Aging impacts basic auditory and timing processing

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Abstract

Deterioration in the peripheral and central auditory systems is common in older adults and often leads to hearing and speech comprehension difficulties. Even when hearing remains intact, electrophysiological data of older adults frequently exhibit altered neural responses across the auditory pathway, reflected in variability in the phase alignment of neural activity to speech sound onsets. However, it remains unclear whether speech processing challenges in older adults stem from more fundamental deficits in auditory and timing processing. Here, we investigated the efficiency of aging individuals in encoding temporal regularities in acoustic sequences and their ability to predict future events. We recorded EEG in older and young individuals listening to simple isochronous tone sequences. A comprehensive analysis pipeline evaluated the amplitude, latency, and variability of event-related responses (ERPs) to each tone onset along the auditory sequences. Spectral parametrization and Inter-Trial Phase Coherence (ITPC) analyses assessed how participants encoded the temporal regularity in the acoustic environment. Our findings indicate that aging individuals exhibit altered temporal processing and reduced capacity to generate and utilize temporal predictions to time-lock and adaptively suppress neural responses to predictable and repeated tones in auditory sequences. Given that deteriorations in these basic timing capacities may affect other higher-order cognitive processes (e.g., attention, perception, and action), our results underscore the need for future research examining the link between timing abilities and general cognition across the lifespan.

Highligths

- Aging individuals (HO) show increased cortical excitability as compared to younger adults (HY);
- HO's neural responses to fully predictable isochronous tones were larger and more variable than HY;
- HO showed reduced inter-trial phase coherence (ITPC) as compared to HY;
- The reduction in ITPC was associated with variability of event-related responses in HO;
- Altogether, results show altered auditory and timing processing in aging.

Keywords: aging, timing, audition, oscillations, predictions

1. Introduction

'Wait, what? Can you repeat it?'

A cascade of biochemical, neuro-functional and -anatomical changes takes place in aging. Deteriorations in the peripheral (e.g., loss of hair, ganglion and/or striatal cells) and central auditory systems [1,2] are particularly common and typically lead to a decline in auditory processing capacity [3–6]. However, structural brain changes often extend more broadly, and include widespread reductions in grey and white matter volume across the brain [7], as well as in cortico-subcortical connectivity [8]. Moreover, modifications within striatal-frontal networks [9], under-recruitment of the cerebellum during challenging cognitive tasks [10], and alterations in cerebellum-basal ganglia connectivity [11] have been linked to diminished cognitive control [12] and a variety of motor and cognitive deficits [11]. However, there is significant heterogeneity in the trajectories of neurocognitive and structural decline, stemming from substantial inter-individual variability in risk and modulating factors [13]. Furthermore, there exists variability in the capacity to compensate for cognitive decline by recruiting additional neural resources and/or adopting compensatory cognitive strategies [13]. For example, despite inevitable hearing loss [1,2], speech comprehension is largely preserved in older adults [14,15]. Performance, however, declines rapidly in challenging listening conditions, and is accompanied by decreased activation of the auditory cortex [15], inferior frontal regions, and reduced connectivity within the speech network [14]. Aging individuals tend to engage more working memory and attentional networks (e.g., frontal and prefrontal regions) in a compensatory manner [15]. Even in the absence of hearing loss, evidence confirms general difficulties in encoding simple and complex sounds, beginning from the brainstem [16]. Auditory nerve modeling has demonstrated that the deterioration of auditory nerve fibers and loss of inner hair cells impact the brain's capacity to precisely phase-lock (i.e., align) neural responses to sound onsets [17], resulting in reduced amplitude and phase-coherence of brainstem responses to simple and complex sounds [16]. This, in turn, can affect speech processing, as indicated by variable brainstem responses, decreased phase-locking to speech sounds [6,18], and a reduction in the connectivity between the brainstem and auditory cortex [4]. The weakened sensitivity to auditory input via the brainstem is typically compensated by increased excitability of the auditory cortex [19] and altered responses to sounds [3,6,20]. Consequently, , event-related potentials (ERPs) recorded by electroencephalography (EEG) exhibit enhanced amplitude responses in aging individuals, particularly in the N100 component [3,19–24]. There is consensus in

associating these larger ERP responses with the reduced ability to employ 'sensory gating' [22], an adaptive mechanism to suppress cortical responses to repetitions of predictable stimuli [20,23]. Furthermore, variability in the latency of event-related responses to sounds [21,25] and the reduction in steady-state responses to auditory metronomes [26,27] suggest a change in encoding the precise timing of sensory events, and internalizing the temporal regularity in auditory sequences. These observations suggest that aging may impact the capacities to detect regularities in the sensory environment, generate predictions about future events, and employ these predictions to inform sensory processing and perception.

This perspective prompts the question: Are difficulties in speech comprehension observed in older adults linked to speech-specific processing difficulties or to more fundamental temporal and predictive processing deficits? Therefore, we aimed to investigate whether older adults detect, encode, and employ temporal regularities in the sensory environment to generate predictions and optimize sensory processing similarly to younger adults. We addressed this question by recording EEG in older and younger adults while they listened to isochronous tone sequences. We hypothesized that aging would be associated with increased variability in event-related responses to tone onsets, as indexed by metrics of N100 variability, and reduced Inter-Trial Phase Coherence (ITPC) in delta-band oscillatory activity. Combined results from event-related, Fourier, and ITPC analyses confirmed altered temporal processing and reduced capacity in older adults to predictively time-lock and adaptively suppress neural responses to predictable and repeated tones in auditory sequences. Furthermore, aging was associated with increased excitability at the scalp level, as revealed by spectral parametrization analyses.

These limitations in fundamental timing and temporal predictability in older adults might critically affect not just basic auditory processing but also higher-order cognitive functions such as speech processing. Consequently, the current results motivate future research on the impact of altered timing capacities on cognition in aging and across the lifespan.

2. Materials & Methods

2.1. Participants

Forty-three native German speakers participated in the study and signed written informed consent in accordance with the guidelines of the ethics committee of the University of Leipzig and the declaration of Helsinki. Participants were grouped into 20 younger (HY; 9 females; 21–29 years of age, mean 26.2 years) and 23 older (HO; 9 females; 35-78 years of age, mean 56.3 years) adults. All participants were right-handed, had normal or corrected-to-normal vision, and no known hearing deficits. Participants received 8€/h for taking part in the study. Participants were not asked to indicate musical expertise and/or daily music listening choices.

2.2. Experimental design and procedure

Participants listened to 96 sequences comprising 13-to-16 tones (F0 = 400Hz, duration = 50ms, amplitude = 70dB SPL; standard STD), presented in one recording session of approximately 25min. Each tone sequence included one or two deviant tones (DEV), attenuated by 4dB relative to the STD tones. The inter-onset-interval between successive tones was 650ms, resulting in a stimulation frequency (*Sf*) of 1.54Hz, and a total sequence duration of 8.45-10.4s (13 to 16 tones * 650ms; Fig. 1A). Participants were seated in a dimly lit soundproof chamber facing a computer screen. Every trial started with a fixation cross (500ms), followed by the auditory sequence. The cross was continuously displayed on the screen to prevent excessive eye movements while listening to the auditory sequences. At the end of each sequence, a response screen appeared and prompted participants to immediately press a response button to indicate whether they had heard one or two softer tones. After the response, there was an inter-trial interval of 2000ms. A session was divided into two blocks of approximately 10 minutes each, with a short pause in between (about 25min total duration). Stimulation materials and experimental setups thus mirror those adopted and previously described [28–30].

2.3. EEG recording

The EEG was recorded from 59 Ag/AgCl scalp electrodes (Electrocap International), amplified using a PORTI-32/MREFA amplifier (DC set to 135Hz), and digitized at 500Hz. Electrode impedances were kept below 5kΩ. The left mastoid served as an online reference. Additional vertical and horizontal electro-oculograms (EOGs) were recorded.

2.4. Data Analysis

2.4.1. EEG Preprocessing

The preprocessing pipeline and the analysis approach adopted here mirror and expand those described previously [28–30]. EEG data were analyzed in MATLAB with a combination of custom scripts and functions and the FieldTrip toolbox [31]. Data were first re-referenced to the average of the two mastoid electrodes and band-pass filtered with a 4th order Butterworth filter in the frequency range of 0.1-50 Hz (*ft_preprocessing*). Eye-blinks and other artifacts were identified using independent component analysis. This semi-automated routine combined two steps: in the first iteration, we employed '*fastICA*' (as implemented in FieldTrip) to decompose the original EEG signal into independent components (N= number of EEG channels -1), then automatically identified components with a strong correlation (>.4; labeled as 'bad' components) with the EOG time-courses, removed them with '*ft_rejectcomponent*', and then reconstructed the EEG time-course. In a second step, we again used '*fastICA'* but now with a dimensionality reduction to 20 components. We visually inspected these components via 'ft_*rejectvisual'*, and selected 'outliers' (e.g., based on max values and z-scores). The 20 components were visually inspected after plotting their topographies and time-series, and a new selection of 'outliers' was defined. Lastly, we visually inspected the two lists of outliers and decided which components had to be removed. On average, we removed 2 components via '*ft_rejectcomponent*'. Then EEG time-series were reconstructed. In the next preprocessing step, we performed artifact subspace reconstruction as implemented in the '*pop_clean_rawdata*' function in EEGlab, and with the 'BurstCriterion' parameter set to 20 (all other parameters were set to 'off'). We then employed an automatic channel rejection procedure to remove noisy channels. In this routine, we calculated the median variance across channels (and excluding EOG channels), and 'outliers' were then defined as exceeding 2.5*median variance. Next, we implemented an artifact suppression procedure [28–30], a cleaning routine that interpolates noisy (>absolute mean+2*SD) time-windows on a channel-by-channel basis. Lastly, data were low-pass filtered at 40Hz via '*ft_preprocessing*', segmented to each auditory sequence (starting 4s before the first tone onset and ending 4s after the last tone onset), and downsampled to 100Hz.

2.4.2. Event-related analyses

We assessed the amplitude, latency, and variability of neural responses to tone onsets along the auditory sequences by adopting the event-related potential (ERP) approach. Thus, sequence-level

data as obtained from preprocessing were further segmented into time-windows ranging from -1 to 8s relative to the first tone onset in each auditory sequence and later underwent a low-pass filter with a 20Hz frequency cutoff ('ft_preprocessing'). Next, we centered the data by mean correcting each trial by a global average (calculated from -1 to 8s and across trials) and performed 'peak analyses'. Thus, we calculated the participant-, trial-, and channel-level peak amplitude and latency, and amplitude and latency variability of three ERP components: the P50, N100, and P200. For doing so, we defined three 60ms-long time-windows respectively centered at 50, 100, 200ms (e.g., the window of interest for the P50 component was .02 to .08s relative to each tone onset). Within these time-windows we obtained the amplitude peak and its latency (the max value and its time point). Next, we calculated the intra-individual variability for each ERP component and metric (peak amplitude and latency) and within a fronto-central channel (FC) cluster of interest. The FC cluster encompassed the sensor-level correspondents of prefrontal, pre-, para-, and post-central regions highlighted in previous studies [32] and further highlighted in similar EEG work on rhythm processing [28,29,33]. The cluster included 16 channels: 'AFz', 'AF3', 'AF4', 'F3', 'F4', 'F5', 'F6', 'FCz', 'FC3', 'FC4', 'FC5', 'FC6', 'C1', 'C2', 'C3', 'C4'. As the first tones within an auditory sequence are known to elicit much stronger neural responses compared to later tones, we focused subsequent analyses on tones from the 3rd to the 7th position (STD before the onset of a DEV tone). Furthermore, as most of the surveyed evidence highlighted a specific impact of ageing on the N100 component [3,19–24], subsequent analyses focused on the N100 component only. Analyses of the P50 and P200 components can be found in the Supplementary materials. Statistical analyses assessed group differences in the N100 peak amplitude over tone repetitions along the auditory sequence by means of a repeated-measure ANOVA. Thus, individual N100 peak amplitudes over 5 tonal positions (3rd to 7th) were modelled by the 'fitrm' algorithm by specifying 'Group' and 'Time' as factors and allowing for an interaction term. Next, the model entered a repeated measures analysis of variance via the 'ranova' function. Statistics are reported in Suppl. Materials. In the absence of a Group x Time interaction, we proceeded by testing for the main effect of Group. Then, group differences in N100 peak amplitude and latency were assessed by means of permutation testing and 1000 permutations. A *p*-value lower than .05 was considered statistically significant. Similarly, we performed group comparisons for any difference in variance in the N100 amplitude and latency. Group differences were assessed by

means of permutation testing and with 1000 permutations. A *p*-value lower than .05 was considered statistically significant. Results are provided in Fig. 1B.

2.4.3. Spectral parametrization

To investigate how efficiently participants (i) encoded temporal regularities in auditory sequences, (ii-iii), and whether there were group differences in the excitation/inhibition balance [34,35], we performed spectral parametrization analyses. Differently from typical Fourier (FFT) analyses, the spectral parametrization allows disentangling true oscillatory from non-oscillatory components [36]. Thus, frequency entrainment of neural oscillatory activity to the temporal regularity in an auditory sequence should be visible as a clear amplitude peak in the frequency spectrum at the *Sf*. To test this hypothesis, we first shortened trials into segments of 8s (from the first tone onset (0s) to the 12th tone offset), and then employed the automated spectral parameterization algorithm described in [36] and implemented in FieldTrip in a two-step approach. Thus, 'ft_freqanalysis' was first used in combination with the multi-taper method for FFT ('mtmfft') and power as output ('pow'), and secondly by specific 'fooof_aperiodic' as output. The output frequency resolution was set at 0.2Hz. Next, the aperiodic (fractal) spectrum was removed from the FFT spectrum via calling the 'ft_math' function, finally isolating the 'real' oscillatory component (Fig. 2A).

Subsequent statistical analyses were performed on the same FC cluster as described above. Group differences were statistically assessed by permutation testing (1000 permutations) of (i) the extracted peak amplitude values at the *Sf*, (ii) the amplitude of the fractal component across the frequency spectrum, and (iii) the slope of the fractal component. A *p*-value below .05 was considered statistically significant.

2.4.4. Inter-Trial Phase Coherence

When neural activity precisely encodes the temporal regularities in auditory sequences, it should not only show a clear amplitude peak in the FFT spectrum but also display phase coherence. The inter-trial phase coherence (ITPC) metric is inversely proportional to the variability in the imaginary part of the complex FFT spectrum. Thus, when oscillations are precisely aligned over

trials (same phase), the ITPC is high; when, instead, there is variability in the phase of the oscillations over trials, the ITPC is lower.

The complex FFT spectrum was obtained by performing FFT decomposition at the single-participant, -channel and -trial level on 8s-long segments as above. Next, the ITPC spectrum was calculated by dividing the Fourier coefficients by their absolute values (thus, normalizing the values to be on the unit circle), calculating the mean of these values, and finally taking the absolute value of the complex mean. Further documentation can be found on the FieldTrip website (https://www.fieldtriptoolbox.org/faq/itc/). For illustration purposes, the ITPC spectrum was restricted to 1-4Hz (Fig. 2B). Subsequent statistical analyses were performed on the same FC cluster as for the event-related analyses. Group differences were statistically assessed by permutation testing of the extracted ITPC values at the *Sf* and with 1000 permutations. A *p*-value below .05 was considered statistically significant.

2.4.5. Link between ERP – FFT – ITPC

Exploratory analyses assessed a possible link between extracted ERP metrics (amplitude, latency, and variability of ERP components) and the individual FFT amplitude and ITPC at the *Sf*. These analyses tested the hypothesis that the precise encoding of temporal regularities and the deployment of temporal predictions should lead to suppressed ERP responses and less variable ERP latencies.

These hypotheses were tested by means of a stepwise regression model, and independently for the FFT amplitudes and ITPC. Single-participant FFT/ITPC values at the *Sf* were entered into the stepwise regression model ('stepwiselm' in MATLAB) and regressed against ERP metrics (P50, N100, and P200 amplitude, latency, and variability). The stepwise approach searches for the best combination of predicting variables leading to the best fit to the data, and the winning model was chosen based on adjusted Eta-squared. Separately, we also computed Pearson's correlations assessing the correlations between FFT and ITPC values with ERP metrics. Finally, the results were visualized by means of circular graphs in Fig. 2C (statistics provided in in Suppl. Materials).

2.5. Data and code Availability

The analysis code in use here will be stored in an open repository. The data can be provided upon reasonable request by the corresponding author.

3. Results

3.1. Event-Related Analyses

Event-related analyses tested for group differences in the N100 component of the event-related potential (ERP; Fig. 2B, C). A repeated-measures ANOVA tested for group differences in the N100 peak amplitude over 5 tone positions along the auditory sequences (3^{rd} to 7^{th} position). This analysis specifically assessed a repetition-suppression effect. However, the Group * Time interaction term of the model was not significant (F = .63, p = .49). Thus, we then tested the main effect of Group across the sequence, by pooling the N100 peak amplitudes across the 5 tone positions. The group effect was statistically assessed by permutation testing (1000 permutations) and reported a significant effect, with older (HO) participants showing larger N100 peak amplitudes than younger adults (HY; p < .001; Fig. 2D bottom left). Further analyses tested group differences in the peak latency and variability in the peak amplitude and latency. HO showed shorter N100 peak latency (p = .008), increased variability in peak amplitude (p <.001) and peak latency (p <.001; Fig. 2D bottom).

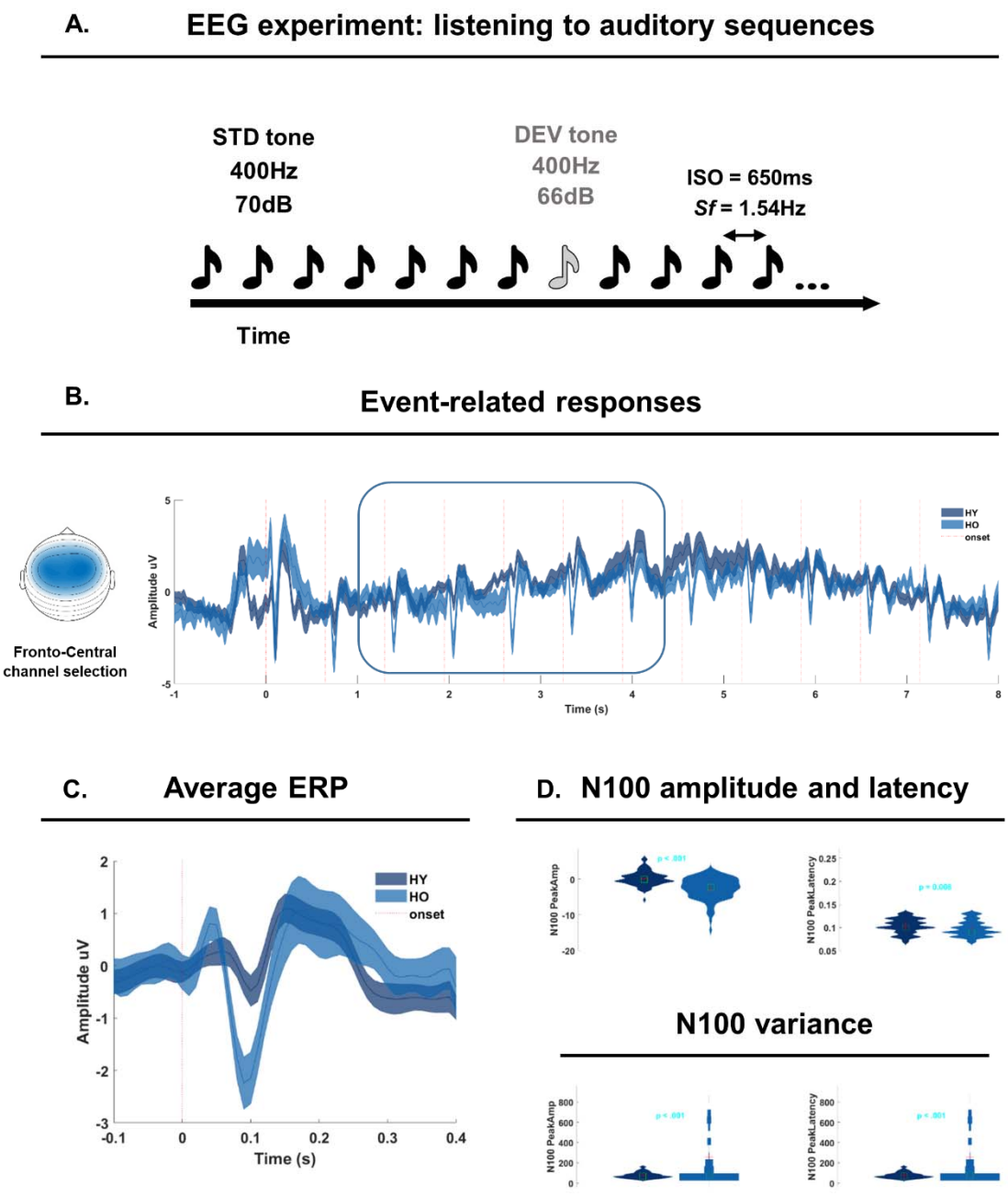

Figure 1 - Experimental setup and Event-related analyses.

A. Participants listened to 96 isochronous tone sequences, containing 13-to-16 tones including standard (STD) tones (F0 = 400 Hz, duration = 50 ms, amplitude = 70dB SPL) and either one or two deviants (DEV; attenuated by 4dB relative to the STD tones). The first DEV could either fall on positions 8,9,10, or 11, while the second DEV always fell on position 12. The inter-onset-interval between successive tones was 650ms, resulting in a stimulation frequency (Sf) of 1.54Hz. B. Event-related analyses focused on a fronto-central (FC) channel cluster (as provided on the left side) and on 5 tones from the 3rd to the 7th position along the auditory sequence (square on the time-series). Dark blue lines report the time-series for younger (HY) participants, while the lighter blue lines report the time-series for older adults (HO) participants. C. Average ERPs over 5 tone positions as

highlighted in B, and in the FC channel cluster. Color coding as in B. D. N100 peak amplitude and latency (top panel) were statistically compared across the two groups by means of permutation testing. At the bottom, the variance in the N100 peak amplitude and latency was statistically compared across the two groups by means of permutation testing.

3.2. Spectral parametrization

After decomposing the Fourier spectrum into an oscillatory component (OSc) and a non-oscillatory (fractal) component (FRc), we statistically assessed group differences in (i) the amplitude of the OSc at the stimulation frequency (1.5Hz; *Sf*), (ii) the amplitude of the FRc across frequencies, and the (iii) slope of the FRs across frequencies by means of permutation testing, and with 1000 permutations.

The group effect for the OSc at the *Sf* was statistically significant and showed larger amplitude responses in the HO than the HY (p = .004; Fig. 3A, left; also see Suppl. Materials). HO also showed a significantly stronger FRc across the spectrum (p < .001; Fig. 3A, right), but there was no significant group difference in the slope of the FRc.

3.3. Inter-Trial Phase Coherence

The imaginary part of the complex Fourier spectrum was used to calculate the Inter-trial phase coherence (ITPC). Statistical analyses assessed group differences in ITPC at the *Sf*. Permutation testing revealed a significant group effect, with HY showing larger ITPC at the *Sf* as compared to HO (p = .007; Fig. 3B).

3.4. Link between OSc, ITPC and ERP

Exploratory analyses assessed the link between ERP's peak amplitude, latency, and variability and (i) individual OSc amplitudes at the *Sf*, and (ii) individual ITPC amplitudes at the *Sf*. The stepwise regression model for the ITPC and ERP metrics was statistically significant ($F = 4.69$, $p = .008$, $R2 = .32$) and revealed a positive link between ITPC and the P50 latency, and a negative link with the P200 latency and the N100 amplitude variance (Fig. 3C, right and Suppl. Materials). The stepwise regression model for the OSc and ERP metrics did not reveal a significant effect. Exploratory correlation analyses, however, found a positive link between the OSc amplitudes and the ERP metrics of variability across P50, N100, and P200 components (Fig. 3C, left and Suppl. Materials).

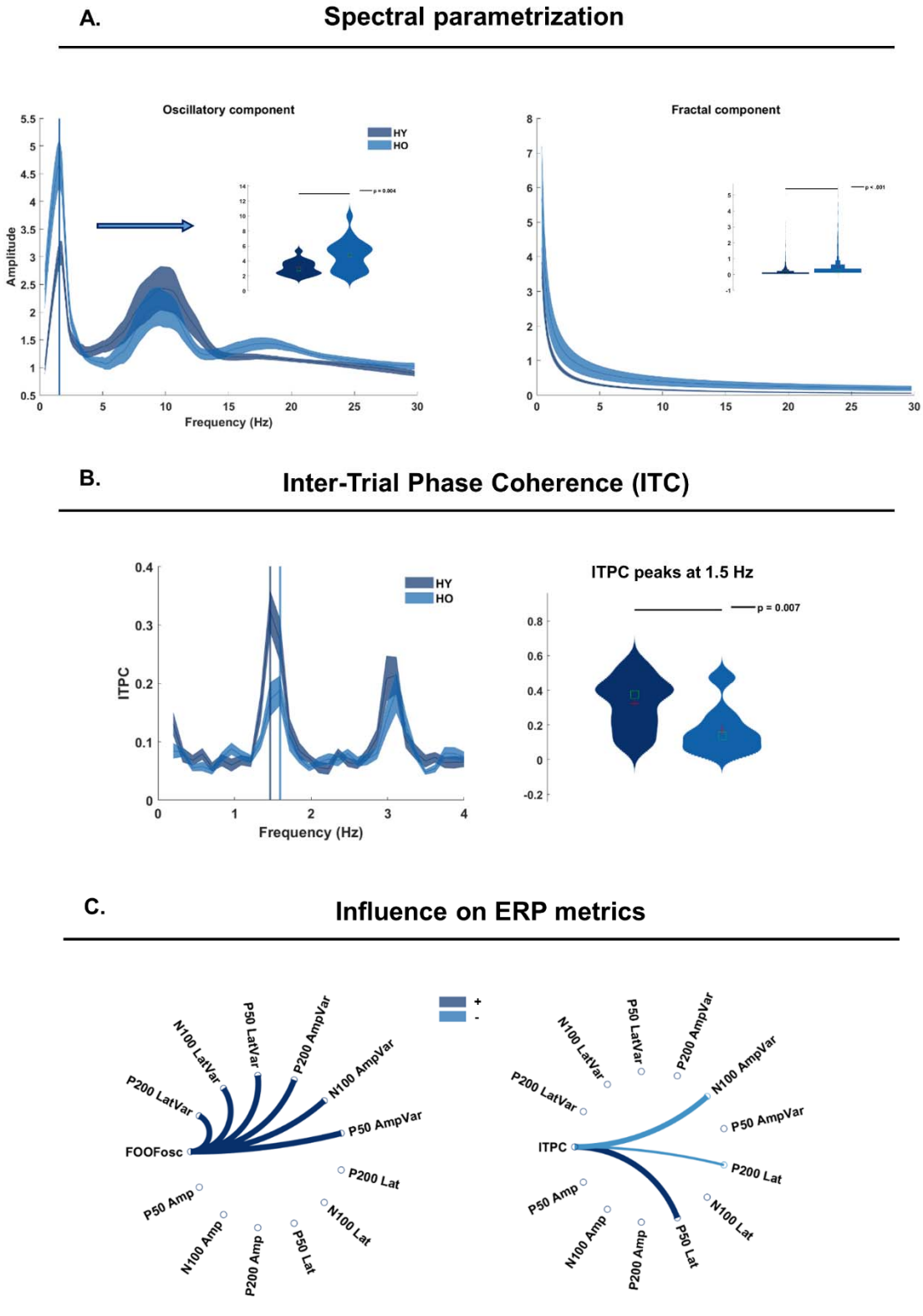

Figure 2 – Spectral parametrization and Inter-trial phase coherence analyses

A. Spectral parametrization analyses allowed to decompose the Fourier spectrum into an oscillatory component (left) and into a non-oscillatory (fractal) component (right). Both spectra provide frequencies on the x-axis and amplitude values on the y-axis. Dark blue lines report the data for younger (HY) participants, while the lighter blue lines report the data for older (HO) participants. The inserts on top of the main panel provide the statistical comparisons on individual data as assessed by permutation testing. On the left, the group comparison assessed the amplitude peak at the stimulation frequency (1.5Hz). On the right, the group comparison assessed for amplitude differences across the entire spectrum.
B. Inter-trial phase coherence (ITPC) analyses assessed group differences in the ITPC at the stimulation frequency by means of permutation testing (right). The ITPC spectrum (left) provides frequencies on the x-axis and coherence values on the y-axis. The two vertical lines on the spectrum report the group coherence peak.
C. Exploratory analyses assessed the link between peak amplitudes in the oscillatory component (on the left, FooFosc) and in the ITPC (right) with ERP metrics of peak amplitude (Amp), latency (Lat) and variance (Var) across three ERP components (P50, N100, P200). Dark blue lines report positive relations, while lighter blue lines report negative relations.

4. Discussion

Throughout the lifespan, brain neuroanatomical changes typically follow an inverted U-shape trajectory [37]. Grey and white matter increase from childhood to adulthood and then decline with aging. Concurrently, primary sensory systems often undergo gradual deterioration, potentially leading to decline in auditory processing [3,5,19]. Changes within both peripheral and central auditory systems, such as the deterioration of auditory nerve fibers and loss of inner hair cells, affect the brain's ability to accurately encode sensory events in the auditory environment [17], consequently impacting speech comprehension, social interactions, and cognition more broadly [38]. Importantly, even in the absence of hearing loss, older individuals experience difficulties in processing both simple and complex auditory sequences in noisy environments [16,21,22,25].

In this study, we posited that the challenges observed in higher cognitive processes such as speech processing during aging might stem form an underlying decline in the ability to detect, encode, and employ temporal regularities in the sensory environment to predict future events and optimize sensory processing. To investigate this hypothesis , we recruited younger and older individuals and recorded their neural activity using EEG while they listened to simple isochronous equitone sequences presented at a stimulation frequency (*Sf*) of 1.5Hz. Analyses on event-related potentials (ERP) revealed that older adults exhibited heightened, more variable, and faster N100 responses, consistent with previous findings [3,19–24]. These results support the notion that aging affects the ability to engage in 'sensory gating' [22], specifically the suppression of cortical responses to repetitive and predictable stimuli [20,23]. Additionally, the increased variability in the N100 amplitude and latency suggests altered encoding of tone onsets in aging.

Subsequently, we aimed to replicate previous findings that have demonstrated increased excitability of the auditory cortex [19] and altered responses to sounds [3,6,20] in aging. To achieve this, we conducted spectral parametrization analyses to discern the 'oscillatory' component (OSc) from a 'fractal' component in the Fourier spectrum. Older adults exhibited increased OSc amplitude at the *Sf* compared to younger participants, along with an increase in the amplitude of the fractal component across frequencies. These results are consistent with the enhanced event-related responses described earlier and support the notion of heightened excitability or reduced inhibition of the auditory cortex in aging [19]. However, the increase in OSc at the *Sf* contrasts with prior evidence showing diminished encoding of temporal regularity in metronome-like auditory sequences obtained through typical Fourier analyses [26,27].

Lastly, inter-trial phase coherence (ITPC) analyses were conducted to assess the coherence of phase alignment of neural oscillations along the auditory sequences and across trials. Older adults exhibited lower ITPC at the *Sf*, indicating increased variability in the encoding of the temporal regularities in auditory sequences. These findings are consistent with previous observations of reduced coherence and phase alignment of neural activity to sounds in simple and more complex auditory sequences [6,16–18].

Taken together, these observations suggest that aging impacts the ability to generate temporal predictions about future events and to utilize these predictions to optimize sensory processing. The increased amplitudes of neural responses to repeated and regular sounds (ERP and OSc) and the increased variability in the N100 amplitude and latency were accompanied by increased variability and reduced coherence in the ITPC. Thus, as hypothesized, aging is associated with alterations in fundamental auditory and timing processing and in the ability to generate and employ temporal predictions to optimize sensory processing. These findings underscore the importance of future research investigating the relationship between timing capacities and higher-order cognitive processes (e.g., speech processing) across the lifespan.

This evidence, however, challenges the 'exploration-exploitation shift' hypothesis [12]. According to this perspective, most aging individuals attempt to counteract sensory and cognitive decline by adopting compensatory cognitive strategies and leveraging on previous knowledge predictively [39]. For example, they may utilize long-term knowledge, generalizations, and predictions to mitigate increased difficulty with learning and the decline of executive functions due to striatal

cholinergic changes [40]. To operationalize and test this notion, Brown et al., [39] referred to the predictive coding framework: given the reduced certainty of sensory signals, aging individuals rely more on memory and consequently generate predictions about future events [41]. These predictions serve the purpose of adaptation aiming to optimize perception and cognition despite cognitive decline [42]. Contrary to these expectations, the current findings indicate that older individuals either did not form predictions, or, at the very least, did not utilize temporal predictions to inform sensory processing at the very fast, millisecond temporal scale. Indeed, consistent with prior electrophysiological evidence, neural responses were not attenuated by top-down modulatory suppression mechanisms [3,19–24].

The abilities to detect and encode temporal regularities, as well as to form temporal predictions, have been linked to widespread cortico-subcortical circuitries including the basal ganglia and the cerebellum [43]. Lesions in either of these circuitries have been shown to causally impact the ability to predictively align neural dynamics to sound onsets [28]. Conversely, aging, is typically characterized by decreased fractional anisotropy and increased diffusivity, indicative of white matter deteriorations, along with bilateral grey [45] and white matter loss in the cerebellum (CE) and reduced connectivity within the dentato-thalamo-cortical network [10]. Additionally, functional connectivity patterns undergo alterations [46], such as reduced within-network connectivity and variegated patterns of increase and decrease in between-network connectivity [47]. Notably, deteriorations within the striatal-frontal networks [9], the under-recruitment of the cerebellum during challenging cognitive tasks [10], and changes within the cerebellum-basal ganglia circuitries [11] have been associated with reduced cognitive control [12] and numerous motor and cognitive deficits [11].

Aligned with the original hypotheses and bolstered by these novel findings, we propose that neuroanatomical and functional alterations in cortico-subcortical circuitries, including the basal ganglia (BG) and the cerebellum (CE) may impact fundamental timing and predictive abilities, which are integral to cognition. These changes could impact the documented declines in processing speed, working memory, inhibition, memory, and reasoning capacities [13,48,49]. However, establishing a causal link between timing, predictive functions, and general cognition presents a challenge due to the substantial heterogeneity in aging trajectories. Indeed, neuroanatomical and cognitive changes throughout the life are subject to modulation by a

complex interplay of vascular, metabolic, and inflammatory risk factors [7], which, in turn, are influenced by the intricate interaction of environmental factors (e.g., socioeconomic status and education) and genetic predispositions [49]. Variability in any of these modulating variables inevitably results in significant diversity in cognitive capacities among older adults, impeding generalizations. Therefore, systematic, longitudinal, and comprehensive assessments of timing and cognitive functions across the lifespan are imperative.

5. Conclusions

Here, we examined the effects of aging on the ability to detect and encode temporal regularities in the auditory environment. The integration of findings from three complementary analytical methods highlights the adverse effects of aging on fundamental temporal and predictive auditory processes. This evidence implies that cognitive decline in aging could be preceded by or linked to diminished abilities to use temporal regularities for predicting future auditory events.

Author contributions

S.A.K., M.S., conceptualized the study.

S.A.K., M.S., collected the data.

A.C. designed and performed data analyses.

A.C., S.A.K., M.S., L.B. interpreted the results.

A.C. wrote the first draft of manuscript.

All authors contributed to, revised, and approved the final version of the manuscript.

Declaration of Competing Interest

The authors declare no competing interests.

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