Age Effects on Preattentive and Early Attentive Auditory Processing of Redundant Stimuli: Is Sensory Gating Affected by Physiological Aging?

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The frontal hypothesis of aging predicts an age-related decline in cognitive functions requiring inhibitory or attentional regulation. In Alzheimer’s disease, preattentive gating out of redundant information is impaired. Our study aimed to examine changes associated with physiological aging in both pre- and early attentive inhibition of recurrent acoustic information. Using a passive double-click paradigm, we recorded mid-latency (P30–P50) and late-latency (N100 and P200) evoked potentials in healthy young (26 ± 5 years) and healthy elderly subjects (72 ± 5 years). Physiological aging did not affect auditory gating in amplitude measures. Both age groups exhibited clear inhibition in preattentive P50 and attention-modulated (N100) components, whereas P30 was not attenuated. Irrespective of age, the magnitude of inhibition differed significantly, being most pronounced for N100 gating. Inhibition of redundant information seems to be preserved with physiological aging. Early attentive N100 gating showed the maximum effect. Further studies are warranted to evaluate sensory gating as a suitable biomarker of underlying neurodegenerative disease.

Key Words: Auditory sensory gating—Evoked potentials—Physiological aging—Inhibition.

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In auditory processing, physiological aging first affects the peripheral auditory system, which causes difficulties when sounds have to be detected, localized, or distinguished. Age-related changes in the cerebral cortex also contribute to auditory processing difficulties. On the other hand, not only cerebral plasticity (1) and compensatory mechanisms (2) but also modifications in attentional processing (3) have the potential to maintain auditory discrimination in later life.

Age-related changes in the auditory system affect inhibitory neurotransmission of subcortical and cortical neurons and may result in changes of response properties of neurons, temporal processing, and response reliability (4). Inhibition is an important modulatory mechanism for various brain processes which influence synaptic plasticity, network oscillations, and response control. Inhibitory modulation is crucial for sensory and supra-modal processing; abnormal inhibitory circuits have been described in schizophrenia, epilepsy, and Alzheimer’s disease (AD) (5).

In contrast to visual processing, the auditory system is especially sensitive to particular combinations of sounds. Not only special temporal organization of auditory perception but also its extensive corticothalamic control accounts for its context dependency and high plasticity (6). The cholinergic thalamo-cortico-thalamic feedback loop for instance modulates sensory information in various time frames and mechanisms (7,8) and thus elucidates the special suggestibility of auditory perception by wakefulness, arousal, and attention (6).

The frontal hypothesis of aging (9) postulates an age-related decline in cognitive functions requiring inhibitory or attentional regulation. In the light of this assumption (10), the question arises as to whether the effective processing of redundant acoustic stimuli, that is, identical information at a short interval, is preserved with normal aging. Recently, a deficit in the inhibition of redundant preattentive acoustic information was described and linked to cognitive performance associated with pathological aging, such as in AD (11,12). Auditory attentional mechanisms are active in subcortical as well as cortical areas and are stimulus dependent. They comprise an early, automated, or “bottom-up” system, including unspecific alertness and automated reaction to sensory input, as well as more complex top–down mechanisms that allow for modulation of acoustic features, stimulus recognition, and processing (3). This raises the question whether the early inhibition of redundant acoustical information is different during the time course of passive auditory processing and whether age effects arise in different time windows.
By studying acoustically evoked electrical potentials, various components reflecting different stages of auditory processing can be assessed. A summation of the electroencephalogram (EEG) potentials in response to auditory stimulation provides a time resolution in the range of milliseconds. Thus, rapid modulations of sensory processing can be studied, for example, inhibition as a basic modulation to prevent further processing of unimportant information—the so-called gating out.

Sensory gating (SG) has been conceptualized as the ability of the brain to suppress responses to the same sensory stimuli. This inhibition of responsiveness provides a mechanism that protects the brain from information overflow by filtering out redundant information (13). SG appears to be an early but presumable active control of repetitive information that has no further meaning. SG occurs in various sensory modalities and time frames and can be attenuated by state and trait conditions of schizophrenia spectrum (14,15) and disease states of schizophrenia (16), migraine (17), posttraumatic stress disorder (18), and neurodegeneration-like Parkinson’s disease (19) or AD (12,20).

In contrast to refractoriness and continuing adaptation processes that occur with trains of shortly spaced stimuli (21) and depend on the refractory period of nerve cells, SG seems to be a short-term habituation (22) including an active inhibitory process (23). There is evidence from source analysis (24,25), electrocorticography (26), and brain imaging techniques for the involvement of a prefrontal control in SG (27,28).

**Sensory Gating Paradigm**

Auditory SG is assessed by a passive test, using a conditioning (C) testing (T) paradigm. The electrical response to the second of two identical shortly separated clicks (500 ms apart) is compared with the first; the difference is then quantified by calculating the T/C ratio of evoked potentials.

Evidence accumulated that SG may be a multistage process (29) appearing between 40 and 250 ms after stimulus onset. Different electrophysiological components of the mid-latency (P30 and P50) and the long-latency range (N100–P200) seem to reflect distinct biological functions and might have specific neural generating networks. This is underlined by different functional correlations of the various components with cognitive tests (20,30).

A gating effect on very early auditory processing reflected by the P30 component was mostly denied (31), but P30 results are rarely reported. SG of the P50 component is largely a preattentive process and thus is preserved in sleep (31). In contrast, N100 and P200 gating can be affected by attention (32), are diminished in sleep (31), and might therefore be subject to particular age-dependant changes. Recently, interest in long-latency SG arose, as N100 and P200 gating were shown to be more heritable (14), and—in spite of an attentional modulation—retest reliability was better than for P50 gating (33). Moreover, results from phase locking studies indicate that P50 gating relates to gamma oscillations, whereas N100 gating comprises oscillations of slower frequencies (34). Again, this argues for a multistage inhibitory action that allows for excellent fine tuning and high temporal variability.

Similarities have been reported between age- and schizophrenia-associated cognitive deficits, particularly in SG and inhibition paradigms (35). Thus, it seems sensible to assess the effects of physiological aging within a paradigm originally conceptualized to track deficits in information processing in schizophrenia. SG deficits in the schizophrenia spectrum were found to be related to alpha-7 nicotinergic ACh receptor function (36). Attentional deficits in physiological aging are also thought to stem from reduced cholinergic modulation of the sensory input located in the prefrontal cortex, which regulates the salience of a stimulus in a bottom–up direction. Age-related alterations of cholinergic transmission not only involve muscarinergic receptors but also different nicotinergic receptor subtypes in the frontal and hippocampal areas (37), whereas choline acetyltransferase activity does not seem to be affected (38).

Attentional networks are affected by aging [ie, the frontal hypothesis of aging (9,10)]. This holds predominantly true for voluntary and divided attention. However, it remains unclear to date whether very early inhibitory processes, like preattentive and early attentive filtering out of dispensable acoustic information is also altered. If it is in fact preserved, it could possibly act as a biomarker and distinguish physiological aging from neurodegenerative processes such as AD.

**Effects of Aging in Acoustically Evoked Potentials**

Effects of aging in the acoustic domain have been thoroughly assessed by means of event-related potentials, predominantly in the long-latency range (39). These potentials reflect more complex networks of sustained attention, memory, and higher association areas. Age-related changes include prolongation of P300 latency and topography (40,41), mismatch negativity enhancement (42,43), and frontal shifts with more complex working memory and speech tasks (44). However, with respect to age-related differences in the ability to ignore dispensable information, SG of mid- and long-latency responses [AEP components are largely named according to Picton (45). P1, however, which he had classified as long-latency component later, was commonly named P50 and then classified as middle-latency peak. From an electrophysiological standpoint, it seems reasonable to classify P50 as a middle-latency component as it comprises mainly from 40 Hz activity and thus requires different filter settings than the long-latency components. Others, however, extended the term “mid-latency” evoked response up to the P200 (14,46).
SG has only rarely been assessed in healthy older adults. The vast majority of studies were conducted in young schizophrenic patients and controls (16,46,47) and were limited mainly to assessing preattentive input modulation between 40 and 80 ms (P50/Pb or P1). In our recent study on preattentive SG in AD (11), we compared our results with a younger control group and reported that P50 SG was not affected by age, but data on the long-latency SG in elderly persons is still lacking.

Pharmacologic reaction to the anticholinergic properties of scopolamine (a muscarinic antagonist) acts as a model of aging and dementia—cholinergic innervation has been shown to be down regulated in both. Under scopolamine challenge, P50 and N100 waves showed similar patterns (48), whereas mismatch negativity and P200 did not react to muscarinergic blockade (49). Elderly patients, classified to be “at risk for AD,” revealed increased sensitivity to incoming stimuli as reflected by enhanced P50 and N100 but not P200 amplitudes (50). With more complex auditory stimuli (speech) and tasks requiring memory involvement, moreover, latencies of N100 and P200 are both found prolonged with age (51,52). Based on its age-related amplitude increase, P200 was considered to be independent from N100 (53) and potentially to show a differential association with age.

P300 latency prolongation is particularly well known in conjunction with aging (54). In the light of correlation studies in schizophrenic individuals (54), which suggest that longer P300 latency might be linked to an N100 gating deficit, one could also expect N100 gating to be less efficient in older participants. Thus, SG of early attentive components such as the N100 gating ratio seems to have an impact on later auditory processing and thus might be affected differentially by aging.

The aforementioned findings suggest that age-related changes in auditory gating are not restricted to the P50. Furthermore, changes might differ between the components P50, N100, and P200. Hence, a more thorough comparison of the effects of age on SG in mid-latency (P30 and P50) and long-latency components (P50, N100, and P200) is warranted. As the development of auditory gating mechanisms has been shown to be completed in late adolescence (55), we decided to compare young adults and elderly individuals, which were neuropsychologically approved to be cognitively intact. By contrasting these two groups of extremely different ages, we aimed to assess age differences in healthy individuals in preattentive and early attentive auditory SG, an established paradigm to assess the passive processing of acoustic stimuli with respect to the inhibition of redundant information.

**Materials and Methods**

**Participants**

Auditory evoked responses (P30, P50, N100, and P200) were obtained from a younger and an older-aged group of healthy participants in order to maximize possible age-dependent differences. Participants were carefully screened for neurological or psychiatric diseases, a family history of schizophrenia, and drug use. Furthermore, all participants refrained from smoking for at least 12 hours prior to the test and from drinking beverages containing caffeine on the morning of the EEG.

Young subjects (YS; mean age 26 ± 5 years, n = 20) were recruited from the staff of the University Hospital Heidelberg. The group of elderly subjects (ES; mean age 72 ± 5 years, n = 23) were recruited from a local senior citizen’s program. After the study had been explained in detail, all participants signed informed consent forms. The experiments were performed in accordance with a protocol approved by the University of Heidelberg Ethical Board in accordance with the Declaration of Helsinki.

ES additionally underwent thorough neuropsychological testing in order to exclude mild cognitive deficits and beginning dementia. Testing was based on the CERAD battery complemented by the Trail Making Test, Clock Drawing Test, logical memory subtest (Wechsler memory scale revised), digit spans, Geriatric Depression Scale, and the Global Deterioration Scale. Participants were excluded from the study when performance in more than one subtest was more than 1 SD below the mean given by the norms of the applied tests (z-score < −1.0).

Three ES had to be excluded because of mild cognitive deficits detected by neuropsychological evaluation. One ES reported a first-degree relative with schizophrenia. In two ES and three YS, event-related potentials could not be evaluated because of technical artifacts. Ultimately, 17 young controls (YC) and 17 elderly controls (EC) were evaluated.

**Evoked Potentials Procedures**

Auditory evoked potentials were recorded in the morning using a 32-channel EEG system (Nihon Kohden) with Ag/AgCl electrodes positioned according to the extended 10/20 System (FP1/2, F3/4, F7/8, F9/10, Fz, FC5/6, C3/4, Cz, CP5/6, T7/8, TP9/10, P3/4, P7/8, Pz, O1/2, O9/10). Additionally, four VEOG/HEOG electrodes were used for ocular artifact control. Data were recorded in direct currency (DC) with a high cutoff filter of 200 Hz and a sampling rate of 1000 Hz. Impedances were kept below 5 kOhm.

Stimuli consisted of a minimum of 130 pairs of identical clicks (duration 0.04 ms, interstimulus interval 500 ms) presented at a level of 60 dB above individual hearing threshold. The intertrial interval varied between 9 and 10s and was Poisson distributed to avoid habituation. Stimuli were presented diotically using a PC equipped with an AWE64 Soundblaster (Creative Labs, Inc.) and presented via intraauricular earphones. Seated upright in a shielded quiet room, the participants received the instruction that random clicks will be presented with no need to pay attention or react to them. To prevent drowsiness, a silent movie was presented in the center of a computer screen at a 1-m...
distance. EEG scalp potential processing was analyzed offline (BrainVision; Brain Products, Inc.) on Fz, Cz, and Pz with average reference. After reducing artifacts semiautomatically, all segments were visually controlled and remaining artifacts, mostly eye movements, were manually removed by two independent experimenters blinded to group affiliation. The 1,000-ms segments containing the paired clicks were divided into two sweeps of 500 ms. For the components P30, N40, and P50, each sweep was filtered with a high cutoff at 150 Hz (12 db/oct) and then corrected to the 100-ms preclick baseline by an experienced technician blinded to the purpose of the study. Afterward, the averages were low cutoff filtered at 3 Hz (6db/oct.). Apart from adjusted filter characteristics (high cutoff: 20 Hz, 12 dB/oct; low cutoff: 1 Hz, 12 dB/oct), the same approach was applied to the components N100 and P200. Finally, a mean of 82 averaged sweeps (range 56–111) was used to calculate the individual averages for all components.

As all EP components could be detected best at the vertex, both amplitude and latency measurements were obtained at Cz, whereas all midline electrodes were used for component detection. The P50 evoked by the first conditioning click (S1–P50, C) was defined as the most prominent positive peak in the range of 40–70 ms poststimulus. The second P50 peak (S2–P50, test peak T) was identified similarly to the S1–P50. If more than one peak was elicited by S2 in the critical time window, the peak with the latency closest to the S1-P50 response (maximum 10 ms difference) was defined as the S2-P50, according to Clementz and colleagues (56). P50 amplitude was measured relative to the preceding negativity, N40, occurring between 30 and 50 ms poststimulus. The P30, N100, and P200 evoked by the first and second click were identified in a similar way: P30 was defined as the most prominent positive peak in the range of 20–40 ms poststimulus, N100 as the most negative deflection in the 80- to 140-ms poststimulus window, and P200 as the most positive peak between 150 and 250 ms. Amplitudes were reported as peak-to-peak measures, with the P30 and P50 related to the N40 component, the N100 related to the preceding P50, and the P200 related to the preceding N100 waveform. In each case, SG was expressed as the S2/S1 or T/C ratio.

As the P200 is a rather broad component and the peak amplitude alone might not provide a sufficient measure for this potential, we additionally calculated the corresponding area under the curve (AUC). As systematic latency differences for the P200 component were found for EC and YC, separate time windows were derived form the corresponding GAs for both age groups (EC: S1 = 120–245 ms, S2 = 115–249 ms; YC: S1 = 127–243 ms, S2 = 121–206 ms; see Figure 2). The resulting P200 gating ratio of areas (S2/S1) was calculated similar to the amplitude-gating ratio and compared between age groups.

Statistics

Confirmative analysis.—Statistical analyses were calculated using STATISTICA 8 (Statsoft, Tulsa, OK). As the dependent variables (gating ratios) were more or less skewed, we applied the linear transformation log10 (y + 1) in order to approximate a normal distribution. Only minor violations to the normal distribution for the transformed variables for the P30 component were observed according to the Kolmogorov–Smirnov test (based on Lilliefors statistics). Given the robustness of the analysis of variance procedures under the condition of homogenous variances (based on the Levene’s test), we were able to use parametric statistics. Consequently, an analysis of variance for repeated measures was conducted to examine the effects of the factors “age,” “sex,” and “component” and any possible interactions on gating ratios. The between-subjects factors “age” and “sex” compared YS with ES and males with females. The within-subjects factor “component” contrasted P30, P50, N100, and P200 gating ratios. Additionally, we employed adjusted post hoc t tests to elucidate differences between the levels of the factor “component.” As Mauchley’s test of sphericity did not indicate a violation of the assumption of sphericity, W(5) = 0.849, p = .43, within-subjects effects were interpreted without further correction. On the basis of the Holm procedure, all comparisons were adjusted according to an overall level of significance of α = .05. U tests were used to compare P200 gating ratio on the basis of AUC information between age groups and sexes. Additionally, effect sizes (d) for P30, P50, N100, and P200 gating and the factor “age” were calculated in order to evaluate the magnitude of suppression independent of the sample size.

Explorative Analysis

In a second step, a more explorative approach was chosen in order to identify any possible differences in S1 and S2 amplitudes and the latencies for the components P30, P50, N100, and P200 with reference to age and sex. Given a skewed distribution of the variables in spite of the log10(y + 1) transformation, we applied nonparametric U tests to untransformed variables (including P200 AUC measures). Considering the explorative approach, the level of significance was set to α = .05 for all comparisons. However, we point out that, due to the substantial number of variables and the resulting increase in the frequency of Type I errors, these comparisons must be interpreted with caution and need to be replicated using independent data.

Results

Demographic Data

Young subjects (YS) and elderly subjects (ES) did not differ with reference to gender distribution, \( \chi^2(1) = 0.120 \),
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Results for Confirmative Analysis

Gating effect differs between components.—For the components P50, N100, and P200, all participants showed gating out of redundant information with large effect sizes for N100 (d = 1.46) as well as for P50 (d = 0.96) and P200 gating (d = 1.12) (In the behavioral sciences, small, medium, and large effect sizes are indicated by d ≥ 0.2, d ≥ 0.5, and d ≥ 0.8 (Cohen, J. 1988). Statistical Power Analysis for the Behavioral Sciences (rev. ed.). New York: Academic Press) (d = 1.12). However, we did not find SG in the P30 component (d = 0.07). In line with this pattern, analysis of variance demonstrated a highly significant main effect for the factor “component,” $F(3,93) = 14.443, p < .05$, indicating that the magnitude of SG differs between the components P50, P50, N100, and P200 (see Figures 1 and 2).

Adjusted post hoc tests revealed P50, $t(32) = 4.653, p < .05$, and N100, $t(32) = 5.834, p < .05$, inhibitory reactions to be significantly stronger than P30 response. Moreover, N100 gating was significantly stronger than P200 gating, $t(32) = −3.782, p < .05$. However, the comparison of P50 and N100 gating ratios did not reach significance, $t(32) = 1.998, p = .05$. The same applied to the comparison of P200 and P50 gating, $t(32) = −1.751, p = .09$. P200 gating differed from P30, $t(32) = 2.754, p = .01$, but revealed non-significant after correction for multiple comparisons. Non-transformed gating ratios are depicted in Figure 1 to illustrate the differences in preattentive and attentive gating. P200 area measures revealed a remarkable gating effect and thus confirm the finding of P200 gating in peak ratio evaluation.

Age Differences in SG Are Sparse

Analysis of variance showed no significant effect for the factor “age” on SG, $F(1,31) = 0.609, p = .44$. The corresponding effect sizes for the components P30 (d = 0.02), P50 (d = 0.21), and N100 (d = 0.12) indicated minimal effects. However, P200 gating revealed a small age effect (d = 0.47). Consequently, there was no significant interaction between the factors “age” and “component,” indicating that age effects on SG did not differ significantly between the components P30, P50, N100, and P200, $F(3,93) = 0.149, p = .90$.

In contrast to peak amplitude gating, age-related differences in P200 area gating reached a medium effect size of $d = 0.59$. Though the corresponding $U$ test did not reach significance ($U = 90, Z = 1.877, p = .06$), a medium effect size in combination with our rather small sample size suggests substantial differences between EC and YC with area gating being larger in YC compared with EC.

Results of Explorative Analysis

The peak amplitudes, however, revealed significant age effects, with S1 amplitudes being larger for YS than for ES for N100 ($U = 70, Z = 2.566, p < .05$) and P200 ($U = 69, Z = 2.600, p < .05$). Age effects did not reveal for the P30 ($U = 925, Z = 1.567, p = .12$) and P50 components ($U = 90, Z = 1.877, p = .06$). SG was not affected by higher conditioning amplitudes.

Significant sex differences were only found for the S2 amplitude of the P50 component ($U = 69, Z = −2.392, p < .05$). At this point, a closer examination of the corresponding means shows that test amplitudes were larger in females than in males, but SG effects were comparable. Mean amplitudes for S1 and S2 and T/C gating ratios (S2/S1) for the P30, P50, N100, and P200 wave can be derived from Table 2 (age effects) and Table 3 (sex effects). S1-AUC information for the P2 wave did not differ significantly with regard to age (S1: $U = 141, Z = 0.121, p = .90$). S2-AUC measures seemed to be larger for EC compared with YC but were not significant (S2: $U = 92, Z = 1.808, p = .07$). No sex differences revealed in the P2 area measures (S1: $U = 94, Z = 1.506, p = .13$, S2: $U = 102, Z = 1.223, p = .22$).

Regarding latency, no significant differences were observed between age groups for the components P30, P50, and N100, in either trial, S1 and S2. However, for later information processing (P200), we found longer S2 latencies for ES ($M = 186.35, SD = 27.92$) than for YS ($M = 169.59, SD = 15.99$, $U = 83, Z = −2.118, p < .05$). P200–S1 latency was not significantly affected by age.
We did not find any latency differences with respect to participants’ sex in all measures.

**DISCUSSION**

The present study aimed to assess age-related differences in neural processing of redundant and thus dispensable acoustic stimuli in the preattentive and early attentive range of auditory information processing. Mid- and long-latency acoustic responses to a passive standard double-click paradigm evoked in elderly individuals were compared with those of young adults. Elderly individuals were carefully screened in order to exclude mild cognitive deficits and beginning dementia.

**Gating of Redundant Auditory Information Is Preserved With Aging**

We clearly demonstrated effective SG, irrespective of age, in the P50, N100, and in P200 waves, representing both pre-attentive and potentially attention-modulated components.
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Table 1. Demographic Information With Regard to Age Groups and Gender

|                      | Elderly Subjects | Young Subjects |
|----------------------|------------------|----------------|
|                      | Men   | Women | Men   | Women |
| N                    | 6     | 11    | 7     | 10    |
| Age (y), M ± SD      | 74 ± 3.69 | 71.36 ± 5.66 | 26.71 ± 5.41 | 13.7 ± 1.79 |
| Education (y), M ± SD| 14.67 ± 3.83 | 12.64 ± 2.46 | 14.3 ± 0.67 | 13.67 ± 1.21 |
| MMSE (points), M ± SD| 29.3 ± 0.82 | 29.55 ± 0.52 | 1; 0–1 | 1; 0–1 |
| Global Deterioration Scale, median; range | 1; 0–1 | 1; 0–1 |

Note: There were no significant differences between both ES/YS and m/f for age, education, MMSE, and the Global Deterioration Scale. MMSE = Mini-Mental State Examination.

However, based on area, instead of common peak amplitude measures, we found some but inconclusive evidence for reduced P200 gating in healthy EC. With respect to the frontal hypothesis of aging (9), these findings speak in favor of the notion that both early and—at least with regard to the N100 component—later SG are conserved with physiological aging. Based on peak amplitude measures both young adults and elderly individuals exhibited the most effective gating out of redundant information in the range of the N100 component (d = 1.46), with an average response suppression of 56%, whereas P200 (d = 1.12; 36%) and also P50 (d = 0.96; 45%) gating was less pronounced. In contrast, the earlier P30 component did not show any gating.

Effects of physiological aging on SG are not well established. Longitudinal studies in adults are lacking, and older participants have only rarely been tested. P50 gating was found to be preserved in a small life-span study (57). Furthermore, a pilot study (58) reported conserved SG in the P50 and N100 range, which is in line with our data. However, they describe a lack of P200 attenuation in 10 elderly subjects based on amplitude measures. In our study, AUC measures provide some evidence that P200 gating may be reduced in EC. As the P200 is a rather broad component area, measures may provide more valid information than peak amplitude measures.

Kisley and colleagues (59) observed diminished N100 gating in the elderly individuals. Referring to a correlation with decreased mismatch negativity and psychometric results, Kisley and colleagues interpreted their finding as a decline in automatic information processing with age. However, their slightly different stimulation and evaluation technique has caused debate as to whether these data can be compared with other studies (16). The reduction in S1-C amplitude seems to be a likely reason for their finding of an N100 gating deficit with age, as they based it on the difference between S1 and S2. In line with this assumption, it was recently shown that difference gating measures are strongly influenced by changes in S1 amplitudes (47). In our study, using the ratio of peak-to-peak amplitudes, both, S2 and S1, amplitudes were smaller in the older group, resulting in a preserved S2/S1 or T/C gating. SG ratio therefore is not influenced by age-dependent amplitude reduction. The shorter time window that Kisley and colleagues applied to assess N1 could be another explanation, as changes caused by short ISI tend to occur in the latest phase of the N1 range (60).

P200 gating, although clearly demonstrated in peak-to-peak-ratios of 0.64, was less pronounced than P50 and N100 gating in both age groups. In this context, nonsignificant differences between age groups were shown on the basis of P200 peak-to-peak amplitude measures. However,

Table 2. Gender Effects: Peak-to-Peak Amplitudes and T/C Ratios for P30, P50, N100, and P200 for Men and Women

| ERP Components | Sex | Amplitude S1 (M ± SD) | Amplitude S2 (M ± SD) | S2/S1 Ratio† (M ± SD) |
|----------------|-----|----------------------|----------------------|----------------------|
| P30            | Men | 0.96 ± 0.57          | 0.83 ± 0.40          | 0.78 ± 0.21          |
|                | Women | 1.20 ± 0.76 | 1.20 ± 0.79 | 0.85 ± 0.26 |
| P50            | Men | 1.17 ± 0.79          | 0.50 ± 0.42          | 0.48 ± 0.29          |
|                | Women | 1.50 ± 0.73 | 0.91 ± 0.51* | 0.62 ± 0.27 |
| N100           | Men | 3.10 ± 1.80          | 1.28 ± 0.84          | 0.44 ± 0.26          |
|                | Women | 3.10 ± 1.40 | 1.31 ± 0.83 | 0.44 ± 0.29 |
| P200           | Men | 4.31 ± 2.05          | 2.42 ± 1.02          | 0.61 ± 0.17          |
|                | Women | 4.75 ± 1.89 | 3.01 ± 1.25 | 0.67 ± 0.22 |

Notes: Asterisks indicate significant results according to the Mann–Whitney U test: *p < .05. ERP = event-related potentials.
†As sensory gating (SG) is defined as the S2/S1 or task/conditioning ratio, stronger SG is indicated by smaller values.
AUC measures provide some evidence that there might be an age effect in the time frame of the P200 wave, indicating that gating may be reduced in EC. The comparison of AUCs might capture a moderate age effect that is masked in the ratio gating. Support for an age effect in later auditory processing also comes from the P200 latency increase for EC.

With stimulus trains, short- and long-term effects on N100 habituation are frequently reported (53), but some authors have challenged the reports that a P200 habituation is present (61). Typically, habituation effects are strongest to the second tone of a stimulus train (62). However, in response to high stimulus rates (<30 ms), amplitudes decrease but stimuli are not gated out but rather evoke a pitch response in the primary auditory cortex. This is due to different time constants at high stimulus rates. Finally, a steady state response (40 Hz response) can be recorded. Phase locking studies moreover reveal a gamma-band response as the underlying mechanism of P50 wave, whereas N100 waves are related to theta-band response (34). Others, in contrast, have recently shown stable N100 and P200 gating effects in younger participants that were even more reliable on retest than the P50 gating (33). In addition, gating heritability seems to be more pronounced for the later AEPs (14) than for P50. Assessing two groups of extremely different age, our data confirm that SG in the preattentive time frame (P50) as well as the potentially attention-modulated N100 gating is clearly independent of age. Moreover, inhibition is found to be most pronounced for the N100 wave.

**P200 Latency Increases With Age**

In general, the latencies of P30, P50, and N100 components were not found to be age dependent. This is in line with results from earlier studies on P50 and N100 gating (57,58) and N100 stimulus trains (63). The P200 component, however, showed increased latency in the elderly participants, particularly for the second stimulus, indicating that older participants needed more time for gating out. In a similar vein, a word presentation task resulted in longer N100/P200 latencies with aging (52), reflecting a slowing down in perception while lexical access remained stable. Latency prolongation has been reported in several studies [see (53) for review], but others found no latency change with age. One reason for those differences might be that topographical changes occur with age that cause a frontal shift of P200 maximum (64).

**Age Effects Include Smaller Conditioning Amplitude**

Although all mean amplitudes were somewhat smaller in older participants, significant age effects were only found for conditioning (S1) amplitudes in the explorative analysis. Smaller S1 amplitudes were shown in all three components in the elderly participants, but this result was most marked for the N100. Amplitude differences did not affect SG in a significant way.

Age effects of the P50 component were recently interpreted as a compensatory mechanism by Golob and colleagues (65). The authors found a P50 amplitude increase with age; however, they used a different analysis protocol, filtering out activities above 20 Hz. As the P50 is thought to consist mainly of a 30–40-Hz activity (34,66), we applied a high cutoff filter of 150 Hz. Filtering affects P50 amplitude strongly (16); thus, the results across studies are unfeasible to compare since filter characteristics are not similar. On the other hand, in both later components, where filter settings are much more comparable to the present study, the authors reported nonsignificantly reduced amplitudes in older controls, which is in line with our data.

Amplitude reductions observed with stimulus trains, however, might be different from paired tone presentation, although latent inhibition rather than habituation seems to account for N1 amplitude reductions of the second stimulus (23), particularly in that study the following tones do not contribute further to response. Comparing short-term habituation and SG, Rosburg and colleagues (22) confirmed these results for P50 and N100.

Thus, in both mid-latency and long-latency components, we did not find amplitude increases but rather amplitude reductions in elderly individuals using a passive design. Therefore, our results argue against a compensatory activation in healthy elderly subjects, as observed in some functional magnetic resonance imaging studies, that is, for inhibition of saccades (67).

In another experiment requiring a decision on the second tone, an age-related increase was found in conditioning N100 amplitude (68), whereas distraction caused higher amplitudes in all ages. A task-related higher attention level, most likely reflecting a prefrontally modulated top-down process (69),

### Table 3. Age Effects on SG: Peak-to-Peak Amplitudes and T/C Ratios for P30, P50, N100, and P200 for Young Subjects (YS) and Elderly Subjects (ES)

| ERP Components | Age Group (YS, ES) | Amplitude S1 (M ± SD) | Amplitude S2 (M ± SD) | S2/S1 Ratio1 (M ± SD) |
|----------------|--------------------|----------------------|----------------------|----------------------|
| P30            | YS                 | 1.34 ± 0.82          | 1.13 ± 0.72          | 0.82 ± 0.23          |
|                | ES                 | 0.88 ± 0.46          | 0.99 ± 0.66          | 0.82 ± 0.26          |
| P50            | YS                 | 1.62 ± 0.81          | 0.88 ± 0.62          | 0.52 ± 0.29          |
|                | ES                 | 1.12 ± 0.62**        | 0.63 ± 0.35          | 0.58 ± 0.30          |
| N100           | YS                 | 3.78 ± 1.25          | 1.50 ± 0.77          | 0.41 ± 0.22          |
|                | ES                 | 2.41 ± 1.51**        | 1.09 ± 0.84          | 0.46 ± 0.33          |
| P200           | YS                 | 5.42 ± 1.95          | 3.07 ± 1.34          | 0.60 ± 0.19          |
|                | ES                 | 3.75 ± 1.56**        | 2.51 ± 0.97          | 0.69 ± 0.21          |

**Notes:** Asterisks indicate significant results according to the Mann–Whitney U test: **p = .01; *p < .05; **p < .01. ERP = event-related potentials; SG = sensory gating.

1As SG is defined as the S2/S1 or task/conditioning ratio, stronger SG is indicated by smaller values.
might be the cause for that difference. N100 amplitudes, evoked by an active task, were reported to be independent of subjects' age (63), but lower passive N100 amplitudes in older participants were found in a visual distraction task (63). This finding indicates a presumably arousal-driven control mechanism not affected by aging that might not be active with cross-modal distraction. As our paradigm was entirely passive, a general amplitude reduction might occur with aging. However, this amplitude reduction did not affect the gating process. Contrary to others (53) Vandoolaege and colleagues (70) report higher peak-to-peak amplitudes in younger patients, which is confirmed by our results.

The observed amplitude reduction with age concerning all three AEP components might indicate a more localized efficient auditory processing in the elderly participants, but the effect has to be replicated in a larger study. Age-dependent changes in frequency power and phase locking as have been described in the theta-band by Yordanova and colleagues (71) for EEG maturation and in the gamma-band very recently by Werkle-Bergner and colleagues (72), who assessed visual perception over the life span, may provide another explanation.

Recently, it was demonstrated that in P3a and P3b components known to show latency increases with aging jitter effects on amplitudes are negligible. Hence, mere latency jitter seems to be a less likely explanation (73). Age-related decline in hearing sensitivity has been proposed to account for the speech perception problems commonly observed in individuals of older age and thus might also account for smaller amplitudes.

By making the stimuli equally discriminable to all participants, we minimized the possibility that any observed age effects result from differences in peripheral processing. However, sensational perception of the clicks was not adjusted. In a recent meta-analysis, age effects on P50 gating were more dependent on filter settings than intensity levels (16).

Our study utilized a well-established paradigm for auditory information processing and applied high diligence in evaluating mid- and long-latency components as claimed recently (16). Limitations of our approach include a solely passive study design and the restriction to a gating paradigm that does not allow for the assessment of P300 or mismatch negativity as it did not include deviant stimuli. By using a simple passive task, however, very old, cognitively impaired, and demented patients can be assessed. Further studies that combine a gating paradigm with interspersed deviant stimuli are warranted. Also, as clicks do not represent realistic sounds, gating studies with various auditory stimuli, including environmental and communication sounds have to be performed. Moreover, we did not evaluate possible oscillatory mechanisms underlying averaged evoked components so far; therefore, additional research focusing on time-frequency measures (eg, single trial phase locking and evoked and induced power) is to be done on this data (47).

Finally, we limited our evaluation to midline electrodes and especially Cz so far, which is in accordance with most literature on SG. Thus, age-related changes in topography, as reported especially in P200 (53), could not be assessed in depth for the gating effect so far. However, an additional explorative topographic analysis (see Figure 3) suggested more widespread and frontal activation in EC compared with YC for both P200 peak and area measures. These effects are merely descriptive, so they have to be analyzed in more detail in a consecutive study.

Figure 3. Maps of P200 topography for both elderly controls (EC) and young controls (YC) Topographic maps for P200 peaks (left) and P200 area under the curve (AUC; right) displayed in Figure 2 are shown for S1 and S2 for both EC (top) and YC (bottom). Maps are based on a spherical spline interpolation.
CONCLUSION

In summary, physiological aging does not seem to affect the inhibition of redundant information. Different components of the preattentive (P50) and early attentive time range (N100) showed a similar suppression pattern, whereas N100 gating proved to be most efficient in both age groups. With respect to signal-to-noise-problems leading to less reliable gating measure in P50, the assessment of N100 gating seems to be more effective and might be a better choice for assessing SG in the elderly.

However, amplitudes of both the test and conditioning stimuli were found to decrease with aging, but this did not affect the inhibition of redundant information as measured with the gating ratio. Amplitude reduction with age might indicate a more localized, efficient primary auditory processing in the elderly, but the effect has to be replicated in a larger study.

SG in the mid- and long-latency range is preserved with aging. However, age effects were found in a reduced P200 area gating, prolonged P200 latency and a possible topographically more widespread activation in the elderly. Our results indicate that auditory SG has the potential to distinguish healthy elderly individuals from those with an underlying neurodegenerative disorder such as AD. An even more suitable biomarker of the disease may be the SG of later attentive components, especially N100 gating.

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Conflict of Interest

No conflicting financial interests.

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