Erratum

Erratum to “Age-related change in neural processing of time-dependent stimulus features” [Cognit. Brain Res. 25 (2005) 913–925]

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Due to a typesetting error at a late stage of production, all in-text references after Reference 43 should be decreased by one number to correspond with the references listed in the References section. For example, Ref. 45 in the text corresponds to Ref. 44 in the References section.

This erratum applies to the print and online PDF versions only. All reference citations in the full-text version of this article on ScienceDirect are correct.

The publisher apologizes for the error.
Aging is associated with changes in automatic processing of task-irrelevant stimuli, and this may lead to functional disturbances including repeated orienting to nonnovel events and distraction from task. The effect of age on automatic processing of time-dependent stimulus features was investigated by measurement of the auditory mismatch negativity (MMN) in younger (18–23) and older (55–85) adults. Amplitude of MMN recorded during a paradigm involving low-probability deviation in interstimulus interval (from 500 ms to 250 ms) was found to be reduced in the older group at fronto-central sites. This effect was paralleled by, and correlated to, decreased sensory gating efficiency for component N1 recorded during a separate paradigm involving alternate presentation of auditory stimuli at long (9 s) and short (0.5 s) interstimulus intervals. Further, MMN amplitude was correlated to behavioral performance on a small subset of neuropsychological tests, including the Rey Auditory Verbal Learning Test, within a group of healthy older adults. The results support the hypothesis that aging is associated with declines in automatic processing of time-dependent stimulus features, and this is related to cognitive function. These conclusions are considered in the context of age-related declines in prefrontal cortex function and associated increases in susceptibility to task-irrelevant stimuli.

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### 1. Introduction

Aging is associated with changes in automatic processing of task-irrelevant stimuli [5,43], and this may lead to functional disturbances including repeated orienting to nonnovel events [45,85] and distraction from task [22,48]. Whereas studies employing behavioral measures have largely investigated age-related changes in top-down regulation of attention [58,107] (reviewed in [116]), event-related potential (ERP) methodology, because of fast temporal resolution and independence from overt behavioral responses, has allowed for assessment of bottom-up, stimulus-driven processing. For example, age-related reductions in amplitude of the mismatch negativity (MMN: [48,104,134]) and novelty-P300 (i.e., P3a: [46,69]) waveforms provide evidence for changes in automatic identification and exogenous attention switching to novel stimuli (reviewed by [72]). It has recently been argued that the full extent of changes in automatic stimulus-driven processing might be difficult to document with behavioral methods, as top-down systems may provide some amount of compensation in older adults [5,31,43] (but see [74]).

Automatic processing of the temporal (i.e., timing) properties of stimuli may be particularly compromised by age. For example, amplitude of the auditory MMN, elicited...
in the absence of selective attention to the stimulus, has exhibited the most consistent aging effects when variation of stimuli involved temporal parameters [104] (stimulus duration: [61,65,134], silent gap duration [5,18]) as opposed to parameters such as pitch or intensity, where a number of negative results have been reported [8,47,54]. The present study involved an investigation of age-related change in automatic processing of a different temporal parameter: the time between auditory stimuli. Further, we tested whether this function is correlated to decreased efficiency in the suppression of neural processing of low-salience stimuli (i.e., “sensory gating”), and examined possible cognitive correlates of observed changes.

The specific MMN paradigm employed in this study [66] involves variation in the time between serially-presented auditory stimuli, or the interstimulus interval (ISI) [41,97]. Like similar paradigms involving change in parameters such as stimulus loudness or duration, the MMN waveform is elicited by sudden “deviation” in a stimulus parameter, and is presumed to reflect a neural signal regarding the potential importance of the novel stimulus (reviewed by [88,106]). This idea is supported by demonstrations that larger (i.e., more salient) deviations, including deviations of ISI [4,66,76,92], lead to larger MMN amplitude [64,91,128,130] and can also cause distraction as assessed both behaviorally and by the presence of a subsequent P3a waveform [115]. Since the auditory stimulus (50 ms, 1000 Hz tone) is physically identical for both “standards” (repeatedly presented stimulus) and “deviants” (occasional novel stimulus) in the present paradigm, the MMN waveform in this case can be assumed to result predominantly from automatic neural processing of the temporal interval between stimuli, as opposed to automatic processing of the stimulus itself [92]. Nevertheless, an observed age-related reduction in MMN amplitude elicited in this paradigm could arise from disrupted suppression of responding to the standard interval, and/or disrupted detection of the deviant interval [90]. Although present study design does not allow an explicit test between these two alternatives, it does provide for a preliminary investigation into this possibility by comparing, through correlational analysis, MMN waveform-generation to ERP-measures of sensory gating.

Sensory gating studies typically involve documenting reduced neural responding as a function of reduced stimulus-driven salience (i.e., “gating out” stimuli of low importance). Amplitude of specific ERP components elicited by low salience stimuli – presented at short-ISIs such as 0.5 s – is typically compared to amplitude in response to higher salience stimuli—physically identical but presented at longer ISIs such as 9 s [1]. This manipulation is based on the premise that, in addition to stimulus properties including semantic content (e.g., your name) and stimulus intensity, stimulus salience is proportional to “novelty” [16,63,88,99,124,125]. In this context, novelty is inversely proportional to the total number of exposures to a given stimulus, and directly proportional to the time since last exposure (i.e., the ISI). For the present study, sensory gating was assessed by measuring amplitude of auditory N1 as a function of ISI manipulation. Sensory gating of component N1 in this paradigm has recently been shown to correlate with behavioral observations concerning the tendency to be distracted by task-irrelevant stimuli [67]. Also, reductions in N1 amplitude with decreased stimulus salience appear to involve active suppression as opposed to simple habituation [119]. Thus, measures of N1 sensory gating are taken here to reflect reduced neural processing in response to stimuli of low stimulus-driven salience. For the present study, after demonstrating an age-related change in this neural function, we tested the hypothesis that sensory gating efficiency is correlated to MMN amplitude in older adults. We expected that stronger suppression of response to low salience stimuli in the sensory gating paradigm would be associated with more robust MMN waveform-generation.

Possible cognitive correlates of age-related changes in MMN amplitude elicited by time-dependent variation of the stimulus train were also investigated here. Specific neuropsychological tests were selected based on previously-documented sensitivity to age (e.g., Rey Auditory Verbal Learning Task, Reaction-Time Speed of Processing Task) and on posited relationships to prefrontal cortex (e.g., Stroop Color–Word task, Tower of London Task, Wisconsin Card-Sorting Task) which is known to be involved in generation of the MMN waveform [3,7,87,100,113].

2. Material and methods

Procedures were approved by the University of Colorado at Colorado Springs Institute Review Board. Subjects gave written informed consent before participating, and received monetary compensation or academic extra credit upon completion of the study.

2.1. Participants and general procedures

A total of 60 healthy adults participated: 20 younger adults (13 female) aged 18 to 23 (mean = 19.9), and 40 older adults (22 female) aged 55 to 85 (mean = 68.4). Exclusion criteria for all subjects included current diagnosis of psychiatric or neurological illness, current psychoactive drug use (prescriptive or illicit), and past traumatic brain injury (including loss of consciousness lasting at least 5 min after head injury). Older adults were also administered the Mini Mental State Exam [40], and all scored 27 or higher (mean = 29.4) out of 30. Hearing was tested at 1000 Hz (binaural, method of limits), and all subjects included exhibited less than 10 dB hearing loss. Auditory stimuli were individually adjusted for hearing loss.

Electrophysiological signals were recorded during two separate, randomly-counterbalanced paradigms. Both paradigms were passive, as participants did not respond to stimuli and watched silent, closed-captioned movies (all
movies satisfied a subjective criterion of being appropriate for a general audience). For the temporal deviation paradigm, the MMN waveform was measured in response to deviation in the interstimulus interval (ISI) of an ongoing stimulus train. In particular, interruption of a “standard” ISI by a “deviant” ISI was found to elicit this waveform, as expected from previous studies \[25,66,92\]. In the sensory gating paradigm, suppression of component N1 amplitude was measured as a function of short- compared to long-ISI: previous studies have shown that N1 amplitude in response to an auditory stimulus is proportional to the preceding ISI \[1,29\]. Both paradigms are illustrated schematically in Fig. 1 and described in more detail below.

2.2. Electrophysiology

Electrophysiological activity was recorded with a NuAmps multi-channel amplifier system and Scan 4.2 software (Neuroscan; Sterling, VA). Sounds, adjusted for individual hearing threshold, were presented binaurally through headphones while participants sat in a reclining chair watching a silent, closed-captioned movie. ERP paradigms were programmed and presented with Eprime (Psychology Software Tools, Inc.; Pittsburgh, PA).

Before recording began, disposable Ag/Ag–Cl electrodes (Vermed; Bellows Falls, VT) were affixed at Cz, Fz, right and left mastoids (RM and LM), directly superior and lateral to the left eye, and the tip of the nose. Ground was affixed to the forehead. During recording, signals were amplified 5000 times, filtered between 0.05 and 100 Hz, and sampled at 1000 Hz. All electrodes were referenced to nose, and impedances were maintained below 10 kΩ. Individuals who fell asleep during any portion of a recording were excluded from further analysis.

2.2.1. Mismatch negativity (MMN) paradigm and analysis

Tones (1000 Hz, 50 ms duration, 5 ms rise/fall, 45 dB hearing level) were presented continuously in a train at a standard offset-to-onset ISI of 500 ms. “Standard” tones were randomly replaced, on average every 20th trial, by a “deviant” tone at an ISI of 250 ms. Thus, this particular paradigm involves a “temporal deviation,” or deviation in a timing variable, with otherwise physically-identical stimuli \[41,66,92,97\]. A total of 2850 standard and 150 deviant tones were presented during a 30 min recording. Single-trial evoked responses, epoched from 100 ms before to 300 ms after tone onset, were baseline corrected and trials for which any channel exceeded ±75 μV were discarded. Individuals that had fewer than 75 deviant trials remaining after artifact rejection were excluded from further analysis. Average waveforms were computed separately for standard and deviant tones, and band-pass filtered from 1 to 30 Hz (48 and 96 dB/octave slope at these corner frequencies). This filter was applied both forward and reverse to eliminate phase distortion.

Because the ISI preceding standard and deviant stimuli were different (500 ms and 250 ms, respectively), an analytical approach was employed to address the possible differences in ongoing activity present at stimulus-onset. Specifically, before filtering, a time-shifted average of the standard evoked waveform was subtracted from the deviant waveform to eliminate the overlap of these responses that results from a sudden decrease of ISI from 500 ms to 250 ms: a standard response waveform shifted forward in time by 250 ms was subtracted, point-by-point, from the deviant response (eliminating this subtraction step from the analysis was found to produce substantively similar results: not shown).

Difference waveforms were computed by subtracting standard from deviant waveforms, point-by-point. For each participant, MMN was identified on electrodes Fz and Cz as the most negative trough between 100 and 200 ms poststimulus, and on electrodes RM and LM as the most positive peak between 100 and 200 ms poststimulus (MMN inverts polarity at the mastoids in a temporal deviation paradigm: \[92\]). Peak waveform amplitudes were measured relative to a 100 ms prestimulus baseline. Although not shown here, MMN amplitude was also measured as the mean voltage of the difference wave between 100 and 200 ms poststimulus. The correlation between MMN amplitudes determined in the two different manners was 0.96 \(N = 36, P < 0.001\), and the basic pattern of results presented below was essentially the same between methods.

![Fig. 1. Schematic diagrams of electrophysiological paradigms. Top: In the MMN paradigm, standard stimuli preceded by a 500 ms “standard” ISI were randomly interrupted by stimuli preceded by a 250 ms “deviant” ISI. Auditory stimuli consisted of 50 ms tones. Bottom: In the sensory gating paradigm, auditory click stimuli were presented alternately at long (9 s) and short (0.5 s) ISIs. Within each paradigm, physical stimulus properties were held constant; only ISI was manipulated.](image-url)
2.2. Sensory gating paradigm and analysis

Acoustic clicks were alternately presented at 9 s and 0.5 s ISIs throughout the recording session at 60 dB hearing level (HL). The evoked response at electrodes FZ and Cz to the clicks, termed “long-ISI” and “short-ISI” responses, respectively, were analyzed separately as follows: single trial ERPs, epoched from 100 ms before to 300 ms after each click, were baseline corrected and subject to artifact rejection (±75 µV). Individuals that had fewer than 75 long-ISI or 75 short-ISI trials remaining after artifact rejection were excluded from further analysis. Average long- and short-ISI waveforms were band-pass filtered, forward and reverse, between 1 and 30 Hz (48 and 96 dB/octave slope, respectively).

N1 was defined for the long-ISI click as the largest negative trough between 75 and 125 ms. Short-ISI N1 was similarly identified, with the added restriction that the trough must be within ±20 ms of the long-ISI latency. N1 amplitude was measured relative to a 100 ms prestimulus baseline. Sensory gating was then quantified for component N1 by computing long-ISI suppression ratio:

\[
\frac{\text{long-ISI amplitude} - \text{short-ISI amplitude}}{\text{long-ISI amplitude}}
\]

A suppression ratio close to 1 indicates robust suppression (very small short-ISI response compared with long-ISI response) and a ratio of 0 indicates essentially no suppression (short- and long-ISI responses comparable in magnitude). A negative value indicates “augmentation,” where the evoked response to the short-ISI stimulus is actually larger than that to the long-ISI stimulus.

2.3. Neuropsychological tests

Several domains of cognitive function were assessed with select neuropsychological tests. 25 of the older participants completed all tests described below. All tests, except Rey Auditory Verbal Learning and Stroop Color–Word tests, were conducted through a computerized battery (Colorado Assessment Test v. 1.0, Colorado Springs, CO) [28,30,36] administered by a trained research assistant.

2.3.1. Tests of memory function

The Rey Auditory Verbal Learning Test (RAVLT) was administered by a trained research assistant. The RAVLT was used to assess declarative memory at different delays [111,117,126] and performance on this task declines with advancing age [30]. During 5 “acquisition” or “immediate recall” trials, participants were read a list of 15 words and asked to recall as many as possible. Dependent measures were number of words recalled on the first trial, and the total number of words recalled during trials 1–5 (“total acquisition”). After a 20 min delay, participants were asked to recall as many of the 15 words as possible. Dependent variables assessed were number of words recalled after the delay period and the “forgetting” score, which is the difference between the recall trial and trial 5 of the acquisition phase. A subset of these participants was later administered a separate word list, and the delay trial occurred either 1 h or 1 week after acquisition. Nonverbal memory was assessed with a visuospatial memory task similar to the card game of Concentration or Memory [15,27]. The participant matched 12 card pairs by turning over two cards per match attempt. The dependent variable was the number of repeat errors.

2.3.2. Frontal lobe tasks

The Tower of London (TOL) task was developed by Shallice [122] to study problem solving in patients with frontal lobe damage, and has since been shown by regional cerebral blood-flow studies to engage the frontal cortex [86,95]. Participants moved 3 to 5 beads to and from 3 to 5 pegs, according to specific rules, with the goal of achieving a particular configuration shown on the right half of the computer screen. The dependent measures were the number of unnecessary moves and total time elapsed for 21 increasingly-difficult problems. The Wisconsin Card Sorting Test (WCST: [59]) involves classifying cards based on a sorting rule (shape, color or number of symbols) that is not explicitly stated to the participant. The rule changes, again without explicit notification to the participant, after 10 correct matches. After a rule change, repeated perseveration on incorrect response strategies (“perseveration errors”) during the WCST is associated with an inability to inhibit prepotent responses [10,35], a function commonly attributed to the frontal lobe [34,112,121]. An abbreviated Golden Color–Word Test was administered by a trained research assistant to measure susceptibility to Stroop interference [52]. The primary measure taken from this test is the increase in reaction time required by an individual to name an ink color (e.g., blue) that is used to print an incongruent word (e.g., “red”) compared to a condition in which ink colors are named in isolation from words (e.g., blue symbols). Clinical patients who, after sustaining frontal lobe damage, perform poorly on the Stroop test tend to have difficulty staying focused on task [77,82]. West and Alain [132] have attributed an increased Stroop effect among older adults to a decline in inhibitory control.

2.3.3. Speed of processing task

Speed of processing, known to decrease with advancing age [120], was assessed with three separate reaction-time (RT) tasks: simple, choice, and conditional. The three tasks require the same manual responses, but different amounts of cognitive processing [127]. The simple task involves pressing a key when a symbol appears on the screen. The choice task involves pressing one of two keys, depending on the symbol that appears (i.e., press left arrow if left arrow appears, press right arrow if right arrow appears). The conditional RT task requires participants to consider a
2.4. Statistical analysis

Repeated measures ANOVA were conducted to assess age-related changes in electrophysiological variables between 20 younger adults and 20 randomly-selected older adults. Planned one-way ANOVA comparisons were also conducted between these groups for selected variables. Hearing loss, though corrected for by adjusting stimulus intensities for each individual, was originally included as a covariate, but found to be nonsignificant and subsequently dropped from all analyses. Within the full older adult group (N = 40), partial Pearson’s correlation coefficients, controlled for age, were computed to examine relationships between selected ERP and behavioral measures.

All significance tests were two-tailed at the 0.05 level. To protect against Type I errors, the degrees of freedom for all repeated measures ANOVAs were adjusted by the method of Greenhouse and Geisser [53]. All waveform amplitudes, whether from positive- or negative-going waves, are reported here as absolute values.

3. Results

A significant age-related reduction in MMN amplitude elicited by temporal deviation of the stimulus train was detected. Specifically, after excluding for recording problems (N = 1) and artifact rejection (N = 3), MMN variables (summarized in Table 1) were compared between 18 younger and 18 older adults. Repeated-measures ANOVA with electrode as within-subjects and age group as between-subjects factors revealed a main effect of electrode, F = 10.37, df = 1.19, 40.60, P < 0.01, a main effect of group, F = 11.42, df = 1.34, P < 0.01, and an electrode-by-group interaction, F = 3.94, df = 1.19, 40.60, P < 0.05. Planned comparisons showed that MMN amplitude was significantly larger in younger than older adults at central electrodes Fz, F = 41.67, df = 35, P < 0.01, and Cz, F = 60.22, df = 35, P < 0.01 but not at mastoid electrodes (RM, LM). These general findings are also reflected in the grand-averaged difference waveforms (bottom panel of Fig. 2). Although waveform latencies were generally longer for the older adults, no significant difference was detected at any electrode.

Because the MMN waveform is computed as a difference between two waves, a separate analysis was conducted to determine whether the observed age-related difference at central sites related primarily to amplitude of standard (500 ms ISI) or deviant (250 ms ISI) evoked responses. These separable components can be seen for younger and older adults in the top two panels of Fig. 2. A repeated-measures ANOVA was conducted on the voltage of the standard and deviant evoked responses at the latency of the corresponding MMN peak for each individual, with stimulus-type (standard or deviant) and electrode (Fz or Cz) as within-subjects and age group as between-subjects factors. A significant main effect was found for stimulus-type, F = 157.76, df = 1.34, P < 0.001, with a type-by-group interaction, F = 11.15, df = 1.34, P < 0.01. The latter effect reflects a significantly more positive voltage in response to the standard tone for the younger group (marginal M = 2.13 μV above zero) compared to the older group (M = 1.03 μV), in contrast to a more negative voltage in response to the deviant tone for the younger group (M = 3.81 μV below zero) compared to the older group (M = 2.42 μV). In subsequent planned comparisons, the mean waveform voltage at the MMN peak latency was significantly different between age groups for both standard and deviant responses and at both Fz and Cz (α = 0.05). Thus, the larger negative-going MMN difference wave in the younger group seems to depend on both a more positive standard response and a more negative deviant response.

Examination of the standard response waveforms (Fig. 2) also suggests that N1, a negative deflection preceding the MMN latency window, was different between the two age groups. To test this, N1 amplitude was measured as the most negative trough between 75 and 125 ms poststimulus, and a repeated-measures ANOVA with electrode (Fz or Cz) as within-subjects and age group as between-subjects factors was conducted on this variable. Main effects were found for electrode, F = 23.98, df = 1.34, P < 0.001, and age group, F = 6.64, df = 1.34, P < 0.05. The latter effect arose because the mean N1 amplitude evoked by the standard tone was actually larger (i.e., more negative) in the older group (marginal M = 1.16 μV below zero) compared to the younger group (M = 0.12 μV). This general effect can be seen by examining the grand-averaged waveforms in Fig. 2, and suggests that the younger adults exhibit stronger N1

3.1. MMN phase locked to stimulus onset

Figure 2 illustrates the MMN waveform for both age groups at the electrodes Fz and Cz. As can be seen, the MMN is a negative deflection with peak latency at approximately 200 ms, though amplitude may be smaller at the mastoid electrodes (RM, LM). Within this time window, a main effect was found for electrode, F = 5.87, df = 2.98, P < 0.01, and an electrode-by-group interaction, F = 3.19, df = 2.98, P < 0.05. The latter effect reflects a more positive MMN amplitude for younger adults at the midline sites Fz and Cz (marginal M = 3.81 μV below zero) compared to the older group (M = 1.03 μV), in contrast to a more negative MMN amplitude in the mastoid (RM, LM) sites for both age groups.
suppression, in response to the repeating standard stimuli, when compared to the older adults.

### 3.1. Age-related differences in suppression of component N1

In order to test more directly for an age-related difference in the suppression of N1 amplitude at short interstimulus intervals (ISIs), a “sensory gating” paradigm was employed with the same participants (2 further participants were excluded due to recording problems during this paradigm). Stimuli were presented alternately at long (9 s) and short (0.5 s) ISIs. Grand-averaged waveforms for this paradigm are shown in Fig. 3, and summary statistics presented in Table 2. A repeated-measures ANOVA for N1 amplitude on electrode Cz, with ISI as within-subjects and age group as between-subjects factors, revealed a main effect for ISI, $F = 24.30$, $df = 1,32$, $P < 0.001$, and an ISI-by-group interaction, $F = 7.16$, $df = 1,32$, $P < 0.05$.

To explore these effects in a manner more typical of sensory gating studies, the suppression ratios were computed for component N1. For the younger adults, N1 amplitude evoked by the short-ISI stimulus was generally smaller than the long-ISI stimulus, as evidenced by the mean suppression ratio of 0.63 (i.e., mean response amplitude to the short-ISI stimulus was reduced 63% from the long-ISI response). N1 suppression ratio for the older adults, $M = 0.34$, was significantly different, $F = 9.02$, $df = 33$, $P < 0.01$, indicating less robust suppression as a function of ISI manipulation. As seen in Table 2 and Fig. 3, and in contrast to the MMN paradigm, the younger adults actually exhibited larger N1 amplitude in response to the long-ISI stimulus compared to the older adults, $F = 7.22$, $df = 33$, $P < 0.05$. N1 amplitude evoked by the short-ISI stimulus did not differ between groups, $F = 2.09$, $df = 33$, $P = 0.16$. The overall pattern of results at electrode Fz was similar (e.g., see Fig. 3). No effects for age or ISI were found for N1 latency at either electrode.

### 3.2. Comparison of MMN generation and N1 suppression in older adults

To test whether MMN generation is correlated to N1 suppression in older adults, measures of N1 suppression in the sensory gating paradigm were compared to MMN amplitudes within a larger group ($N = 35$ after exclusions for recording problems and artifact rejection in both...
paradigms). MMN amplitude measured from the temporal deviation paradigm was significantly correlated (Pearson’s, controlled for age) to N1 suppression in the sensory gating paradigm at both Cz, \( r = 0.42, df = 34, P < 0.05 \), and Fz, \( r = 0.41, df = 34, P < 0.05 \). This correlation is illustrated for electrode Cz in Fig. 4, and is consistent with the idea that those individuals who exhibit stronger N1 suppression at shorter ISI in the sensory gating paradigm also exhibit larger MMN amplitude in response to temporal deviation in the MMN paradigm.

3.3. Comparison of MMN generation and neuropsychological function in older adults

In order to test whether integrity of the neural system underlying the scalp-recorded MMN waveform is related to cognitive function in older adults, MMN amplitude and latency recorded during the temporal-deviation paradigm were compared to summary measures of 6 neuropsychological tests (Pearson’s, controlled for age). No significant correlations were found with MMN latency, so those tests are not reported here. Although electrophysiological data were available for 38 older adults, only 25 of these individuals completed all neuropsychological tests. To reduce the likelihood of Type I errors, only one electrode (Fz) was considered. MMN amplitude was significantly correlated to the total acquisition score on the RAVLT, \( r = 0.45, df = 22, P < 0.05 \). This relationship, which reflects better immediate recall in those individuals that expressed larger MMN waveforms, is illustrated in the top panel of Fig. 5. MMN amplitude was also correlated to the total time required to perform the TOL task, \( r = -0.42, df = 22, P < 0.05 \), as well as other cognitive measures.

Table 2
Summary of N1 sensory gating measures at electrode Cz for younger \((N = 17)\) and older \((N = 17)\) adults

<table>
<thead>
<tr>
<th>Variable</th>
<th>Younger</th>
<th>Older</th>
<th>Younger</th>
<th>Older</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (SD)</td>
<td>M (SD)</td>
<td>M (SD)</td>
<td>M (SD)</td>
</tr>
<tr>
<td>Long-ISI</td>
<td>8.16 (5.30) μV</td>
<td>4.96* (2.12) μV</td>
<td>102.8 (13.1) ms</td>
<td>96.7 (12.2) ms</td>
</tr>
<tr>
<td>Short-ISI</td>
<td>2.46 (2.02) μV</td>
<td>3.27 (1.13) μV</td>
<td>101.6 (11.8) ms</td>
<td>95.7 (11.2) ms</td>
</tr>
<tr>
<td>Suppression ratio</td>
<td>0.63 (0.34)</td>
<td>0.33** (0.21)</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Bold entries represent a significant difference between groups, one-way ANOVA, *\( P < 0.05 \), **\( P < 0.01 \).
0.05. The direction of this correlation implies that individuals with relatively larger MMN amplitudes completed the TOL task more quickly.

MMN generation was also found to be related to performance on a conditional RT task. Specifically, MMN amplitude was significantly correlated to the total number of correct trials during the task, \( r = 0.57, df = 22, P < 0.01 \), even with an apparent performance "ceiling" (see bottom panel of Fig. 5). In other words, individuals that generated larger MMN waveforms in the temporal deviation paradigm also performed better on the conditional task. MMN amplitude was not, however, correlated to reaction times in simple, choice, or conditional reaction time tasks. Also, no correlation was found when comparisons were made to the differences in reaction times between the separate tasks.

No significant correlations were detected between MMN amplitude and behavioral performance on the WCST, Stroop, and Memory Card tasks, \( df = 22, \alpha = 0.05 \).

### 4. Discussion

The basic finding of this study is consistent with the view that neural processing of stimulus-driven salience, specifically salience as determined by temporal parameters, changes with aging. This was demonstrated as an age-related reduction in amplitude of the scalp-recorded MMN waveform elicited by deviation in the ISI of an ongoing acoustic stimulus train. The direction of change is interpreted to reflect less robust automatic identification of stimulus salience based on time-dependent stimulus features in the older adults. This argument, previously made based on results from MMN studies employing deviation of the temporal parameters of the auditory stimulus itself [5,18,61,65,104,134], is strengthened by the present study for which the stimuli employed were physically identical and only the time between stimuli was varied.

Interpretation of the present results depends upon the assumption that the MMN waveform was elicited automatically, in the absence of selective attention to the deviant stimuli (reviewed by [88,106]), in both age groups. Although the automatic nature of the neural process underlying the scalp-recorded MMN is especially supported by the demonstration that it can be elicited during sleep [14,79,94,96,102], it has been shown previously that MMN amplitude can be modulated by selective attention to the stimulus [33,129,133]. It is unlikely that a systematic difference in attention to the auditory stimuli existed between age groups, as both were instructed to watch the silent movie and ignore the tones. Selective attention directed towards the tones would have led to the elicitation of component N2b, a second negative component evoked by the deviant stimulus [98,114]. The peak latency of component N2b is later than that of component MMN for both younger and older adults [8]; however, no significant latency differences were found between groups in the present study. Finally, attention-related component N2b does not exhibit polarity reversal between central and
Age-related change in frontal lobe function (reviewed by [60,109]) provides a parsimonious explanation for the present pattern of electrophysiological results. Robust, statistically significant age-related differences in MMN amplitude were seen at fronto-central sites, but not at mastoid sites. The mastoid MMN waveform is believed to reflect primarily activity in the superior temporal lobe (i.e., auditory cortex), whereas the frontal lobe contributes to the MMN waveform at Fz and Cz [3,7,87,100,113]. In addition to the role of the frontal lobes in generation of both N1 and MMN, prefrontal cortex appears to be involved in “gating out” irrelevant stimuli and in coding temporal intervals (reviewed by [70]). Regarding the former, both older adults [21,22,135] and prefrontal patients [71] exhibit enhanced primary auditory cortical processing (i.e., larger Pa amplitudes) of task-irrelevant sounds. In the domain of time processing, both groups exhibit deficits in the perception of intervals on the order of hundreds to thousands of milliseconds (older adults: [38,84,108], prefrontal patients: [56]). Interestingly, another patient population with pronounced “hypofrontality” exhibits a similar constellation of deficits to healthy older adults, though of greater severity: schizophrenia patients exhibit reduced MMN amplitude in an ISI-deviation paradigm [25], N1 suppression deficits [1,20], and temporal processing impairments [24,26].

Frontal lobe changes in older adults could also be responsible for the observed positive correlation between MMN amplitude and total acquisition score on the RAVLT. The acquisition or “immediate recall” portion of this task involves short-term memory which depends upon the integrity of prefrontal cortex (for recent reviews see [23,103]). On the other hand, words immediately recalled after trial 1 might be considered to provide a purer estimate of short-term memory – no repetition and/or consolidation have occurred yet – but this variable was not significantly correlated to MMN amplitude, although the direction of relationship was as expected: \( r = 0.29, P = 0.13 \). Nevertheless, the acquisition phase of the RAVLT task has been shown to involve increased metabolism in prefrontal cortex [11].

Another possible explanation for the correlation between MMN amplitude and RAVLT acquisition, particularly in light of the overall paucity of relationships detected here, is the modality of presentation. Of the tests administered, only the RAVLT involved auditory presentation of stimuli. In this context, a somewhat trivial explanation for the observed correlation is that those older adults with poorer auditory acuity exhibited smaller MMN amplitudes due to reduced activation of the auditory system, and worse performance on the RAVLT due to difficulty hearing the verbally-presented words. However, this explanation is unlikely because all auditory stimuli in the MMN paradigm were adjusted for individual hearing loss. Also, the correlation between MMN amplitude and total acquisition was retested with both age and individual hearing loss controlled for, and a significant
correlation remained \( (r = 0.41, df = 22, P < 0.05) \). Another possible explanation involves age-related changes in temporal (i.e., time) processing. First, temporal perception is generally more closely related to auditory than to visual stimulation [37,55,110,123]; the opposite is true for spatial perception [17,68,131]. Second, age-related declines in temporal processing have been shown to be related to reduced auditory verbal comprehension [105]. Thus, it remains possible that the neural system studied here (i.e., the population of neurons underlying the scalp-recorded MMN elicited by deviation of time-dependent stimulus parameters) is involved in, or at least related to, temporal processing of auditory stimuli including some types of verbal material. In this very speculative scenario, older adults with relatively smaller MMN amplitudes would process time-dependent stimulus features with degraded fidelity, and as a consequence process auditory information less robustly.

MMN amplitude was not found to be significantly related to performance on several other tasks including Stroop, Memory Cards, and WCST which are commonly associated with frontal lobe function. On the other hand, MMN was significantly correlated to performance on TOL; this task requires a number of psychological processes attributed to prefrontal cortex including planning and working memory [86,122]. Also, correct performance on the conditioning RT task, which was positively correlated to MMN amplitude, involves responding to a stimulus (e.g., a right arrow) with an opposing response (e.g., a left arrow). This behavior could be considered to require inhibition of the default response (e.g., press right arrow in response to right arrow), another function typically attributed to the prefrontal cortex [13,50,73,118]. In past studies of age-related changes in automatic neural processing of task-irrelevant stimuli, significant correlations have been found between performance on the WCST and component Pa (primary auditory cortex response, approximately 30 ms poststimulus: [75,136]) within a group of older adults [22], and between Stroop performance and component P3a elicited by unexpected stimuli in an adult “lifespan” sample [39].

In conclusion, neural processing of temporal stimulus features changes with age. In particular, the robustness with which low-probability deviant ISIs are identified automatically, as assessed by MMN amplitude appears to decline. This is consistent with the hypothesis that aging is particularly associated with changes in the identification of (and subsequent exogenous attention switching to) stimuli based on their temporal features [18,104]. Further, in agreement with previous aging studies (see especially [22,48]), age-related impairments in the “gating in” [19] of high salience stimuli appear to be related to impairments in “gating out” of low salience stimuli, demonstrated here by a correlation between MMN amplitude in the ISI-deviation paradigm and N1 suppression in the sensory gating paradigm. The potential behavioral significance of age-related changes in the neural system that underlies the scalp-recorded MMN waveform is suggested by observed correlations between MMN amplitude and cognitive function. However, the basis for this correlation – whether related to select aspects of prefrontal cortex function, auditory temporal processing, or otherwise – remains to be determined. But the present results are at least consistent with broader theories linking age-related prefrontal functional declines with impaired filtering of task-irrelevant information [12,32,57,69].

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