Reduced Suppression or Labile Memory? Mechanisms of Inefficient Filtering of Irrelevant Information in Older Adults

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Abstract

■ Cognitive aging theories emphasize the decrease in efficiency of inhibitory processes and attention control in normal aging, which, in turn, may result in reduction of working memory function. Accordingly, some of these age-related changes may be due to faster sensory memory decay or to inefficient filtering of irrelevant sensory information (sensory gating). Here, event-related brain potentials and the event-related optical signal were recorded in younger and older adults passively listening to tone trains. To determine whether age differentially affects decay of sensory memory templates over short intervals, trains were separated by delays of either 1 or 5 sec. To determine whether age affects the suppression of responses to unattended repeated stimuli, we evaluated the brain activity elicited by successive train stimuli. Some trains started with a shorter-duration stimulus (deviant trains). Results showed that both electrical and optical responses to tones were more persistent with repeated stimulation in older adults than in younger adults, whereas the effects of delay were similar in the two groups. A mismatch negativity (MMN) was elicited by the first stimulus in deviant trains. This MMN was larger for 1- than 5-sec delay, but did not differ across groups. These data suggest that age-related changes in sensory processing are likely due to inefficient filtering of repeated information, rather than to faster sensory memory decay. This inefficient filtering may be due to, or interact with, reduced attention control. Furthermore, it may increase the noise levels in the information processing system and thus contribute to problems with working memory and speed of processing. ■

INTRODUCTION

Several theories have emphasized that aging brings forth a reduction in the capacity to control attention and an increased susceptibility to distraction (Braver & Barch, 2002; Alain & Woods, 1999; McDowd & Filion, 1992; Hasher & Zacks, 1988). These age-related problems may be the outcome of a diminished efficiency of inhibitory processes, present at several levels of the information processing system (Rykhlevskaia et al., in press), or may be due to a faster decay of the sensory memory templates used to filter out irrelevant information. In this article, we examined the relative contributions of these two mechanisms. We found that brain responses to repeated, unattended tones are quickly suppressed in younger adults, whereas they are more persistent in older adults. However, the recovery rate of these responses after a blank interval, as well as the brain responses to deviant stimuli, appear to be largely unaffected by age, suggesting that a faster decay of stimulus templates in older adults is not the primary cause of the reduced suppression. These findings are consistent with the view that older adults may have difficulty in filtering out irrelevant information, with an ensuing overload of the information processing system. In turn, this may have consequences for working memory function and speed of processing.

Theories emphasizing reduced inhibitory and attentional control in aging were originally based on evidence from the performance outcomes of complex cognitive tasks (Hasher & Zacks, 1988). Consistently with this view, recent data from psychophysiological studies have shown that old adults exhibit increased attention to irrelevant information (Alain & Woods, 1999; McDowd & Filion, 1992). Furthermore, brain imaging studies have found that old adults sometimes exhibit increased, widespread activation, often encompassing both brain hemispheres, in tasks in which young adults show more focused and unilateral activation (dedifferentiation/widespread activation hypothesis; e.g., Logan, Sanders, Snyder, Morris, & Buckner, 2002; Reuter-Lorentz et al., 2000; Cabeza et al., 1997). The tasks in which these effects are observed are usually complex, and performance differences are typically found between age groups,

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leading to a debate about whether the additional activity observed in aging may be an index of compensatory processes.

Similarly, studies in which event-related brain potentials (ERPs) are recorded have found that older adults orient to repeated stimuli as if they were novel, whereas younger adults cease to produce orienting responses as soon as the stimuli are repeated a few times (P3a or novelty P3 responses; Fabiani, Friedman, & Cheng, 1998; Fabiani & Friedman, 1995). These findings have been obtained in the context of very simple tasks in which there are no performance differences between younger and older adults. Nonetheless, individual differences in the brain responses recorded in these simple paradigms are predictive of performance in neuropsychological tests of frontal function (Fabiani et al., 1998; Fabiani & Friedman, 1995; see also Barcelo, Perianez, & Knight, 2002; Herrmann & Knight, 2001), suggesting that they may be indicative of widespread age-related problems. In fact, it is possible to hypothesize that these effects may be pervasive and may be present even at the earliest processing stages. Data from neurological patients with frontal lesions and from schizophrenic adults indicate that these individuals exhibit changes in sensory gating phenomena, characterized by increased responses to irrelevant/unattended input (P50 and N1 responses; e.g., Light & Braff, 1999; for a review see Knight & Grabowecky, 1995), and possibly mediated by reduced frontal inhibitory function over the sensory areas. Similar ERP results in older adults led Chao and Knight (1997) to propose frontal inhibitory decrements in normal aging (see also Gazzaley, Cooney, Rissman, & D'Esposito, 2005, for recent data obtained with functional magnetic resonance imaging).

Suppression of irrelevant/repeated information is typically thought to require two steps: (a) identification of a particular type of information as irrelevant/repeated through matching with memory templates of previously presented stimuli and (b) suppression of the processing channels carrying this information. Accordingly, we expect both sensory memory and attention control to be involved in the filtering process. Therefore, two possible (nonmutually exclusive) mechanisms for the impaired suppression of responses in older adults can be considered: (a) older adults may fail to maintain appropriate memory templates (faster memory decay), (b) they may have problems inhibiting the processing of irrelevant information (reduced attention control and filtering), or both.

In this article we contrast these two possibilities by examining event-related brain responses in young and old adults in a passive task in which the subjects' attention is directed elsewhere. A critical element of our paradigm is that the latent inhibition process eliciting the suppression is estimated separately from the memory decay process. This is achieved by using short stimulus trains (comprising five auditory tones) separated by variable silent intervals. The repeated stimuli within the trains are expected to induce suppression of the sensory-evoked potentials, whereas the silent intervals are expected to allow for the recovery process to occur because of decay of the existing memory templates. The variable duration of the interval allows us to study the memory decay process. Similar paradigms were used in previous studies by Sable, Low, Maclin, Fabiani, and Gratton (2004), Winkler, Schröger, and Cowan (2001), and Cowan, Winkler, Teder, and Näätänen (1993).

Two ERP components are of particular interest within this framework: the N1 and the mismatch negativity (MMN). The auditory N1 response is elicited by perceived sounds regardless of whether they are attended, although its amplitude is modulated by attention (for a review, see Näätänen & Picton, 1987). At least one of the generators of the N1 is located in the auditory cortex (Rosburg, Haueisen, & Kreitschmann-Andermahr, 2004; Lutkenhoner, Krumbholz, & Seither-Preisler, 2003; Alho, Huotilainen, & Näätänen, 1995; Verkindt, Bertrand, Perrin, Echallier, & Pernier, 1995; Vaughan & Ritter, 1970; see Woods, 1995; Näätänen, 1992; Näätänen & Picton, 1987, for reviews of N1 components; see Rinne et al., 1999, for evidence of an optical homolog of the N1).

Stimulus repetition attenuates the amplitude of the N1, and the degree of attenuation depends on the stimulation rate (e.g., Sussman, Ritter, & Vaughan, 1999; Vaz Pato & Jones, 1999; Yabe et al., 1998; Yabe, Tervaniemi, Reinikainen, & Näätänen, 1997). However, when short stimulus trains are used, a more complex picture emerges. For tone pairs, the maximum attenuation occurs with a stimulus onset asynchrony (SOA) of 400 msec (Todd, Michie, Budd, Rock, & Jablenski, 2000; Budd & Michie, 1994). In a recent study using five-tone trains, we showed that N1 attenuation with stimulus repetition is not due to refractoriness–habituation, but it is likely to be *actively* imposed on the N1 generators (Sable et al., 2004; see also McEvoy, Levänen, & Loveless, 1997). In fact, at SOAs *shorter* than 400 msec, the N1 amplitude is relatively unattenuated, regardless of the number of stimuli interposed in the interval. This suggests that some other mechanism(s), possibly involving latent inhibition, takes about 400 msec to be fully deployed (Sable et al., 2004; McEvoy et al., 1997). In any case, 400 msec is the optimum SOA for eliciting maximum N1 attenuation to individual stimuli in short trains, as well as for allowing time for activity to return to near-baseline levels following each stimulus.

Several investigators have reported age-related increases in N1 amplitude (e.g., Amenedo & Díaz, 1999; Chao & Knight, 1997; Anderer, Semlitsch, & Saletu, 1996) as well as in the amplitude of the P2 response (Amenedo & Díaz, 1998). The P1 has also been reported to increase with age (Smith, Michalewski, Brent, & Thompson, 1980). Less N1 attenuation to the second tone in a pair (600-msec interstimulus interval) has also

been reported for older adults, relative to young adults (Golob, Miranda, Johnson, & Starr, 2001), but in that study this phenomenon was significant only when the first stimulus in the pair was a visual stimulus (cross-modal suppression). Taken together, these data indicate that older adults process repeated irrelevant information more than younger adults. This may be due to faster decay of the memory templates for the stimuli, decrease in filtering of irrelevant input (possibly mediated by reduced or delayed inhibitory phenomena), or both.[1]

The paradigm used in the current study allowed us to examine these hypotheses more closely. To evaluate whether age differentially affects N1 suppression with stimulus repetition, we examined the N1s elicited by the five successive tones in each train (separated by fixed 400 msec SOAs, at which N1 suppression is well established by the second stimulus; Sable et al., 2004; Todd et al., 2000; Budd & Michie, 1994). As mentioned earlier, Sable et al. (2004) showed that under this stimulation condition, the suppression of N1 is not due to refractoriness or habituation, but to some other mechanisms—possibly involving latent inhibition. If inhibitory mechanisms become less effective with age, it can be hypothesized that the rate of N1 suppression will be steeper in younger than older adults over the five tone presentations.

To determine whether age differentially affects decay of sensory memory templates over short intervals, we compared the amplitudes of the N1s elicited by the first stimulus in the train across the two groups of subjects and the two delay intervals (i.e., 1 and 5 sec). If sensory memory templates decay more rapidly in older adults, then the amplitude of the N1 elicited by the first stimulus should be larger for this group. Furthermore, if the amount of decay depends on the duration of the interval, then the N1 amplitude may interact with both age and interval duration.

The second ERP component of interest for the purposes of this study is the MMN, elicited by stimuli that are deviant compared to a template generated by previous stimuli. For this reason, in the current study, half of the trains started with a tone of different (shorter) duration than the other tones in the train (deviant trains). The MMN is typically considered to reflect sensory memory processes (Ritter, Deacon, Gomes, Javitt, & Vaughan, 1995). This provided us with another means for studying the decay of sensory memory representations: A larger MMN would be expected to occur when the memory representation of the standard is more intact (i.e., in the 1-sec compared to the 5-sec delay condition). Thus, if memory representations decay faster in older than in younger adults, the former should also show a smaller MMN difference between the two delay conditions.

Most ERP components, including the N1 and the MMN, represent the summated activity of several generators. In addition, component overlap can further limit the possibility of attributing the observed brain activity to one component/generator. In an effort to isolate activity originating in auditory cortex, in this study we also recorded optical brain measures (the event-related optical signal, or EROS; Gratton & Fabiani, 2001) from auditory areas in the right hemisphere, simultaneously with the ERP recordings. These measures possess both high temporal and spatial resolution, and can therefore be used to corroborate the ERP results. Rinne et al. (1999) showed the feasibility of recording optical measures from the auditory cortex of young adults and demonstrated that optical equivalents of the N1 and MMN responses could be measured from distinct regions of the temporal lobe. In this study, which is the first in which EROS data were recorded in older people, we are testing the feasibility and usefulness of using this approach to compare younger and older subjects.

METHODS

Subjects

Sixteen young (mean age, 26 years; range, 21–33 years; 8 women) and 16 old (mean age, 72 years; range, 65–78 years; 8 women) adults were recruited from the University of Missouri student population and from the Columbia, MO, community to participate in this study. All subjects signed informed consent and were paid for their participation. All subjects reported themselves in good health and were right-handed (based on the Edinburgh Handedness Inventory; Oldfield, 1971), native English speakers, and free from medications that could affect the central nervous system. All subjects admitted into the study were also within normal limits on the modified Mini-Mental Status exam (mMMS; Mayeux, Stern, Rosen, & Leventhal, 1981; young, 56.44; old, 54.75) and had at least average IQ (estimated from the vocabulary and block design scores of the Wechsler Adult Intelligence Scale—Revised [WAIS-R]; Wechsler, 1981; young, 122; old, 117).

All subjects were audiometrically screened to determine auditory thresholds at 500 Hz (the pitch of the tones used in this study). Subjects who had a mean loss greater than 30 dB were excluded from the study. The young adults admitted into the study had an average hearing loss of 5 dB (range 0–15), and the old adults had an average hearing loss of 16 dB (range 5–30). The hearing loss of each subject was compensated for by increasing the intensity of the stimuli by the subject's average decibel loss (across ears). We further checked these volume-adjustment procedures to make sure they would not produce confounds. Specifically, because N1 amplitude is sensitive to intensity, we wanted to make sure that the tone loudness was not overcompensated in older adults, leading to artifactually increased N1 amplitudes, hence to decreased suppression. We reasoned that if this were true, there should be a significant

correlation between N1 amplitude and degree of compensation, with subjects exposed to louder tones also producing larger N1s. In fact, the correlation between N1 amplitude and auditory threshold was not significant and approached zero ($r = -.04$) indicating that the compensation procedure had worked correctly.

Stimuli and Procedures

The sound stimuli were harmonically enriched 500-Hz tones (5-msec Gaussian on-offset, consisting of frequencies of 500, 1000, and 1500 Hz, with the second and third components being 3 and 6 dB lower in intensity, respectively, than the first component; Tervaniemi et al., 1999). The stimuli were presented binaurally via earphones at 70 dB above the subject's hearing threshold. Stimuli were presented while subjects were reading a book of their choice and instructed to ignore the tones. Tones were presented in trains of five, with onset-to-onset intervals of 400 msec. This SOA was chosen because it is the one at which the N1 shows maximum suppression by the second tone with stimulus repetition (Sable et al., 2004; Todd et al., 2000; Budd & Michie, 1994). The delay between trains was either 1 or 5 sec. The duration of the first tone in each train varied. On half of the trains, all tones were 75 msec (standard) in duration, whereas on the other half, the first tone was 25 msec (deviant) followed by four 75-msec tones. Standard and deviant trains were randomly intermixed, with 17 trains per block presented for 75 blocks. Short breaks were offered to the subjects in between blocks. The first train in each block was considered ''warm-up'' and was excluded from further analyses.

Subjects were tested over two sessions. During the first session, subjects were administered the auditory screening and neuropsychological tests. During the second session, ERPs and EROS were recorded simultaneously while subjects were seated comfortably in a sound-attenuated booth.

ERP Recording and Analysis

Electroencephalographic (EEG) activity was recorded from six gold scalp electrodes (Fz, Cz, Pz, C3 and C4, and A2), referred to the left mastoid (a limited EEG montage was used to avoid interference with the optical sensors, which were placed on the scalp at the same time). An average mastoid reference was derived off-line. Vertical and horizontal electrooculographic (EOG) activity was recorded from electrodes placed above and below the right eye and at the outer canthus of each eye, respectively. EEG and EOG data were digitized at 100 Hz, and filtered on-line with 0.01–30 Hz band-pass (Model 12 Neurodata Acquisition System, Grass Instruments Co., Quincy, MA). Each recording epoch started 200 msec before the onset of the first stimulus in the train and lasted 2400 msec.

Eye movement artifacts were corrected off-line (Gratton, Coles, & Donchin, 1983). Trials exceeding the A/D converter range and those with activity above 150 μV were excluded. Data were averaged for each subject, electrode, and condition. Amplitude measures were taken on the average waveforms of each subject at the three midline electrodes within the following windows: P1 (largest positive peak, 40–90 msec), N1 (largest negative peak, 90–180 msec), P2 (largest positive peak, 180–300 msec), all from stimulus onset. The MMN amplitude was quantified as the largest negative peak in the interval between 120 and 220 msec on the Fz difference waveforms.

EROS Recording and Analysis

Optical (EROS) data were recorded using a frequency-domain 16-channel Omnia Tissue Oxymeter (ISS Inc.; Champaign, IL). Light sources consisted of laser diodes emitting light at 750 nm (near-infrared range), with a power of ≈1 mW. The current powering the laser diodes was modulated at 110 MHz. The light emitted by the laser diodes was channeled to the surface of the scalp through 400-μm-diameter optic fibers, which were held in place using a modified motorbike helmet. The two detectors were fiber-optic bundles (diameter, 3 mm) connected to photomultiplier tubes (PMTs). The current feeding into the PMTs was modulated at 110.005 MHz. This generated a 5-kHz heterodyning frequency, making it possible to use inexpensive A/D cards for the recording. The output current from the PMTs was sampled at 50 kHz and subjected to FFT for computation of DC (average) intensity, relative phase delay, and amplitude measures. Only phase delay data, which are most commonly used for the computation of EROS, are presented here.

Data were recorded from a total of 24 source–detector pairs in locations that covered the scalp projection of the auditory cortex of the right hemisphere. Two detectors and four sources were used at a time; the stimulus sequences were repeated three times with different sensor configurations to generate maps. This afforded a spatial sampling of approximately 1.5 cm along the anterior–posterior (y) axis and 0.5 cm along the dorsal–ventral (z) axis.

The stimulation and recording systems were synchronized using a parallel cable. The recording of the optical data began simultaneously with the beginning of each block (and with the onset of the EEG recording), and continued for 92.16 sec, sampled every 20 msec (50-Hz sampling rate). The pulse artifact on the optical data was compensated off-line using an algorithm described by Gratton and Corballis (1995).

Analysis comprised the following steps. The phase delay data were used for the computation of EROS by segmenting the recording period into shorter epochs

corresponding to each train, beginning 100 msec before the first train tone and lasting for 2400 msec. These segments were then averaged separately for each channel, condition, and subject. Channels with a standard deviation exceeding 6° were not included in the analysis. A baseline composed of the 100 msec before train onset was subtracted from each trial record. To reduce high-frequency noise, an 8-Hz low-pass filter was applied to the data (see Maclin, Gratton, & Fabiani, 2003); to eliminate slow drifts the data were linearly detrended before the analysis.

The average data were then analyzed using a computer program (Gratton, 2000) that allows the user to produce maps of the optical response for each data point and overlay them onto sample images of the surface of the cortex. For each data point, the maps were computed by back-projecting the value recorded at each channel (i.e., source–detector pair) on the cortical surface. We digitized the locations of the optical sources and detectors referenced to fiducials (nasion and preauricular points) in one representative young and one representative old participant, for whom structural magnetic resonance (MR) images were also obtained. These data were used to coregister the optical data on the structural MR images and for plotting them according to Talairach coordinates (Talairach & Tournoux, 1988).

In many cases, the regions investigated by different channels overlapped partially. In these cases, the values of overlapping channels were averaged (pi detector; Wolf et al., 2000). Statistical analyses (means, standard errors, *t* values, and associated *Z* scores) were derived across subjects for each data point or preset intervals. Note that, because data were surface projected over the right hemisphere, the *x* (left–right) coordinate is arbitrary, and only the *y* (anterior–posterior) and *z* (dorsal–ventral) coordinates are relevant.

Peak activity analysis was carried out by selecting the point with the maximum value in a specific region of interest (ROI) corresponding to the superior temporal gyrus. The statistical significance of the data was determined by comparing the obtained value with a criterion that takes into consideration the spatial smoothness of the data (SPM; Poline, Worsley, Evans, & Friston, 1997).

RESULTS

ERP Data

N1 Suppression by Train Position and Delay

Figure 1A and B shows the grand average train data for the two delay conditions (1 and 5 sec), separately for the two groups, and for deviant and nondeviant trains. Several effects are evident in this figure. First, a large N1 is evident in response to the first stimulus in the train for both groups, especially for the 5-sec delay condition. The amplitude of the N1, which is largest at Cz, is considerably suppressed for the following train stimuli (positions 2–5), especially for the young adults. This suppression is less evident in the old adults, who still exhibit a clear N1 response to the fifth stimulus in the train.

Figure 2 shows the amplitude of the N1 response (at Cz) to each train stimulus. This figure indicates that for stimuli in position 1, data were segregated by delay interval, with a larger N1 response after the 5-sec delay for both groups. However, by the end of the train, data were segregated by age, with larger N1 amplitudes for the old adults in both delay conditions. This suggests that age influences the degree to which the N1 response is suppressed over repeated stimulation.

To corroborate these visual impressions, the N1 amplitude measures were submitted to two mixed-design, repeated measures analyses of variance (ANOVAs). Both analyses were conducted collapsing across deviance conditions (i.e., across trains starting with standard and deviant stimuli). The first analysis focused on the N1 recovery after a blank interval. It was therefore restricted to the first item in the series, and included age group (young, old), and delay interval (1 sec, 5 sec) as factors. There was a main effect of delay interval, $F(1,30) = 87.82$, $p < .0001$, but not a main effect of age or an interaction between age and delay interval; in both cases, $F(1,30) = 0.00$. These results support the claim that N1 recovers at a similar rate in both age groups when no stimuli are interposed in the interval. To further test that our sound intensity adjustment procedures had worked as planned, we also repeated this analysis using tone intensity as a covariate. The results of this analysis of covariance (ANCOVA) matched those of the ANOVA reported above. There was no significant effect of group, $F(1,29) = .21$, *ns*, and no significant interaction between group and delay interval, $F(1,30) = .00$, *ns*. As in the ANOVA case, the effect of delay was significant, $F(1,30) = 87.82$, $p < .001$. This confirms the absence of a difference in amplitude at tone one (with intensity factored out) and the fact that the two age groups appear to have the same N1 modulation in response to the delay intervals.

The second analysis focused on the suppression process and included age group, position (1 to 5), and delay interval (1 sec, 5 sec) as factors. There were main effects of position, $F(4,120) = 71.30$, $p < .0001$, and delay interval, $F(1,30) = 20.54$, $p < .0001$, as well as a significant interaction between these two variables, $F(4,120) = 39.88$, $p < .0001$. These findings support the claim that N1 is suppressed over the course of the train, recovers only slightly in the 1-sec delay compared to the 5-sec delay.

Most important for the purposes of this article, there was also a significant interaction between position and age, $F(4,120) = 3.83$, $p < .01$, indicating that less suppression occurred in the older compared to the

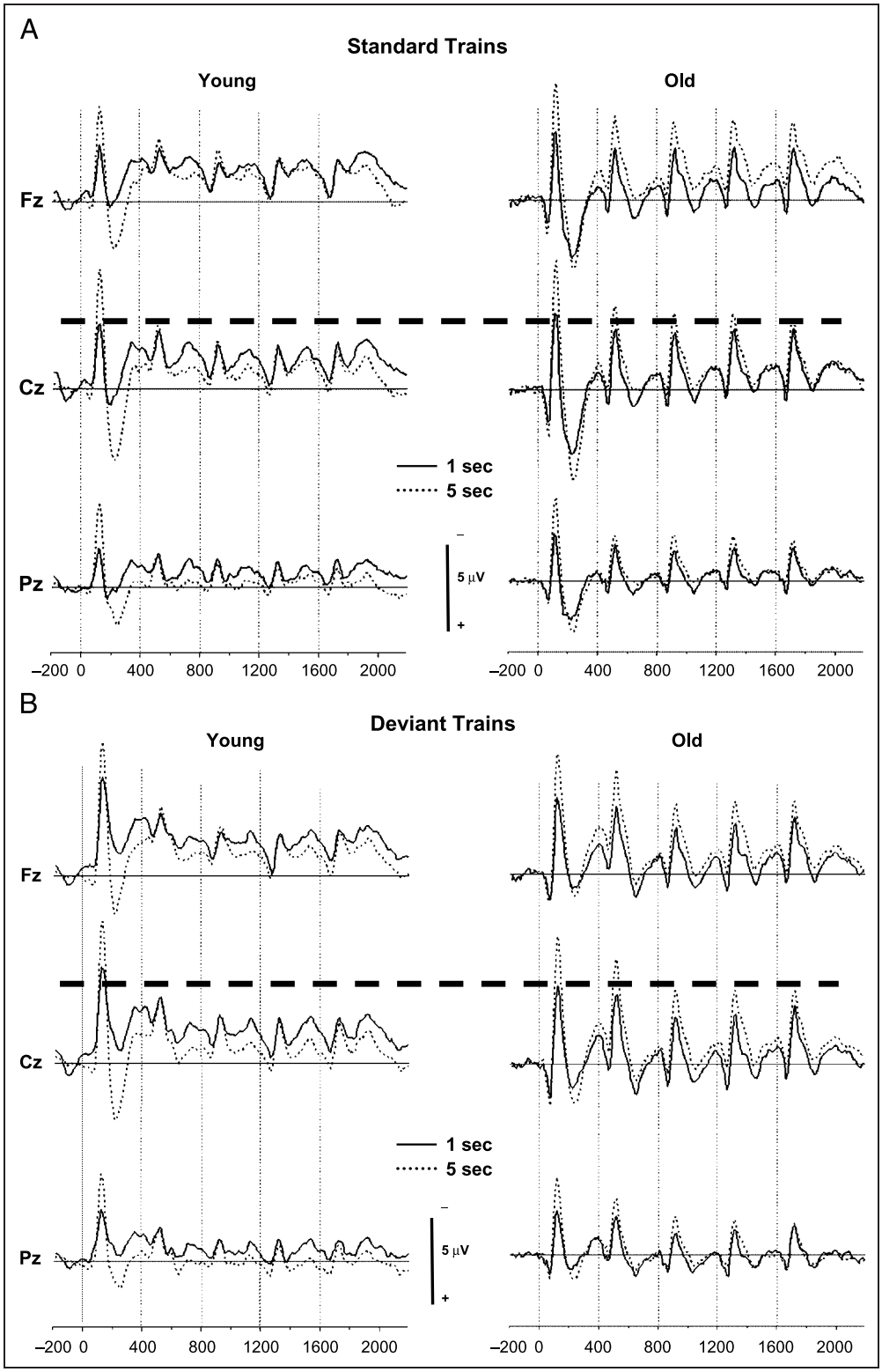

Figure 1. Grand average ERPs to standard (A) and deviant (B) trains at three midline electrode locations (Fz, Cz, and Pz). Young adults are on the left, old adults on the right. Solid lines refer to data from the 1-sec delay condition, and dotted lines to data from the 5-sec delay condition. The thin dotted vertical lines indicate the onset of each train stimulus. Positive values are plotted downward. The thick dashed horizontal line at the Cz electrodes is displayed to facilitate the visualization of the differential N1 suppression across the two groups.

younger subjects. Age group also interacted with delay, $F(1,30) = 4.75$, $p < .05$, and there was a significant three-way interaction between age, delay, and position, $F(4,120) = 2.90$, $p < .05$. Inspection of Figure 2 shows that both of these interactions are due to the different efficacy of the suppression process, which in the young is practically completed by the third stimulus in the 5-sec, second delay series, whereas in the old is still operating (although to a lesser degree) through the last item in the series.

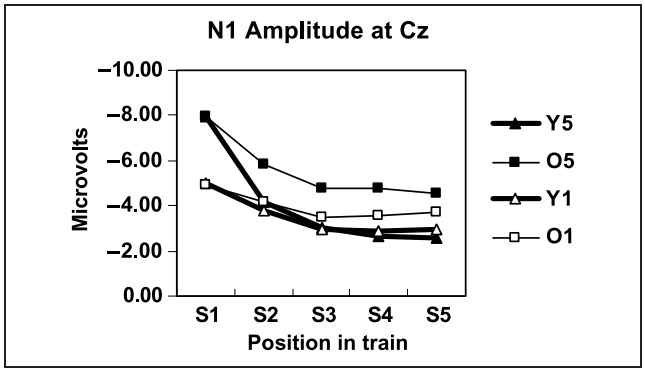

Figure 2. Grand average peak measures (taken at the Cz electrode) of N1s for the two groups, delay conditions, and positions in the train. Data are averaged across standard and deviant trains. Y = young; O = old; 5 = 5-sec delay; 1 = 1-sec delay.

P1 and P2 Effects

An inspection of Figure 1 suggests that age and delay interval have effects on two additional responses—the P1 and the P2—which are both clearly evident in the two groups in response to the first train stimulus. Specifically, it appears that whereas for the younger adults both of these components are suppressed at the 1-sec delay interval (compared to the 5-sec delay condition), for the older adults they are larger and are maintained even at the short (1 sec) delay. ANOVAs including age group and delay interval as factors were conducted using peak amplitude measures taken at Cz (where these two components were largest).

The P1 response was larger after the 5-sec delay than after the 1-sec delay, $F(1,30) = 12.0$, $p < .01$, and for older than for younger adults, $F(1,30) = 8.4$, $p = .01$. Furthermore, age interacted with delay, $F(1,30) = 4.9$, $p < .05$. Follow-up analyses revealed that a reliable difference in P1 amplitude between the 1-sec and 5-sec delay conditions was only evident for the young adults (mean 5 sec = −0.08 μV, mean 1 sec = −0.62 μV) but not for the older adults, for whom P1 amplitude was similar in the two cases: mean 5 sec = .68 μV; mean 1 sec = .56 μV; young adults: $F(1,15) = 13.9$, $p < .01$; old adults: $F(1,15) < 1$.

Similar to the P1, the P2 response was more positive after the 5-sec delay, $F(1,30) = 48.9$, $p < .001$. Older adults had larger P2 amplitudes compared to younger adults, $F(1,30) = 5.8$, $p < .05$, but this effect interacted with delay, $F(1,30) = 26.2$, $p < .001$. Follow-up analyses of the group by delay interaction revealed that the increase in P2 amplitude following the 5-sec compared to the 1-sec delay condition was only reliable for young adults: young adults: $F(1,15) = 114.5$, $p < .001$; old adults: $F(1,15) = 1.3$, *ns*. In fact, P2 amplitude was not statistically different for the two groups under the 5-sec delay condition. Only at the 1-sec delay were the groups different, with older adults displaying more positivity than younger adults.

In summary, the P1 and P2 analyses confirm the observation that older adults show larger brain responses than younger adults (at least for the 1-sec delay condition). They further indicate that for these brain responses (differently from the N1), age interacted with delay, with younger but not older adults showing a reduction of these components with short intertrain delays.

Mismatch Negativity

Grand average MMN waveforms from Fz, Cz, and Pz, sorted by age group and delay interval, are presented in Figure 3. These waveforms were obtained by subtracting the average waveforms elicited by the standard trains (i.e., trains starting with a standard 75-msec-duration stimulus) from the waveforms elicited by the deviant trains (i.e., trains starting with a deviant 25-msec-duration stimulus). These waveforms are characterized by a frontocentral negative deflection with latency between 150 and 200 msec from stimulation (MMN).

The peak amplitude values for the MMN were submitted to an ANOVA with two factors—age group and delay interval. The MMN was more negative after the 1-sec delay (−1.99 μV) compared to the 5-sec delay (−1.26 μV), $F(1,30) = 26.5$, $p < .001$. There was no main effect of group (young = −1.62 μV, old = −1.63 μV; $F < 1$), and the difference between the 1-sec and 5-sec delay was not statistically different in the two groups, $F(1,30) = 3.4$, *ns*. These data are consistent with the idea that sensory memory representations for the standards decay more during the 5-sec delay interval than during the 1-sec delay interval (leading to a smaller MMN after 5 sec), but that this phenomenon occurred in a similar manner in the two subject groups. This supports the claim that decay of the sensory memory representations supporting the MMN does not differ significantly as a function of age in this paradigm.

Optical Data

Optical data were collected in this study for two reasons: first, to demonstrate the feasibility of obtaining such measures in older adults and second, to isolate activity originating in auditory cortex, so that the N1 effects observed with ERPs could be corroborated by data in which component overlap is not an issue (Gratton & Fabiani, 2003).

Figure 4 shows surface projection maps of the right hemisphere (from which the recordings were obtained). The area shaded in dark gray is the area probed by the measure, whereas the green square indicates the ROI used for the analysis. In these maps, the areas in red indicate Z scores above 2.0 (corresponding to $p < .02275$, uncorrected for multiple comparisons). Results indicate that a clear activity is present between 80 and 120 msec latency (latency of the N1 response to the first train stimulus) in the 5-sec delay condition (right), averaged

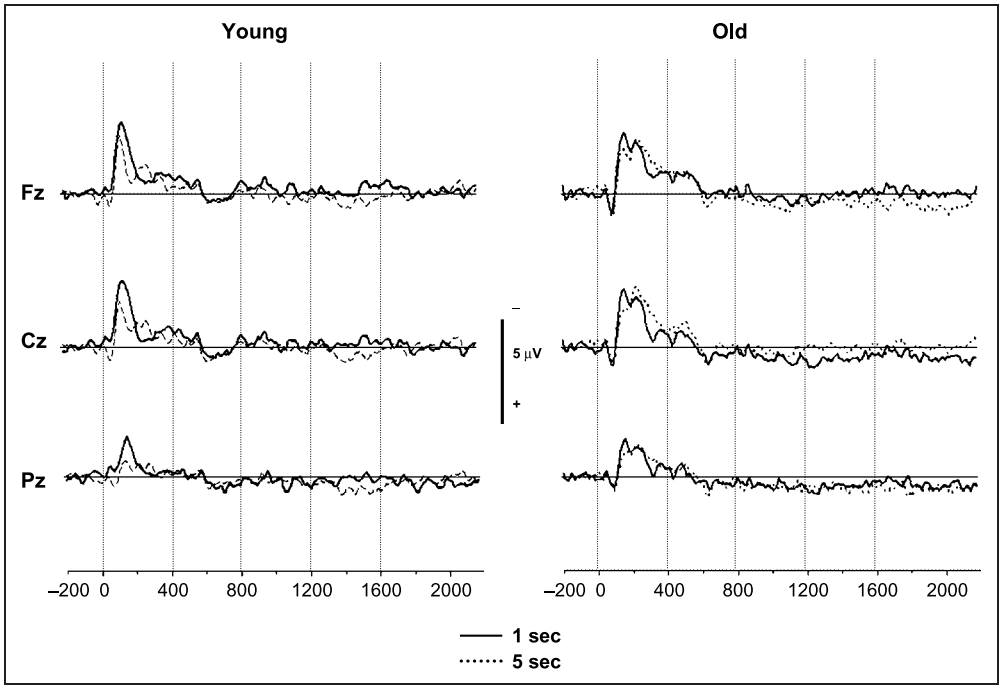

Figure 3. Grand average difference waveforms between deviant and standard trains at Fz, Cz, and Pz. Young adults are on the left, old adults on the right. Solid lines refer to the 1-sec delay condition, and dotted lines to the 5-sec delay condition.

across all subjects. The peak location showed a significant Z score of 3.81 (corrected critical $Z = 3.13$, $p < .05$). Reduced activity is apparent in the 1-sec condition (left), with a nonsignificant peak Z score of 1.85. The peak locations were very similar in the two conditions (5 sec: $y = -25$, $z = 1$; 1 sec: $y = -27$, $z = 4$), and both were within the superior temporal gyrus in Brodmann's area (BA) 22.

Figure 5 shows the average activity across all subjects for the 5-sec delay condition, in the same latency interval as above, as well as a comparison of the activity for younger and older adults separately (in this figure, red indicates a Z score exceeding 2.5, $p < .006$, uncorrected). At this latency (first stimulus in the train), both groups show clear responses, similar to the ERP results. Figure 6 shows a comparison between the first and second train stimulus in the 5-sec delay condition in younger and older adults. Similarly to the ERP results, both groups show a clear N1 response to the first train stimulus, but this activity is much reduced in the young adults in response to the second stimulus (latency 80–120 msec from the onset of the second stimulus).

Figure 7 provides a quantitative comparison between the ERP and EROS measures, both rescaled based on the activity obtained in response to stimulus 1 in the 5-sec delay (at Cz for the ERP measures; at the location of peak activity within the ROI for the EROS measures). For both measures, younger adults show a greater reduction with stimulus repetition than older adults. The reduction, which is significant for both measures, $t(30) = 2.88$ (for ERPs), $t(30) = 1.97$ (for EROS), both $p < .05$, one-tailed, is more pronounced for the EROS than for the

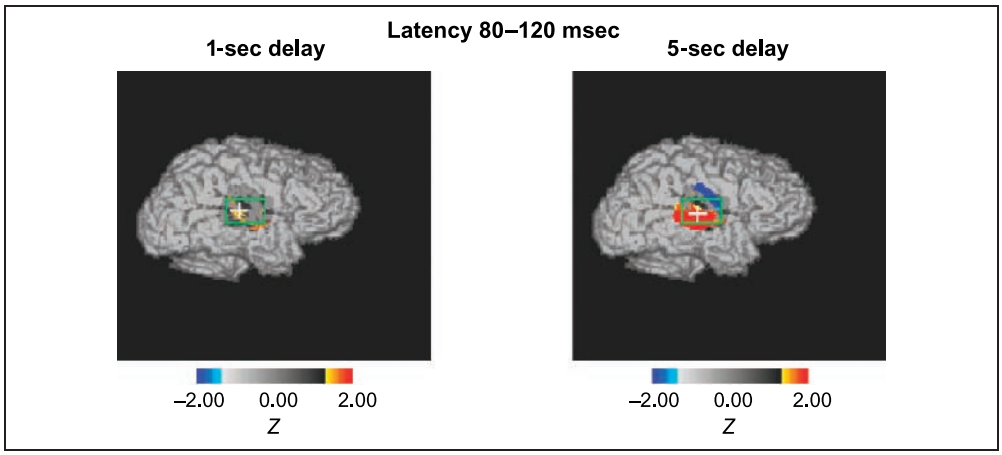

Figure 4. Surface projections (Z-score maps) of the optical data over the right hemisphere for young and old adults combined, for the 1-sec (left) and the 5-sec (right) delay condition at a latency of 80–120 msec from the first train stimulus. The dark gray shading indicates the area from which data were obtained. The green box indicates the ROI used for the analysis. The color scale indicates the Z value. The white cross indicates the peak point.

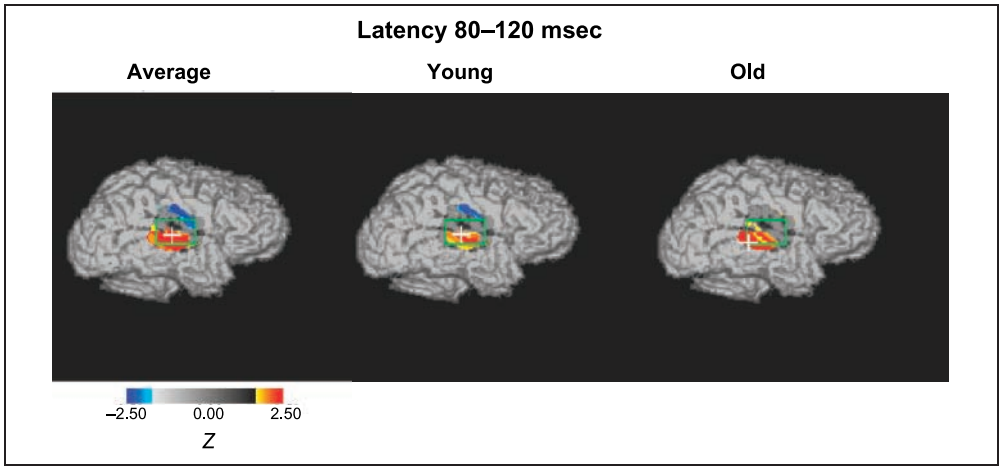

Figure 5. Surface projections (*Z*-score maps) of the optical data over the right hemisphere for the 5-sec delay for young and old adults combined (left) and for each group separately (middle, young; right, old) at a latency of 80–120 msec from the first train stimulus. The dark gray shading indicates the area from which data were obtained. The green box indicates the ROI used for the analysis. The color scale indicates the *Z* values. The white cross indicates the peak point.

ERP data. This may be because the EROS measure may isolate a subset of the activities that are instead summated in the ERP component measures and/or because the signal-to-noise ratio is poorer for the EROS measures. In particular, the optical signal becomes increasingly noisy at greater tissue depths, and the N1 generators may extend into the sylvian fissure beyond the practical range of the recording equipment.

DISCUSSION

This study aimed at testing whether age differentially affects (a) the suppression of responses to repeated unattended stimuli, (b) the decay of sensory memory templates over short time intervals in which stimuli are not presented, or both. We found that the recovery of N1 amplitude after an interval is affected by the duration of the interval but not by age. This supports the hypothesis that age is *not* associated with a faster decay of sensory memory templates. This finding is also supported by the analysis of the MMN data, which also shows no difference as a function of age but is modulated only by the delay interval duration. However, this conclusion is somewhat mitigated by the P1 and P2 measures, which indicate that at short intervals older adults have larger amplitude responses than younger adults. This suggests that the processes indexed by these components have a faster recovery cycle (or are under less inhibition) in older adults.

The examination of the N1 suppression across train stimuli shows that this response decreases faster with stimulus repetition in younger than older adults. Sable et al. (2004) (see also McEvoy et al., 1997) had reported data suggesting that some active mechanism, possibly

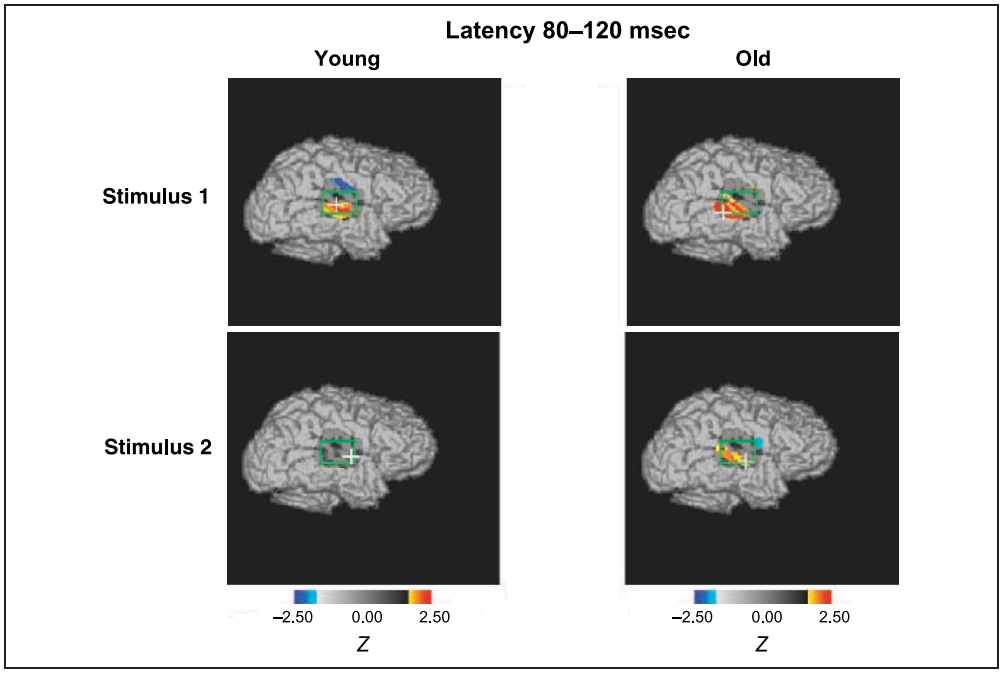

Figure 6. Surface projections (*Z*-score maps) of the optical data over the right hemisphere for the 5-sec delay for young (left column) and old adults (right column), at a latency of 80–120 msec from stimulus onset (top row, first stimulus; bottom row, second stimulus). The dark gray shading indicates the area from which data were obtained. The green box indicates the ROI used for the analysis. The color scale indicates the *Z* values. The white cross indicates the peak point.

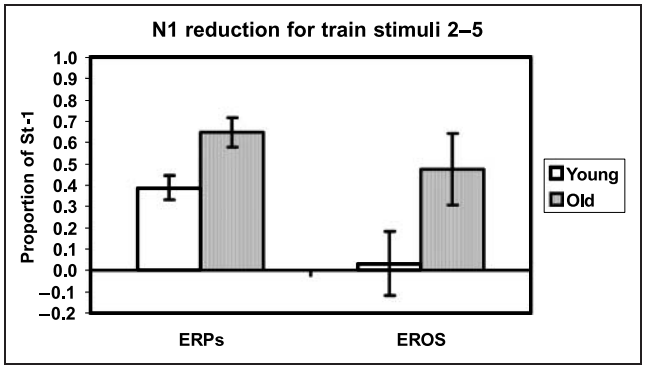

Figure 7. Comparison of the relative amplitude of N1 for train stimuli in positions 2–5 with respect to the first train stimulus in younger (white bars) and older (gray bars) adults for ERPs (left) and EROS (right).

involving latent inhibition, is at the basis of the N1 suppression with stimulus repetition. The decrease in age-related suppression reported here may be indicative of the fact that inhibitory processes are reduced or become slower and more sluggish with age (Hasher & Zacks, 1988). Furthermore, it could be hypothesized that the P1 and P2 effects observed in this study may have a role in a feedback loop involving inhibitory control. For example, one might conceive that the P1, N1, and P2 each reflect a different functional level in an auditory processing circuit with the frontal cortex. The P1 is generally considered to reflect sensory gating processes in the auditory system—an input level phenomenon (with a frontal component; see Weisser et al., 2001). The N1, which is affected by attention, may reflect a processing stage. The P2 may reflect a feedback signal.

Consistent with this view of the role of early auditory components, Kisley, Noecker, and Guinther (2004) recently found that reduced N1 attenuation correlated with subjective reports of ''overinclusion'' of sensory information (e.g., ''I seem to always notice when automatic appliances turn on and off—like the refrigerator or the heating and cooling system''), whereas reduced P1 attenuation correlated with reports of ''perceptual modulation'' difficulties, particularly related to filtering (e.g., ''I have feelings of being flooded by sounds''). Similarly, Jääskeläinen et al. (2004) also ascribe a gating role to the posterior N1 response, suggesting that it serves as a preattentive gating mechanism determining the extent to which unattended novel sounds enter a person's awareness.

The optical data recorded from the auditory cortex corroborate the electrical N1 suppression findings and support the feasibility of using optical brain measures with older adults. In fact, EROS activity from the superior temporal gyrus (at a latency approximately equivalent to that of the electrical N1) in response to the first train stimulus is clearly evident in both subject groups but is largely suppressed in the younger adults by the second train stimulus. In contrast, older adults continue to exhibit this response across train stimuli. The differential rate of response reduction for the two age groups is larger for the EROS data than for the ERP data. This may be because the EROS data are limited to one of the possible sources of electrical N1 response. The supratemporal component of the auditory N1 is thought to be generated, at least in part, by cells in the primary auditory cortex, but it may include a larger area (e.g., Woods, 1995; Näätänen, 1992; Näätänen & Picton, 1987; Vaughan & Ritter, 1970). Because the primary cortex extends well into the sylvian fissure on the lateral surface of the temporal lobe, EROS may not be able to acquire useful data from the entire active area. If there is a core area of N1 activation that spreads with a larger response, EROS may be more sensitive to this spread than to the activity in the core area. Such a pattern would produce the difference we see between EROS and ERPs.

An important methodological feature of this study is that we varied the intensity of the auditory stimuli to account for variations in auditory thresholds across subjects. The purpose of this manipulation was to attempt to equalize stimulation levels for all subjects, so that a similar cortical response could be expected. That our compensation process was successful is demonstrated by the observation that the first N1 in the trains are of practically identical amplitude in young and old subjects and that there was no correlation between the amplitude of the N1 and the auditory threshold. Similarly, the duration MMN also appears to be very similar in the two groups. This contrasts with some previous studies showing significantly reduced N1 (e.g., Golob et al., 2001—N1 reduced to the first tone of a pair) and MMN amplitudes (Gaeta, Friedman, Ritter, & Cheng, 1998; Kazmerski, Friedman, & Ritter, 1997; Czigler, Csibra, & Csontos, 1992; Woods, 1992). We believe that this reduced activity may be attributable, at least in part, to the differential amount of cortical stimulation obtained when the physical (but not the perceived) intensity of the stimulus was equalized in young and old subjects. Note, however, that the purpose of this experiment was to study N1 and MMN variations as a function of stimulus repetition and variable intertrain delays. For this purpose, it is not as important to demonstrate that N1 and MMN are similar in the two groups as it is to compare conditions in which the amplitude of these components begins at similar levels and is then modified differentially by the suppression and recovery mechanisms. Thus, it is very useful to obtain conditions in which the cortical response to the first stimulus after the longest delay condition is similar in the two groups.

Several previous studies have reported smaller MMN amplitude in older adults and used this finding to propose that sensory memory declines with age (Alain et al., 2004; Gaeta et al., 1998; Kazmerski et al., 1997; Czigler et al., 1992; Woods, 1992). These studies typically

are not aimed at distinguishing between memory decay and filtering (or suppression) mechanisms in sensory memory, and therefore their conclusions are not contradictory to ours. However, the lack of an age-related reduction of the MMN in the current study does deserve further investigation. Several explanations of this finding are possible including (a) the very strict subject screening criteria, which may have resulted in a particularly healthy old adult sample; (b) the fact that the volume of the tones was adjusted to match the subjects' auditory thresholds, thus reducing confounds due to perceived stimulus intensity; and (c) the fact that the stimuli used (Tervaniemi et al., 1999), combined with duration-based deviance, produce particularly robust MMNs, thus avoiding the issue of the number of subjects *not* displaying an MMN who may be included in the grand average.

Pekkonen et al. (1996) used both duration and frequency manipulations to test the effects of age and SOA (0.5, 1.5, and 4.5 sec) on the amplitude of MMN, in a study in which standard (but not deviant) tone volume was adjusted to match the subjects' auditory thresholds. The three SOAs were only compared under frequency-based deviance conditions, and indicated that at the shorter SOAs (0.5 and 1.5 sec), the MMN did not differ between younger and older adults. Thus, in this respect, this finding is consistent with ours. However, Pekkonen et al. did report a reduced frequency MMN/N2b in the old group at the longer (4.5 sec) SOA, which is close to the 5-sec interval used in the current study. The N2b is not clearly visible in our averages (possibly because of the very short [400 msec] SOA between the stimuli within each train). Thus, it is conceivable that a differential overlap with the N2b may have caused the discrepancy. Future studies using EROS from extended montages may help disentangle results in which differential ERP component overlap may be a factor.

Notwithstanding these issues, taken together, the results of the current study support the claim that reduced filtering, rather than memory decay per se, is the ultimate cause of the N1 persistence in old age. The lack of N1 suppression observed in older adults is in line with the view that older subjects may be more ''distractible'' than younger adults, as is often reported in more complex cognitive paradigms (Hasher & Zacks, 1988; see also Gazzaley et al., 2005). The larger N1 amplitude over stimuli in the elderly may reflect the fact that attention is ''captured'' by the repeated irrelevant stimuli, away from the primary (reading) task. If this were the case, failed N1 suppression should be inversely related to performance in the primary task. In the current study, it was not possible to evaluate this hypothesis, as participants were reading material of their own choice. Future research, manipulating primary task difficulty and measuring the relative performance in conjunction with the ERP activity to the to-be-ignored tones may provide evidence relevant to this issue (see Kazmerski, Lee, Gratton, & Fabiani, 2005).

The lack of N1 suppression reported here may be accounted for by two possible mechanisms: (a) a generalized and diffused age-related impairment of inhibitory processes, which may be implemented by computational changes occurring in all areas of the brain; (b) a specific deficit in a brain process (or region) whose purpose is to control attention and inhibit inappropriate responses; or both. The latter mechanism has been postulated by several researchers, including Perlstein, Dixit, Carter, Noll, and Cohen (2003), Sylvester et al. (2003), and Braver and Barch (2002). Areas that are considered relevant for the control of attention and inhibitory processes include prefrontal regions, as well as parietal areas and the anterior cingulate cortex. It is important to note that the inhibitory control role of the prefrontal cortex is consistent with the results reviewed by Knight and Grabowecky (1995), who reported lack of attention modulation of early auditory evoked responses in frontal-lesioned patients. It is also consistent with data from schizophrenic patients, who are expected to exhibit symptoms of hypofrontality (e.g., Light & Braff, 1999).

The current study does not provide direct support for the existence of either or both mechanisms, although several investigators (e.g., Fabiani & Wee, 2001; Chao & Knight, 1997; West, 1996) have proposed that a decline in frontal lobe function may account for many of the cognitive problems encountered in aging. Measures of functional and effective connectivity between brain areas may help test the relationship between regions that have been implicated in inhibitory function and attention control. We are currently exploring the use of EROS as a measure for studying functional connectivity among brain regions, exploiting the combination of spatial and temporal resolution that this technique affords (Rykhlevskaia et al., in press).

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Note

1. Some studies have found either no changes or sometimes a reduction of N1 as a function of age. Typically these studies have used either an active oddball task or some other task in which all stimuli were relevant to performance and/or had to be attended (e.g., Bennett, Golob, & Starr, 2004; Ostroff, McDonald, Schneider, & Alain, 2003; Anderer, Pascual-Marqui,

Semlitsch, & Saletu, 1998; Picton, Stuss, Champagne, & Nelson, 1984). Note that according to the logic developed in the current study, no filtering is expected to occur in these conditions, and therefore age-related increases in N1 should not be expected. In fact, if older adults are more distractible than younger adults, N1 attenuation to target stimuli in these conditions may indicate that attention has been shifted to other less relevant stimuli in the environment.

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