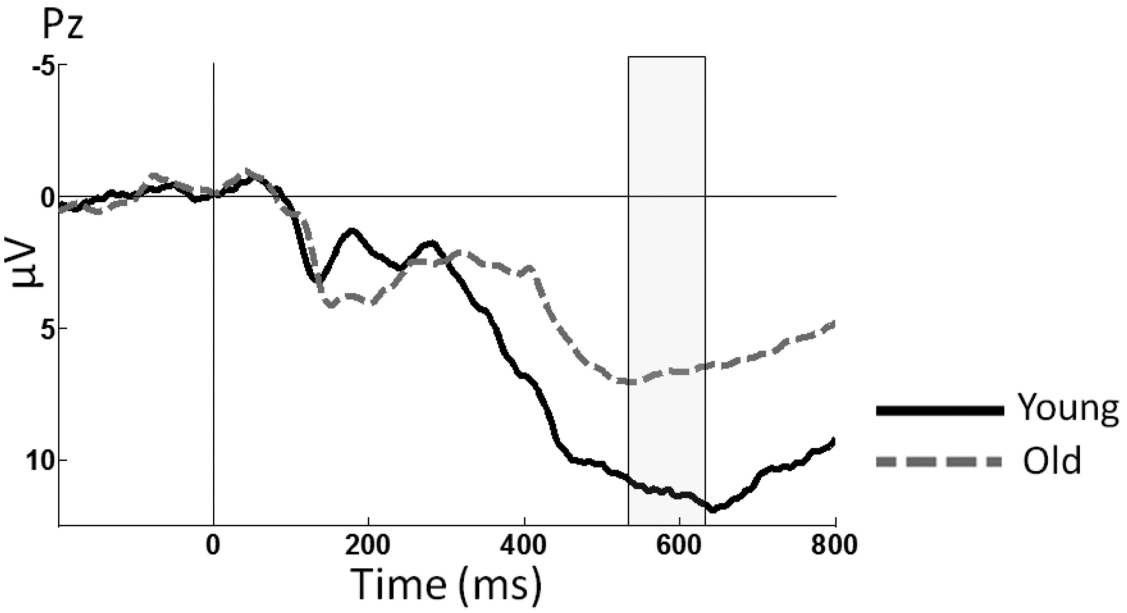

Figure 2.
Grand-average ERP waveforms at midline electrode site Pz in response to target stimuli. The shaded area represents the approximate temporal interval in which the average amplitutude was measured for the P3b.

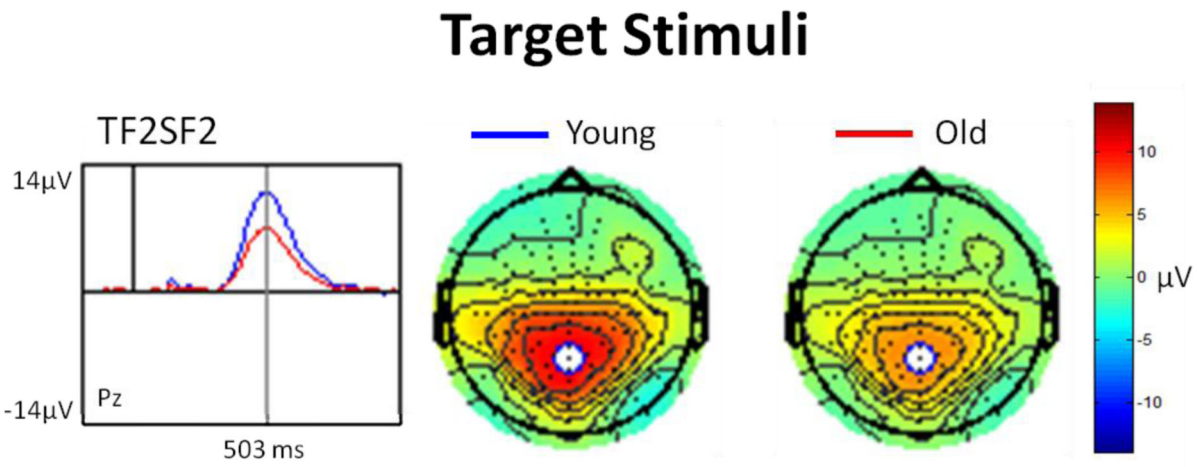

Figure 3.
PCA-derived waveform and topographical distribution of the visual P3b component in response to target stimuli.

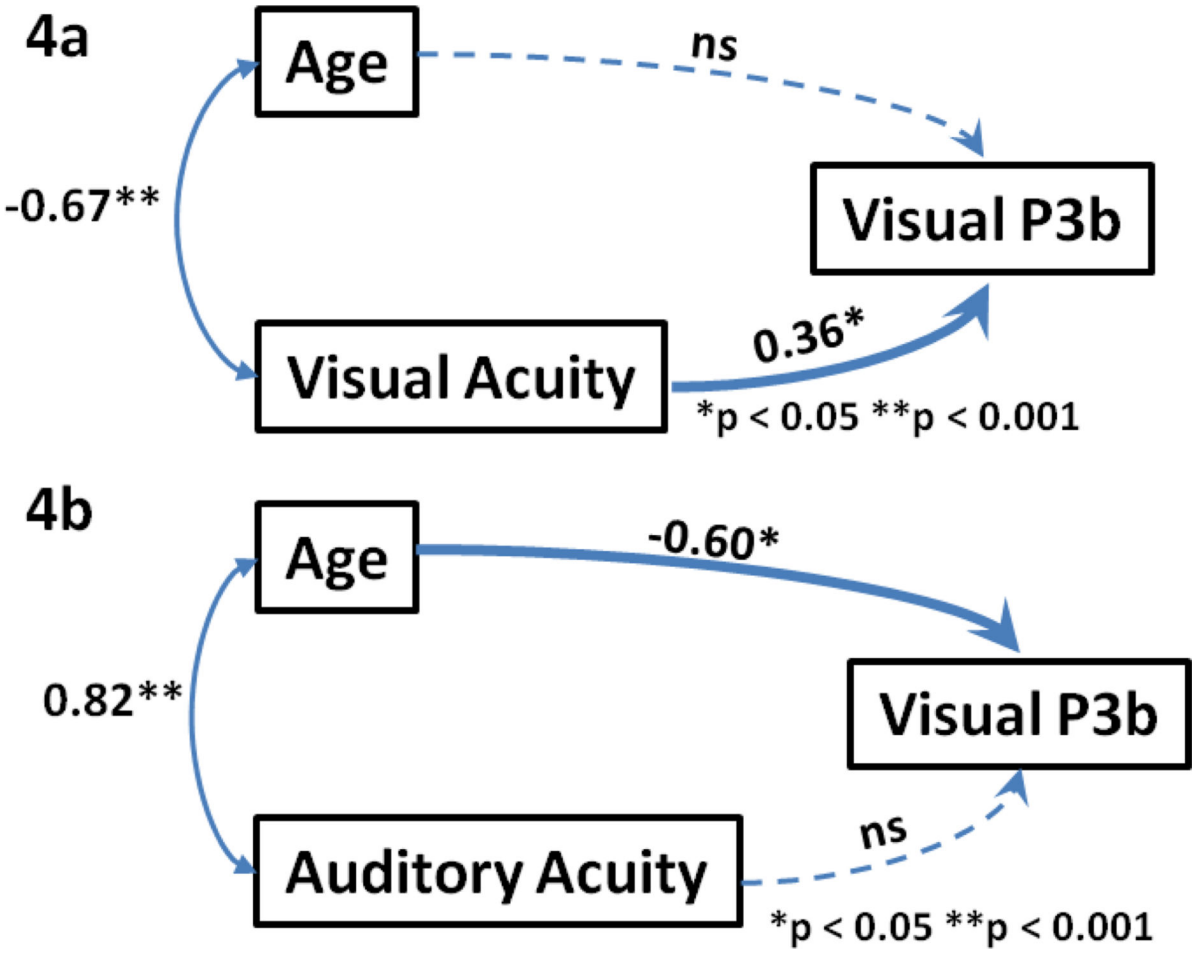

Figure 4.

Path analysis examining the relationships between a) PCA-derived P3b factor, age and visual acuity and b) PCA-derived P3b factor, age and auditory acuity (mean hearing loss). * p < 0.05, ** p < 0.01, ns: non-significant.

Table 1

Subjects 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 (%ile)	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