About time

Biological Psychology 163 (2021) 108135

Contents lists available at ScienceDirect

Biological Psychology

journal homepage: www.elsevier.com/locate/biopsycho

About time: Ageing influences neural markers of temporal predictability

Pia Brinkmann [a,b,c], Simon Rigoulot [a,b,d,e], Melissa Kadi [a,b,e], Michael Schwartze [c], Sonja A. Kotz [a,c], Simone Dalla Bella [a,b,e,f,*]

[a] International Laboratory for Brain, Music, and Sound Research (BRAMS), Montreal, Canada
[b] Dept. of Psychology, University of Montreal, Montreal, Canada
[c] Dept. of Neuropsychology & Psychopharmacology, University of Maastricht, Maastricht, the Netherlands
[d] Dept. of Psychology, Université du Québec à Trois Rivières, Trois Rivières, Canada
[e] Centre for Research on Brain, Language and Music (CRBLM), Montreal, Canada
[f] Dept. of Cognitive Psychology, University of Economics and Human Sciences in Warsaw, Warsaw, Poland

ARTICLE INFO

Keywords:
Ageing
Temporal predictability
Timing
ERP
Rhythm perception
Temporal structure
Formal structure
Oddball

ABSTRACT

Timing abilities help organizing the temporal structure of events but are known to change systematically with age. Yet, how the neuronal signature of temporal predictability changes across the age span remains unclear. Younger ($n = 21$; 23.1 years) and older adults ($n = 21$; 68.5 years) performed an auditory oddball task, consisting of isochronous and random sound sequences. Results confirm an altered P50 response in the older compared to younger participants. P50 amplitudes differed between the isochronous and random temporal structures in younger, and for P200 in the older group. These results suggest less efficient sensory gating in older adults in both isochronous and random auditory sequences. N100 amplitudes were more negative for deviant tones. P300 amplitudes were parietally enhanced in younger, but not in older adults. In younger participants, the P50 results confirm that this component marks temporal predictability, indicating sensitive gating of temporally regular sound sequences.

1. Introduction

Timing abilities are central to our subjective experience of the temporal course of events (Allman & Meck, 2011). For example, when parking a car, a parking assistant helps to estimate the distance of objects using auditory feedback. With sufficient distance to an object, this feedback is a repeated tone presented at temporally regular intervals. However, when approaching an obstacle, tones increase in rate and pitch, attracting attention and optimizing reactions (Nobre & van Ede, 2018). By changing its temporal structure (i.e., increasing rate) and formal structure (i.e., increasing pitch), the isochronous rhythm of the parking assistant thus signals a potential danger. While the formal structure of a stimulus defines an event type (Schwartze, Farrugia, & Kotz, 2013), i.e., "what" is perceived, the temporal structure refers to "when" an event occurs (Fraisse, 1984). Accurate timing abilities may allow predicting "when" something is likely to happen and may complement predictions about "what" can be expected (i.e., formal structure; Nobre & van Ede, 2018; Schwartze et al., 2013; Schwartze, Rothermich, Schmidt-Kassow, & Kotz, 2011). It is known that timing abilities contribute to successful adaptive behavior, such as changing the focus of attention (Nobre & van Ede, 2018; Nobre, Correa, & Coull, 2007). Efficient adaptation to a dynamic environment requires extrapolation from past events to predict future events (Nobre & van Ede, 2018; Nobre et al., 2007). Here, the primary focus was on temporal predictability in temporally manipulated auditory sequences.

At the neural level, the dissociation of formal and temporal structure can also be translated to patterns of oscillatory activity. Neural oscillations occur naturally in the brain, indicating transient rhythmic variations in the excitability of neuronal populations (Canolty & Knight, 2010; Lakatos, Chen, O'Connell, Mills, & Schroeder, 2007). They can be described in terms of repetition rate (i.e., frequency), amplitude (i.e., magnitude) and phase (i.e., a position within a wave cycle; Canolty & Knight, 2010; Kotz, Ravignani, & Fitch, 2018; Large & Jones, 1999). Entrainment of oscillatory activity describes a state in which such activity becomes aligned with external stimulation (i.e., via period and phase adjustment), for example, a periodic auditory rhythm (Kotz et al., 2018; Large, 2008; Large & Kolen, 1994). Entrainment to rhythmic stimulation has also been proposed to modulate attentional processes.

* Corresponding author at: International Laboratory for Brain, Music and Sound Research (BRAMS), Dept. of Psychology, University of Montreal, Pavillon Marie-Victorin, CP 6128 Succursale Centre-Ville, Montréal, QC, H3C 3J7, Canada.
E-mail address: simone.dalla.bella@umontreal.ca (S. Dalla Bella).

https://doi.org/10.1016/j.biopsycho.2021.108135
Received 9 March 2020; Received in revised form 21 May 2021; Accepted 9 June 2021
Available online 11 June 2021

Dynamic Attending Theory (DAT; Large & Jones, 1999) suggests that the allocation of attention is partly driven by the temporal properties of sensory input. According to this theory, internal attending rhythms entrain to external stimulation, thereby generating expectations regarding the future course of events (Jones, 2018; Jones, 1976; Large & Jones, 1999). Note that the processing of temporal structure can be examined in both perceptual and sensorimotor tasks.

To gain a better understanding of the neural mechanisms underlying temporal structure and temporal predictability, thorough investigation of the diseased or ageing brain is needed. The general importance of sensory and sensorimotor timing abilities becomes evident when underlying mechanisms are affected by neural or psychological conditions, such as Parkinson's Disease (Benoit et al., 2014; Cunnington, Iansek, Bradshaw, & Phillips, 1995), schizophrenia (Carroll, Boggs, O'Donnell, Shekhar, & Hetrick, 2008), attention-deficit hyperactivity disorder (Dankner, Shalev, Carrasco, & Yuval-Greenberg, 2017; Hart et al., 2014), cerebellar (Ivry & Keele, 1989; Kotz, Stockert, & Schwartze, 2014) or basal ganglia lesions (Schwartze, Keller, Patel, & Kotz, 2011). For example, timing abilities are compromised in Parkinson's disease patients (Allman & Meck, 2011; Benoit et al., 2014; Dalla Bella et al., 2017; Puyjarinet et al., 2019), leading to impaired temporal predictions (Breska & Ivry, 2018). However, there are also indications that timing abilities vary over the lifespan and change systematically with age (McAuley, Jones, Holub, Johnston, & Miller, 2006). Finger tapping tasks in the absence of a pacing stimulus indicate that the chosen rates slow down with increasing age (Vanneste, Pouthas, & Wearden, 2001). Average spontaneous inter-tap intervals (ITIs) are about 300 ms in children. Younger adults prefer slower rates (~600 ms ITI), while this rate is more variable and further slowed down to about 650 ms in older adults (> 75 years of age; McAuley et al., 2006). In the present study, the emphasis was on the influence of age on temporal predictability.

Age-related changes in timing abilities have been investigated at the neural level by event-related potentials (ERPs), measures of oscillatory activity, and neural entrainment. Henry, Herrmann, Kunke, and Obleser (2017) investigated entrainment patterns in younger and older participants who had to detect a gap in frequency modulated sound sequences. Results indicated that oscillations in older adults entrained less strongly and less adaptively to the target frequency than in younger adults (Henry et al., 2017). Another study focused on the effects of different types of temporal structure on neural entrainment and found reduced entrainment in the vicinity of the target frequencies in older adults, as reflected by decreased mean spectral amplitudes (Sauvé, Bolt, Fleming, & Zendel, 2019).

ERP studies also provide evidence for differential neural activity associated with temporal predictability across different ages. The auditory P50, N100, P200 and P300 components are sensitive to manipulations of temporal and formal structure (Schwartze et al., 2013; Schwartze, Rothermich et al., 2011). The middle-latency P50 is a positive ERP deflection that peaks around 50 ms after sound onset, known to be generated in temporal areas, and functionally interpreted as a marker of sensory gating (Korzyukov et al., 2007; Smith, Boutors, & Schwartzopf, 1994). Sensory gating can be described as a filter of sensory auditory information, where impaired filter mechanisms lead to the unfiltered transmission of auditory information to higher-order brain areas (Korzyukov et al., 2007). Source localization analyses suggest that next to temporal areas, P50 is generated in frontal regions of the brain (Korzyukov et al., 2007). Age effects in classical paired-stimulus paradigms were observed at inter-stimulus intervals (ISI) of 250 ms, suggesting P50 suppression in older but not in younger participants (Rasco, Skinner, & Garcia-Rill, 2000). Another study reported an increased P50 amplitude response with increasing age, based on results obtained with an oddball paradigm (Golob, Irimajiri, & Starr, 2007). Moreover, P50 activity was modulated by manipulations of temporal and formal structure in a sample of younger adults (Schwartze et al., 2013). Taken together, previous research suggests that P50 may serve as a marker of temporal predictability, with overall increased amplitudes observed in older participants.

The N100 is a long-latency negative ERP deflection that peaks approximately 100 ms in response to a sound onset and is generated in the supratemporal planes of the auditory cortex (Näätänen & Picton, 1987). The N100 can be observed after unpredicted stimuli (Schafer & Marcus, 1973) and also distinguishes between self- and other-generated auditory events via amplitude suppression in the former case (Baess, Jacobsen, & Schröger, 2008; Knolle, Schröger, Baess, & Kotz, 2012; Knolle, Schwartze, Schröger, & Kotz, 2019). Previous ERP studies by Schwartze and colleagues used a paradigm that independently manipulated formal and temporal structure in auditory sequences to investigate temporal predictability (Schwartze et al., 2013; Schwartze, Rothermich et al., 2011). In this paradigm, two different sound sequences were utilized. The first sequence followed an isochronous rhythm (i.e., a regular temporal structure), while containing two tones differing in formal structure (i.e., in pitch). The other sequence followed a random temporal structure, while containing identical tones. When recording responses to manipulations of temporal and formal structure in a sample of younger adults, N100 activity patterns did not differentiate between changes in temporal structure (i.e., isochronous versus random), but formal structure (i.e., standard versus deviant; Schwartze, Rothermich et al., 2011). Interestingly, older adults seem to exhibit shorter N100 latencies than younger adults in auditory oddball paradigms (Golob et al., 2007). These findings suggest that ERP latencies shorten with increasing age (Tomé, Barbosa, Nowak, & Marques-Teixeira, 2015). However, there are also indications that the N100 amplitude is not affected by age in attentive conditions, but increases in pre-attentive conditions (Schiff et al., 2008). Further results indicate that N100 latency does not differ in attentive and pre-attentive conditions (Schiff et al., 2008), suggesting that N100 is less affected by age than other components, for example the later P300 complex (Schiff et al., 2008).

The P200 component is a positive ERP deflection peaking at approximately 200 ms after the presentation of an auditory stimulus and is detectable at anterior and central sites (Luck, 2014). Like the P300 complex, the P200 is larger for deviant stimuli in an oddball paradigm. It has been suggested that while the P200 is elicited only by simple stimulus features, the P300 could be elicited by more complex stimulus features (Luck, 2014). Previous research on temporal predictability and the P200 in younger adults found reduced P200 deflections for more temporally predictable cue-target trials (Herbst & Obleser, 2017).

The P300 complex is a positive deflection, generated in centro-parietal areas, and peaks approximately 300 ms after the presentation of an auditory stimulus (Polich & Criado, 2006). In oddball paradigms, the P300 component has long been studied and can be divided between the more frontally located P3a and the more parietally located P3b (Squires, Squires, & Hillyard, 1975). While both sub-components are elicited by infrequent and unpredictable changes, the P3b is only present when changes are task-relevant (i.e., participants count the number of deviants in a stimulus sequence) and is referred to as the P300 component. A related study by Schwartze, Rothermich et al. (2011) investigated the effect of formal structure in an oddball paradigm and assessed P3b activity in an attentive session. When comparing younger with older adults, reduced P300 amplitudes and delayed latencies were observed in the latter, using an oddball paradigm (Golob et al., 2007; Nowak et al., 2016). Notably, in the study by Golob et al. (2007), P300 latencies progressively increased from healthy elderly to patients diagnosed with mild cognitive impairment and mild Alzheimer's disease.

In summary, previous evidence suggests an effect of age on EEG markers of temporal predictability and deviance processing. Based on previous research, it is suggested that P50 is modulated in younger adults by temporal (i.e., isochronous versus random sequences) and formal structure in oddball paradigms (Schwartze et al., 2013). Previous observations suggest increased P50 amplitudes with increasing age. Second, the amplitude of the N100 seems to be sensitive to formal but less or not to manipulations of temporal structure. Moreover, it is

suggested that P300 amplitudes decrease and latencies increase for older relative to younger adults. However, the existing studies did not systematically investigate age-related effects, while directly manipulating the temporal (i.e., temporal predictability by comparing isochronous with random sequences) and formal structure (i.e., standard versus deviant tones) in an oddball paradigm. The advantage of directly manipulating temporal regularity in auditory oddball sequences is to better isolate temporal predictability regarding structural predictability and to pinpoint its neural underpinnings across age groups.

The goal of the present study was to shed light on the effect of age on the underlying neural correlates of temporal predictability measured with EEG. We hypothesized that (1) ERP amplitudes and latencies would be differentially modulated by formal and temporal structure and that, P50 may serve as marker of temporal predictability; (2) that P50 amplitudes will be increased, N100 latencies will be altered and P300 amplitudes and latencies decreased for older adults compared to younger ones. Investigating the effect of age on neural correlates of temporal predictability will expand the current knowledge about systematic changes of timing abilities during ageing.

2. Methods and materials

2.1. Participants and recruitment

A group of younger adults ($n = 21$, 8 males, $M_{age} = 23.1$ years, age range: 18–29 years) and a group of older adults ($n = 21$, 6 males, $M_{age} = 68.5$ years, age range: 59–80 years) participated in the study. All participants were right-handed. Two participants in the younger group were excluded from the analysis, one due to left-handedness and one due to low signal quality (> 70 % of the data had to be removed after artefact correction procedures). All participants ($N = 42$) were non-musicians (i.e., with less than 2 years of formal musical training). Recruitment took place via advertisements, presentations in community centers, elderly homes, and word of mouth. Participants did not have a history of alcohol or drug abuse, did not take medications acting on the nervous system, or had previous head trauma, neurodevelopmental disorders, psychopathology and visual, hearing, or motor disabilities. The study was approved by the *Comité d'éthique de la recherche en éducation et en psychologie* (CEREP) of the University of Montréal (UdeM) and adhered to the Declaration of Helsinki. Written consent was obtained and participants were reimbursed with 10$/h.

2.2. EEG task, data acquisition, preprocessing and ERP analysis

2.2.1. EEG task

The experimental EEG paradigm employed consisted of an adaptation of a previously established oddball paradigm (Schwartze et al., 2013; Schwartze, Rothermich et al., 2011). The paradigm comprised two oddball sequences that differed in their temporal structure, i.e., the ISI was either fixed (ISI =1000 ms; isochronous sequence) or varied randomly between 600 ms and 1400 ms (average ISI =1000 ms; random sequence), while keeping the duration of each auditory stimulus constant (150 ms, 10 ms rise and fall). Each sequence contained 721 tones (deviant = 144, standard = 577). Thus, in total 1442 tones were presented, 1154 standard (600 Hz), and 294 oddball (660 Hz) sinusoidal tones (ratio of 4:1; Fig. 1). To ensure that the participants focused on the task to count the number of deviants, deviants were added to the sequence that was presented last (i.e., deviant = 147, standard = 577). Due to counterbalancing, the order of presentation switched from presenting isochronous - random to random - isochronous sequences. Those additional deviants were not further considered during analysis.

Participants were asked to fixate an asterisk displayed on a computer screen, to count the number of deviants in each sequence, and to report the respective number at the end of each sequence. Stimuli were presented via insert earphones using Presentation software (Neuro-Behavioral Systems, NBS). The presentation of the tones was pseudorandomized, to warrant that each sequence started with four standard tones to establish a memory trace and that maximally two deviants were presented consecutively. The order of the sequences was counterbalanced to avoid carry-over effects.

2.2.2. EEG data acquisition and preprocessing

A Biosemi ActiveTwo system was used to record continuous EEG data. Reference free brain activity from 64 channels, arranged according to the international 10–20 system (Sharbrough, 1991) and grounded to a two electrode feedback loop, was recorded at a sampling rate of 1024 Hz. Six additional electrodes were bilaterally placed at mastoid and lateral ocular sites and unilaterally inferior to one eye and on the nose. Impedances were kept below 5 kOhms.

Preprocessing was performed using EEGlab (Delorme & Makeig, 2004) and the ERPLab toolbox (Lopez-Calderon & Luck, 2014), following Miyakoshi's preprocessing pipeline (Miyakoshi, 2018). The data were first down-sampled to 256 Hz, then a high-pass filter (0.1 Hz) was applied. In the following, the plug-in *clean_rawdata* was used to remove bad channels, which were then interpolated from the original dataset (Mullen, Chi, Kerth, & Cauwenberghs, 2015). Re-referencing was performed to the average and the plug-in *CleanLine* was used to eliminate line noise (Mullen, 2012). To remove muscular and ocular artefacts, independent component analyses (ICA) were applied (Delorme & Makeig, 2004). After baseline correction, epochs starting–200 ms before stimulus onset and ending 535 ms post-stimulus were segmented for each stimulus (standard and deviant tones). Three additional steps of artifact rejection were performed. First, epochs exceeding ± 40 μV were excluded. Then a 100 μV thresholder using a moving window peak to peak was used to exclude remaining epochs containing blinks. Finally, a 30 μV thresholder for detecting step-like artifacts was used to remove trials containing remaining horizontal ocular movements. On average, 10 % of trials were rejected (older adults = 13.9 %, younger adults = 6.1 %).

2.2.3. ERP analysis

Nine regions of interest (ROIs) for further analysis were selected based on Schwartze et al. (2013) and Schwartze, Rothermich et al. (2011), as the current research consisted of an adapted version of the same paradigm. The ROIs were left-anterior (AF7, AF3, F7, F5, F3, Fp1), left-central (T7, C5, C3, TP7, CP5, CP3), left-parietal (P7, P5, P3, PO7, PO3, O1), medial-anterior (Fz, FCz, F1, F2, FC1, FC2), medial-central (Cz, C1, C2, CPz, CP1, CP2), medial-parietal (Pz, P1, P2, POz), right-anterior (AF8, AF4, F8, F6, F4, Fp2), right-central (T8, C6, C4, TP8, CP6, CP4), right-parietal (P8, P6, P4, PO8, PO4, O2). We expected the P50, N100 and P200 components in fronto-central regions, while for the P300 the centro-parietal ROIs were focused on (Korzyukov et al., 2007; Linden, 2005; Polich & Criado, 2006). After visual inspection of the grand averages and individual waveforms, the following time-windows were selected for the respective four ERP components: 35−70 ms (P50), 75−130 ms (N100), 150−220 ms (P200) and 250−525 ms (P300). Variables of interest extracted from these time-windows were local mean amplitudes and local peak latency values in the specified time windows.[1]

2.3. Statistical analyses

Mixed-design 2 Group (younger versus older adults) x 2 Temporal structure (isochronous versus random sequences) x 2 Formal structure (standard versus deviant tones) x 3 Hemisphere (left versus medial versus right) x 3 Region (anterior versus central versus parietal)

[1] Please note that we also analyzed the data using different approaches of applying temporo-spatial PCAs (tsPCA). We performed one tsPCA on conditions and groups combined, as well as 8 tsPCAs, separate per stimuli. Overall, the results were similar to the ones that are reported here.

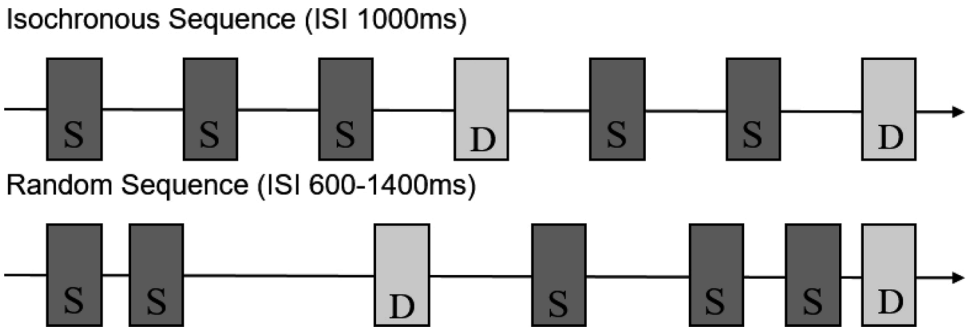

Fig. 1. Examples of the two stimulus sequences. S = Standard, D = Deviant, ISI = inter-stimulus-interval.

ANOVAs were performed per ROI, separately for amplitude and latency values. Group was the between-subject factor, Temporal- and Formal structure, Hemisphere and Region were the within-subject factors. When needed, Greenhouse-Geisser correction was applied to the results reported. Post-hoc analyses consisted of paired t-tests, if necessary, performed after averaging across non-significant factors and were Bonferroni corrected. A threshold of $p = .05$ indicated statistical significance.

3. Results

First, to ensure that participants paid attention to the task, one-sample t-tests were performed on the results of the counting task. There were no significant differences between the number of stimuli to be counted and the numbers reported by the participants for the isochronous (number of stimuli to be counted: 147, $M = 144.65$, SD = 14.41, $t(1,42) = -1.07$, $p = .291$) and the random sequence (number of stimuli to be counted: 147, $M = 149.86$, SD = 23.41, $t(1,42) = .801$, $p = .428$) confirming that participants paid attention to the sequences.

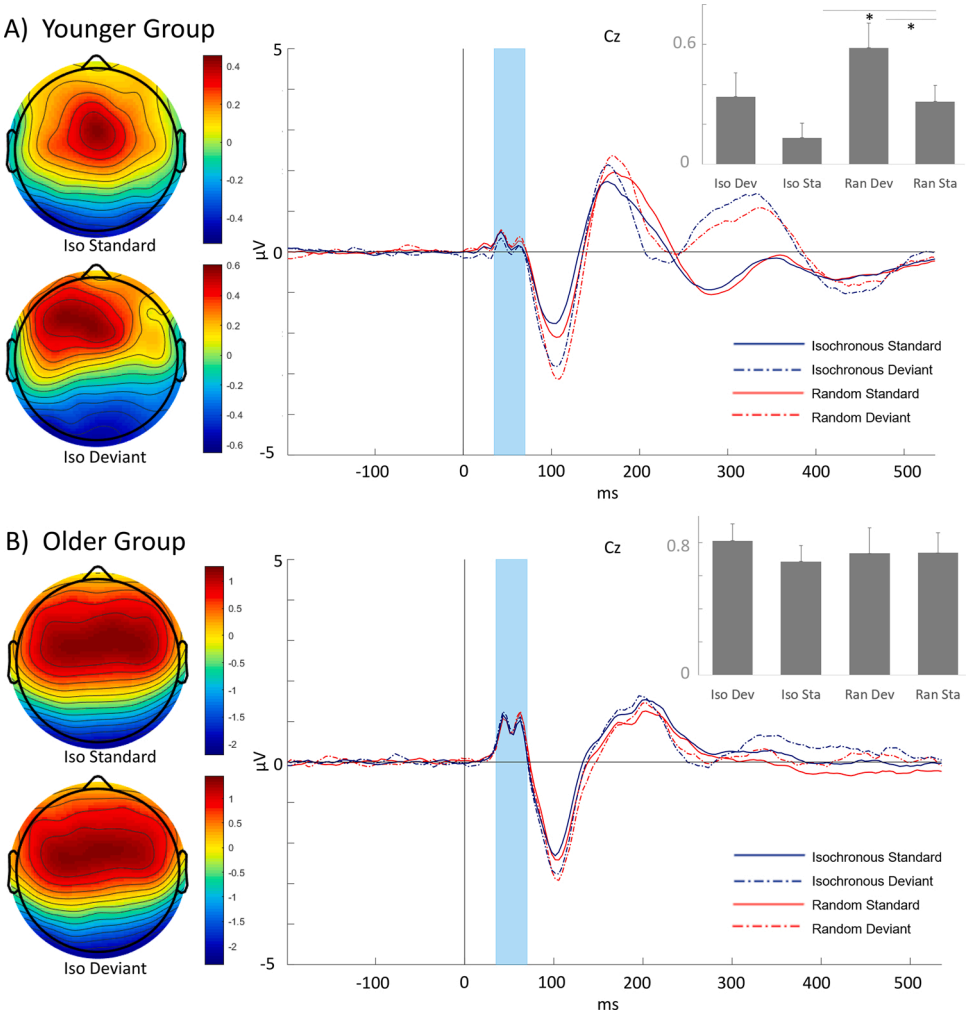

Fig. 2. ERP results for the P50 component. P50 responses and topographical maps for deviant and standard tones in the isochronous and random sequence for (A) younger and (B) older adults. The bar plot reflects local mean amplitudes of the medial-anterior ROI. For more detail see 3.1.

3.1. P50

Results and topographical maps for the P50 are presented in Fig. 2 for younger (Fig. 2A) and older adults (Fig. 2B). Although no significant main effect for Temporal structure was found ($F_{(1, 40)} = .66$; $p = .422$, $\eta^2_{partial} = .016$), main effects of Group ($F_{(1, 40)} = 4.98$; $p = .031$, $\eta^2_{partial} = .111$), Formal structure ($F_{(1, 40)} = 13.71$; $p = .001$, $\eta^2_{partial} = .255$), Region ($F_{(2, 80)} = 71.46$; $p < 001$, $\eta^2_{partial} = .641$) and Hemisphere ($F_{(2, 80)} = 5.83$; $p = .005$, $\eta^2_{partial} = .127$) were further qualified by multiple interactions, including a significant interaction between all five factors ($F_{(4, 160)} = 4.81$; $p = .002$, $\eta^2_{partial} = .107$). As we expected the P50 to be most prominently displayed in fronto-central regions (Bak, Glenthoj, Rostrup, Larsson, & Oranje, 2011), post-hoc analyses for the medial-anterior ROI were performed and indicated, specifically for the younger group, larger amplitudes ($M = 0.582$ μV) for deviant tones as opposed to standard ones ($M = 0.314$ μV) in the random sequence ($t_{(20)} = 3.02$, $p = .007$). The difference between deviant and standard tones for the isochronous sequence was non-significant ($t_{(20)} = 1.63$, $p = .119$) in the younger group. Increased amplitudes for standard tones when comparing the random ($M = 0.314$ μV) and isochronous ($M = 0.132$ μV) sequences were observed in the younger group ($t_{(20)} = -2.82$, $p = .011$). For deviant tones the difference between the isochronous and random sequence was not significant in the younger group ($t_{(20)} = -2.38$, $p = .081$; Bonferroni corrected). For the older group, no significant differences were observed for the post-hoc analyses (Formal structure in isochronous sequence: $t_{(20)} = 1.75$, $p = .096$; Formal structure in random sequence: $t_{(20)} = -.041$, $p = .967$; Temporal structure for deviant tones: $t_{(20)} = .799$, $p = .434$; Temporal structure for standard tones: $t_{(20)} = -.987$, $p = .335$).

The local peak latency measures of the P50 did not show a main effect of Group ($F_{(1, 40)} = .6$; $p = .443$, $\eta^2_{partial} = .015$), nor were the main effects for Temporal structure ($F_{(1, 40)} = 1.48$; $p = .232$, $\eta^2_{partial} = .036$), Formal structure ($F_{(1, 40)} = 2.43$; $p = .127$, $\eta^2_{partial} = .057$), Hemisphere ($F_{(2, 80)} = 1.48$; $p = .234$, $\eta^2_{partial} = .036$) or Region ($F_{(1, 40)} = .29$; $p = .681$, $\eta^2_{partial} = .007$) significant. Local latency measures of the P50 showed a three-way interaction between Deviance, Hemisphere and Group ($F_{(2, 80)} = 3.46$; $p = .039$, $\eta^2_{partial} = .080$). In addition there was a Timing by Region interaction ($F_{(2, 80)} = 3.89$; $p = .037$, $\eta^2_{partial} = .089$). Post-hoc analyses showed significantly delayed local peak latencies for deviant tones across medial regions compared to standard tones in the younger group ($t_{(20)} = 4.14$, $p = .001$). For the left ($t_{(20)} = .83$, $p = .417$) and right ($t_{(20)} = .33$, $p = .745$) regions, the effect of deviance was not significant in the younger group. In the older group, none of the deviance effects were significant for the three regions. Post-hoc tests for the timing by region interaction indicated a significant effect of Temporal structure in parietal regions ($t_{(41)} = 2.52$, $p = .016$), across groups. Moreover, when performing a one-sample *t*-test against zero in the younger group, the results indicated that there was indeed a significant effect for the P50 peak (all p-values were below $p < .000$).

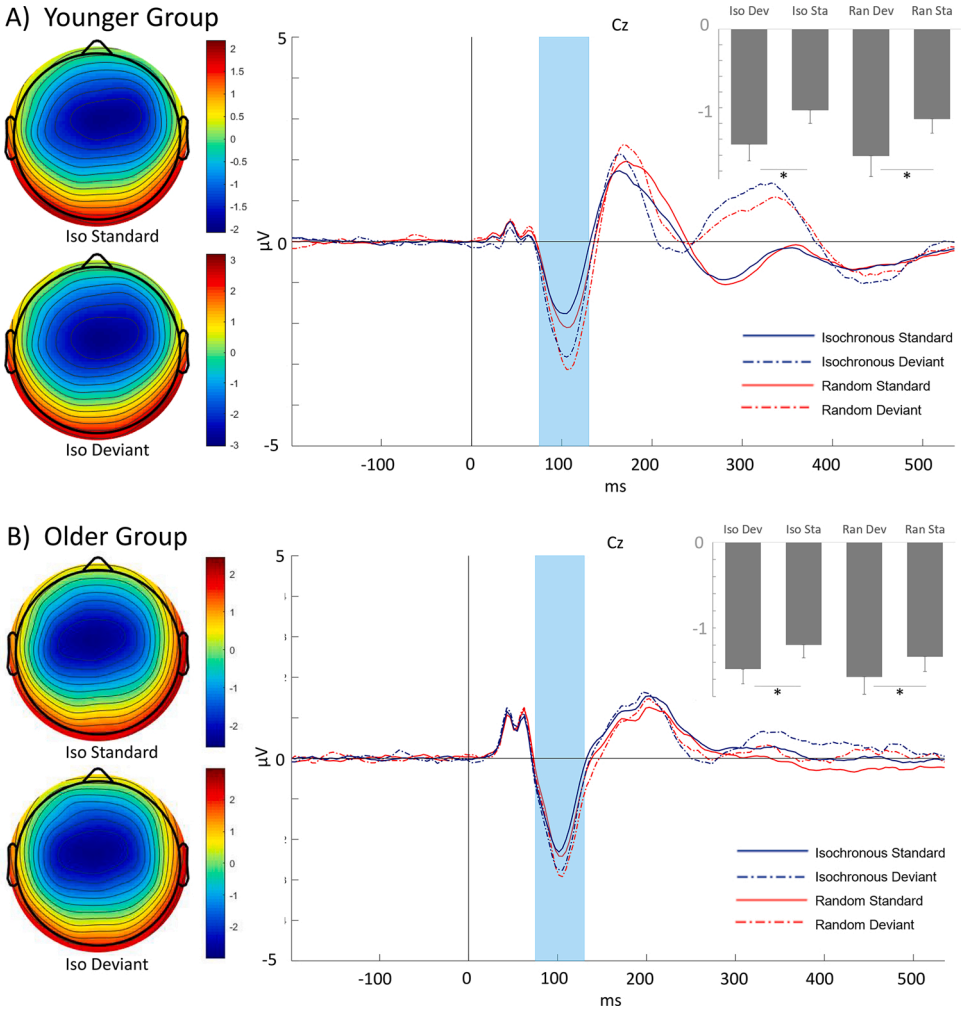

Fig. 3. ERP results for the N100 component. (A) ERP responses and topographical maps for deviant and standard tones in the isochronous or random sequence for the younger and (B) older adult group. The bar plot reflects local mean amplitudes of the medial-anterior ROI. For more detail see 3.2.

3.2. N100

Results for the local mean amplitudes of the N100 component and topographical maps are presented in Fig. 3 for younger (Fig. 3A) and older adults (Fig. 3B). Although the main effects of Group ($F_{(1, 40)} = .25$; $p = .618$, $\eta^2_{partial} = .006$) and Temporal structure ($F_{(1, 40)} = .46$; $p = .503$, $\eta^2_{partial} = .011$) were not significant, the main effects of Formal structure ($F_{(1, 40)} = 67.91$; $p < .001$, $\eta^2_{partial} = .629$), Hemisphere ($F_{(2, 80)} = 119.203$; $p < .001$, $\eta^2_{partial} = .749$) and Region ($F_{(2, 80)} = 57.73$; $p < .001$, $\eta^2_{partial} = .591$) were significant and further qualified by multiple interactions, including a significant interaction between all five factors ($F_{(4, 160)} = 4.42$; $p = .002$, $\eta^2_{partial} = .099$). As we expected the N100 to be most prominently displayed in fronto-central regions (Luck, 2014), post-hoc analyses for the medial-anterior ROI were performed. Results indicated more negative amplitudes for deviant tones ($M = -1.46$ μV) in comparison to standard tones ($M = -1.03$ μV) in the isochronous ($t_{(20)} = -4.69$, $p < .001$) and more negative amplitudes for deviant ($M = -1.61$ μV) as opposed to standard tones ($M = -1.14$ μV) in the random sequence in younger adults ($t_{(20)} = -3.98$, $p < .001$). Similar results were observed in the older group, more negative amplitudes for deviant tones ($M = -1.48$ μV) as compared to standard tones ($M = -1.2$ μV) in the isochronous ($t_{(20)} = -4.52$, $p < .001$) and more negative amplitudes for deviant tones ($M = -1.57$ μV) as opposed to standard tones ($M = -1.33$ μV) in the random ($t_{(20)} = -3.15$, $p = .005$) sequence. The differences between isochronous and random conditions were not significant in younger (deviant: $t_{(20)} = 1.77$, $p = 0.092$; standard: $t_{(20)} = 1.63$, $p = .119$) and older (deviant: $t_{(20)} = 1.25$, $p = 0.226$; standard: $t_{(20)} = 2.34$, $p = .12$; Bonferroni corrected) adults.

Analyses of the local peak latency measures showed main effects for Group ($F_{(1, 40)} = 7.59$; $p = .009$, $\eta^2_{partial} = .159$) and Deviance ($F_{(1, 40)} = 20.06$; $p < .001$, $\eta^2_{partial} = .334$), reflecting overall delayed latencies in the older group (M =101.14 ms, M younger group =99.34 ms) and overall delayed latencies for deviant tones (M =101.09 ms, M standard tones =99.39 ms). There were significant interactions between Region and Group ($F_{(2, 80)} = 14.98$; $p < .001$, $\eta^2_{partial} = .272$), and Timing and Hemisphere ($F_{(2, 80)} = 6.2$; $p = .003$, $\eta^2_{partial} = .134$). Post-hoc analyses across groups indicated an effect of Temporal structure in the medial ($t_{(41)} = -3.82$, $p < .001$) and right ($t_{(41)} = 2.58$, $p = .014$) regions, but not in the left ($t_{(41)} = .92$, $p = .36$) regions. Post-hoc analyses on Region indicated significant latency differences between groups in the anterior ($t_{(40)} = -3.72$, $p = .001$) and parietal region ($t_{(40)} = -3.94$, $p < .001$), reflecting delayed latencies for the former in younger and delayed latencies for the latter in the older group.

3.3. P200

Results for the P200 component and topographical maps are presented in Fig. 4 for younger (Fig. 4A) and older adults (Fig. 4B). While the main effect of Group ($F_{(1, 40)} = 2.52$; $p = .121$, $\eta^2_{partial} = .059$) and Temporal structure ($F_{(1, 40)} = .519$; $p = .475$, $\eta^2_{partial} = .013$) were not significant, the main effects of Formal structure ($F_{(1, 40)} = 5.57$; $p = .026$, $\eta^2_{partial} = .118$), Hemisphere ($F_{(2, 80)} = 56.63$; $p < .001$, $\eta^2_{partial} = .586$)

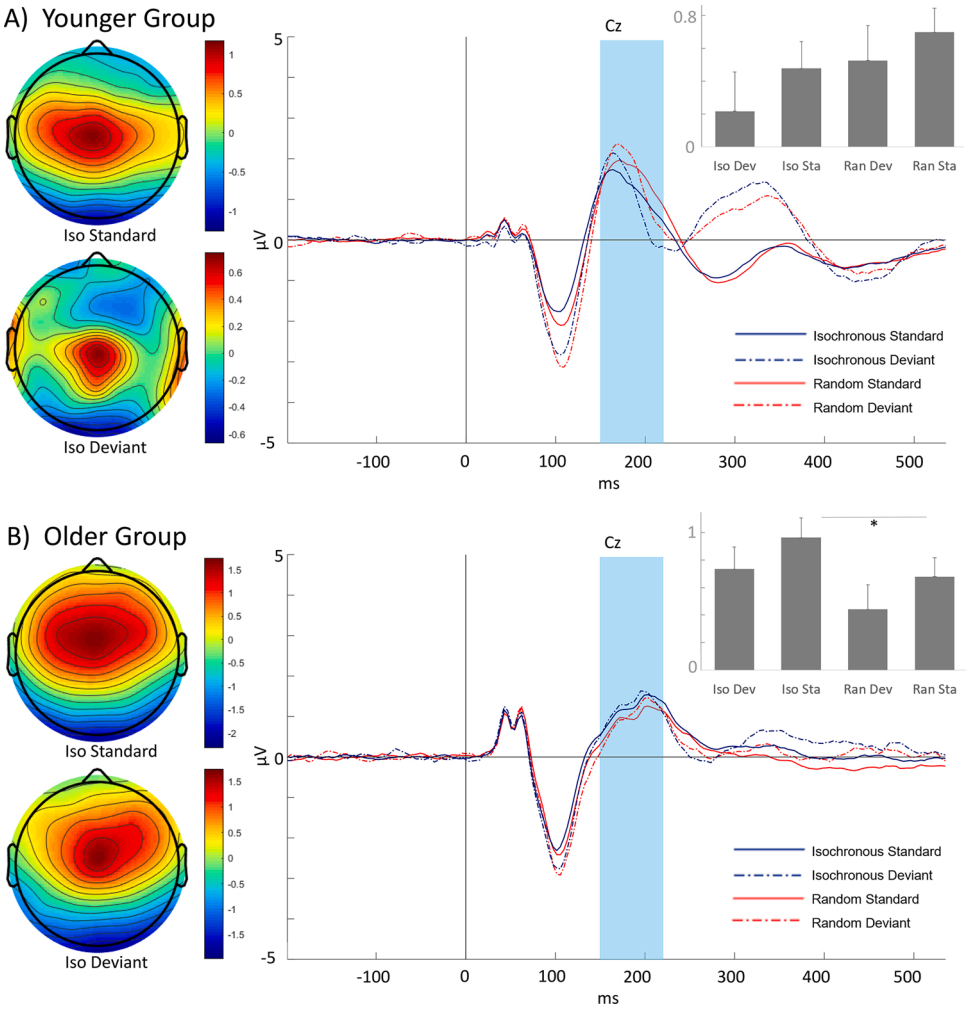

Fig. 4. ERP results for the P200 component. ERP responses and topographical maps for deviant and standard tones in the isochronous or random sequence for the (A) younger and (B) older adult group. The bar plot reflects local mean amplitudes of the medial-anterior ROI. For more detail see 3.3.

and Region ($F_{(2, 80)} = 16.4$; $p < .001$, $\eta^2_{partial} = .291$) were significant and further qualified by multiple interactions, including a significant interaction between all five factors ($F_{(4, 160)} = 2.78$; $p = .038$, $\eta^2_{partial} = .065$). We expected the P200 to be most prominently displayed in fronto-central regions (Luck, 2014). Post-hoc analyses of the medial-anterior ROI showed a marginally significant effect of Temporal structure (i.e., increased amplitudes for the random sequence ($M = .7$ μV) as opposed to the isochronous sequence, $M = .48$ μV) for standard tones in the younger group ($t_{(20)} = -2.68$, $p = .056$; Bonferroni corrected). The effect of Temporal structure for deviant tones was not significant in the younger group ($t_{(20)} = -2.14$, $p = .09$; Bonferroni corrected). Similarly, in the older group, the effect of Temporal structure for deviant tones was also not significant ($t_{(20)} = 2.59$, $p = .072$; Bonferroni corrected). For the Temporal structure, for standard tones, there was a difference between isochronous and random sequences ($t_{(20)} = 3.56$, $p = .002$), suggesting increased amplitudes for standard tones ($M = .96$ μV) in the isochronous sequence as opposed to standard tones in the random sequence ($M = .68$ μV) in the older group. The effects for Formal structure were not significant in the younger (isochronous: $t_{(20)} = -1.49$, $p = .153$; random: ($t_{(20)} = -1.03$, $p = .315$) and older group (isochronous: $t_{(20)} = -1.93$, $p = .069$; random: ($t_{(20)} = -2.29$, $p = .132$), after Bonferroni correction.

Although analyses of the local peak latencies for the P200 indicated non-significant main effects for Temporal structure ($F_{(1, 40)} = 2.37$; $p = .131$, $\eta^2_{partial} = .056$) and Formal structure ($F_{(1, 40)} = 1.64$; $p = .208$, $\eta^2_{partial} = .039$), the main effects of Group ($F_{(1, 40)} = 5.04$; $p = .030$, $\eta^2_{partial} = .112$), Hemisphere ($F_{(2, 80)} = 14.24$; $p < .001$, $\eta^2_{partial} = .262$) and Region ($F_{(2, 80)} = 13.29$; $p < .001$, $\eta^2_{partial} = .249$) were significant and further qualified by a significant five-way interaction between all factors ($F_{(1, 40)} = 5.04$; $p = .030$, $\eta^2_{partial} = .112$). As we expected the P200 to be most prominently displayed in fronto-central regions (Luck, 2014), post-hoc analyses of the medial-anterior ROI were performed and displayed a significant effect of Temporal structure for deviant tones in the younger group ($t_{(20)} = -4.58$, $p < .001$), indicating delayed latencies in the random condition ($M = 175.5$ ms) as opposed to the isochronous ones ($M = 168.56$ ms). The same effect was not significant in the older group ($t_{(20)} = -1.48$, $p = .15$). The effect of Temporal structure for standard tones was not significant in the younger group ($t_{(20)} = -.11$, $p = .915$), similar to the same effect in the older group ($t_{(20)} = .18$, $p = .86$). The effects of Formal structure were not significant in the younger (isochronous: $t_{(20)} = -1.76$, $p = .093$; random: $t_{(20)} = -.08$, $p = .941$) and older group (isochronous: $t_{(20)} = -1.32$, $p = .201$; random: $t_{(20)} = -.24$, $p = .815$). For older adults, the latencies were increasingly delayed in anterior ($M = 192.8$ ms) as opposed to central ($M = 187.6$ ms) or parietal regions ($M = 173.4$ ms).

3.4. P300

Results with respect to the P300 component and topographical maps are presented in Fig. 5 for younger (Fig. 5A) and older adults (Fig. 5B). The main effects of Group ($F_{(1, 40)} = 4.57$; $p = .039$, $\eta^2_{partial} = .102$),

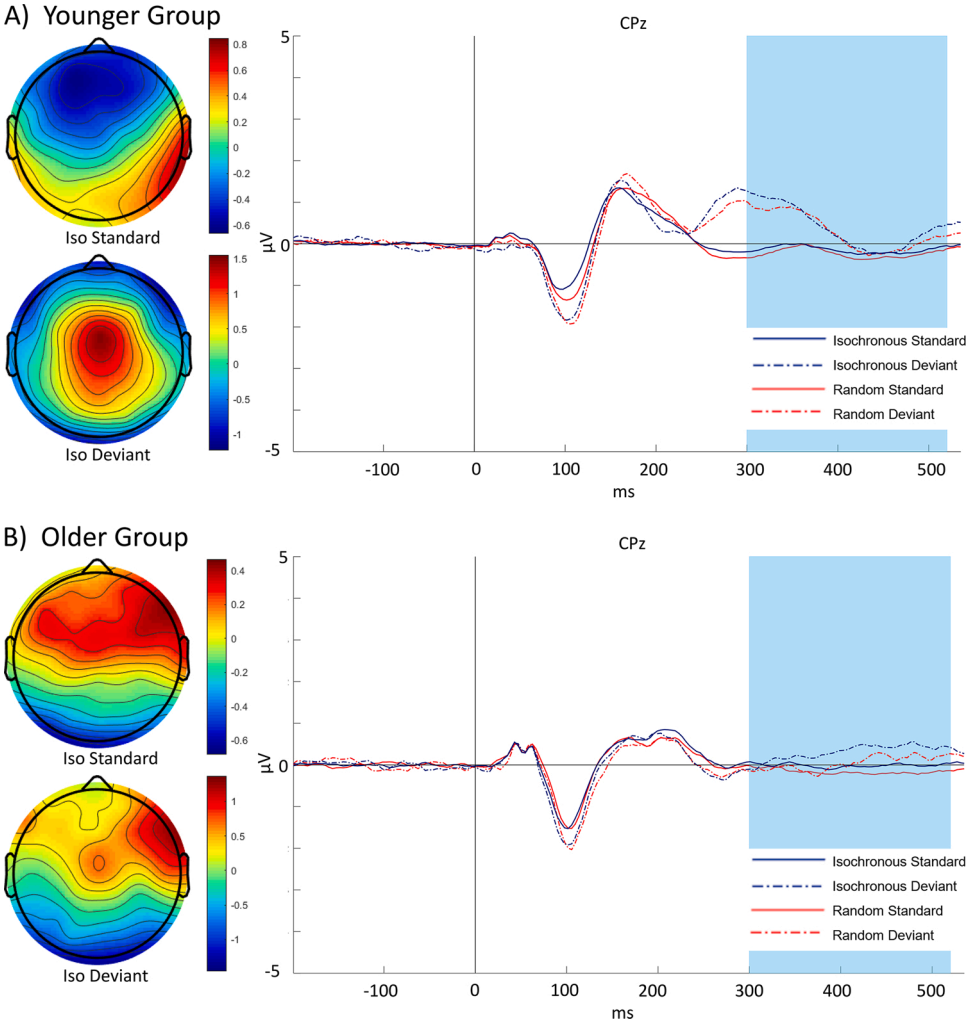

Fig. 5. ERP results for the P300 component. ERP responses and topographical maps for deviant and standard tones in the isochronous or random sequence for (A) younger adults and (B) older adults at 330 ms. For more detail see 3.4.

Temporal structure ($F_{(1, 40)} = 17.82$; $p < .001$, $\eta^2_{partial} = .308$), Formal structure ($F_{(1, 40)} = 51.36$; $p < .001$, $\eta^2_{partial} = .562$), Hemisphere ($F_{(2, 80)} = 4.25$; $p = .020$, $\eta^2_{partial} = .096$) and Region ($F_{(2, 80)} = 16.26$; $p < .001$, $\eta^2_{partial} = .289$) were significant and further qualified by multiple interactions. The analyses of the local mean amplitude for the P300 yielded a significant interaction between Formal structure, Hemisphere, Region and Group ($F_{(4, 160)} = 3.31$; $p = .020$, $\eta^2_{partial} = .076$), between Temporal structure, Region and Group ($F_{(2, 80)} = 4.49$; $p = .033$, $\eta^2_{partial} = .101$) and between Temporal structure, Hemisphere and Group ($F_{(2, 80)} = 3.32$; $p = .045$, $\eta^2_{partial} = .077$). Post-hoc comparisons for the Formal structure, Hemisphere, Region and Group interaction showed significant effects for Formal structure for the medial-central ($t_{(20)} = 4.87$, $p < .001$), medial-parietal ($t_{(20)} = 5.6$, $p < .001$), right-anterior ($t_{(20)} = -3.89$, $p = .001$) and left-anterior ($t_{(20)} = -3.46$, $p = .003$) ROIs in the younger group. For the older group significant effects of formal structure for the medial-anterior ($t_{(20)} = 3.34$, $p = .003$), right-anterior ($t_{(20)} = 4.28$, $p < .001$), left-central ($t_{(20)} = -3.5$, $p = .002$), left-parietal ($t_{(20)} = -3.96$, $p = .001$), and right-parietal ($t_{(20)} = -3.35$, $p = .003$) ROIs were observed. Post-hoc analyses for the Temporal structure, Region and Group indicated an effect for Temporal structure in the in the central region in the younger group ($t_{(20)} = 2.71$, $p = .013$), but not in the anterior ($t_{(20)} = -1.8$, $p = .087$) or parietal ($t_{(20)} = 1.6$, $p = .127$) region. In the older group, none of the regions showed a significant effect of temporal structure (anterior: $t_{(20)} = 1.45$, $p = .162$; central: $t_{(20)} = 1.84$, $p = .08$; parietal: $t_{(20)} = -1.33$, $p = .202$). Post-hoc analyses on the Temporal structure, Hemisphere and Group yielded significantly increased amplitudes in the isochronous condition as compared to the random condition in the older group in medial areas ($t_{(20)} = 3.2$, $p = .005$), but not in left ($t_{(20)} = -2.39$, $p = .081$) or right ($t_{(20)} = -.19$, $p = .85$) areas. In the younger group, none of the effects were significant (left: $t_{(20)} = -.16$, $p = .872$; medial: $t_{(20)} = .65$, $p = .53$; right: $t_{(20)} = 1.4$, $p = .17$). There was a significant Hemisphere by Group ($F_{(2, 80)} = 5.54$; $p = .007$, $\eta^2_{partial} = .122$) and Region by Group interaction ($F_{(2, 80)} = 38.4$; $p < .001$, $\eta^2_{partial} = .490$), indicating hemispheric differences only when comparing medial to right areas in the younger group ($t_{(20)} = -3.44$, $p = .003$), while the differences between left and medial ($t_{(20)} = 2.44$, $p = .072$; Bonferroni corrected), and left and right ($t_{(20)} = -1.28$, $p = .216$) were not significant. In the older group, none of the comparisons were significant (left vs medial: $t_{(20)} = -2.17$, $p = .126$;medial vs right: $t_{(20)} = -.07$, $p = .944$; left vs right: $t_{(20)} = -2.51$, $p = .063$; Bonferroni corrected). For the Region by Group interaction, significant differences were observed between anterior and parietal regions in both groups (younger: $t_{(20)} = -6.16$, $p < .001$; older: $t_{(20)} = 2.75$, $p = .012$), between central and parietal regions in both groups (younger: $t_{(20)} = -3.98$, $p = .001$; older: $t_{(20)} = 2.86$, $p = .010$) and between anterior and central regions only in the younger ($t_{(20)} = -5.58$, $p < .001$), but not in the older group ($t_{(20)} = 1.49$, $p = .153$). These effects for Region showed overall increased amplitudes for anterior regions in older and increased amplitudes for parietal regions in younger adults.

Local peak latency analyses showed main effects of Group ($F_{(1, 40)} = 14.6$; $p < .001$, $\eta^2_{partial} = .267$), Formal structure ($F_{(1, 40)} = 4.15$; $p = .048$, $\eta^2_{partial} = .094$) and Region ($F_{(2, 80)} = 14.6$; $p < .001$, $\eta^2_{partial} = .251$), but not Temporal structure ($F_{(1, 40)} = .167$; $p = .685$, $\eta^2_{partial} = .004$) and Hemisphere ($F_{(2, 80)} = 3.03$; $p = .062$, $\eta^2_{partial} = .07$), which were further qualified by multiple interactions. There was a significant interaction between Formal structure, Region and Group ($F_{(2, 80)} = 15.26$; $p < .001$, $\eta^2_{partial} = .276$), in addition to an interaction between Formal structure, Hemisphere and Group ($F_{(2, 80)} = 23.24$; $p < .001$, $\eta^2_{partial} = .367$). Post-hoc analyses in the younger group showed significant effects for Formal structure in the anterior ($t_{(20)} = 3.46$, $p = .002$) and the parietal ($t_{(20)} = -4.32$, $p < .001$), but not central ROIs ($t_{(20)} = 2.54$, $p = .06$; Bonferroni corrected). In the older group, the difference between standard and deviant tones was significant for anterior and central but not parietal areas (anterior: $t_{(20)} = -3.0$, $p = .007$; central: $t_{(20)} = -2.76$, $p = .012$; parietal: $t_{(20)} = -.39$, $p = .699$). Post-hoc tests for the Formal structure, Hemisphere and Group interaction, revealed an effect of Formal structure in the medial ($t_{(20)} = 3.7$, $p = .001$), but not left ($t_{(20)} = -2.22$, $p = .114$; Bonferroni corrected) and right ($t_{(20)} = -1.54$, $p = .139$) areas for younger adults. Similar results were observed for older adults for the medial ($t_{(20)} = -5.1$, $p = .000$), left ($t_{(20)} = .48$, $p = .636$) and right ($t_{(20)} = -.98$, $p = .341$) areas. The significant Region by Group interaction ($F_{(1, 40)} = 42.2$; $p < .001$, $\eta^2_{partial} = .513$) indicated significant differences between anterior and central ($t_{(20)} = -5.18$, $p < .001$), central and parietal ($t_{(20)} = -9.43$, $p < .001$) and anterior and parietal ($t_{(20)} = -9.64$, $p < .001$) regions in the older group, but not in the younger group (anterior vs central: $t_{(20)} = 1.02$, $p = .321$; central vs parietal: $t_{(20)} = -1.87$, $p = .076$; anterior vs parietal: $t_{(20)} = 1.96$, $p = .064$), suggesting delayed latencies in parietal regions (M =436.63 ms) as compared to central (M =372.1 ms) and anterior (M =334.7 ms) regions in older adults.

In sum, the overall pattern of results indicated an influence of age on P50 amplitude, N100, P200 and P300 latencies. The findings showed that older adults display overall enhanced P50 amplitudes and delayed latencies for N100 P200 and P300. Post-hoc tests showed a difference between isochronous and random sequences in the younger, but not in the older group for the P50. For the P50 latency, the effect of Temporal structure was visible in parietal regions. For the N100, younger and older adults displayed more negative amplitudes for deviant tones. For the P200, marginally significant amplitude reductions for the isochronous sequences were observed for standard tones in younger and increased amplitudes for standard tones in the isochronous sequence as compared to the random sequence in older adults. For the P200 latency, delayed latencies for the deviant tones in the isochronous sequence were observed in younger, but not in older adults. Lastly, for the P300 latencies, stimuli were processed earlier in anterior ROIs, followed by central ROIs and parietal ROIs in the older group. For the P300 latencies the younger group, stimuli were generally processed earlier in parietal, then in central and then anterior regions.

4. Discussion

The goal of the current study was to examine the effect of age on the neural signatures of temporal predictability in auditory sequences. Although several studies investigated the influence of age on timing capacities, few focused on ERP signatures of temporal predictability, while independently manipulating formal and temporal structure. In the present study, younger and older adults were tested and neural activity was recorded in a classic oddball paradigm. We observed differential neural signatures for temporal predictability for younger and older adults. Compared to younger participants, older adults displayed an overall increased P50 amplitude, followed by delayed N100, P200, P300 latencies in response to the manipulation of temporal and formal structure. More specifically, temporal predictability (i.e., isochronous versus random auditory sequences) interacted with age, as altered P50 amplitudes were observed in younger but not older adults. This suggests early differentiation of evoked responses between the two groups. Below, we will discuss these patterns of results in more detail.

4.1. The global effect of age and the effects of age on temporal and formal structure

Based on previous studies, we expected specific age effects on the ERP components of interest (Golob et al., 2007; Nowak et al., 2016). Our findings are generally in line with these expectations, as the results confirmed main effects of age for changes in P50 amplitude and N100, P200 and P300 latencies. The increased P50 response to temporally predictable and random tone sequences is in line with reduced sensory gating in the older group. Previously, with increased age, sensory gating was found to be decreased, as indicated by reduced paired-stimulus suppression of the P50 (Patterson et al., 2008). In turn, reduced sensory gating might be linked to less efficient inhibitory processing, considering that the P50 is at least partly generated in the frontal lobes

that regulate cognitive control (Korzyukov et al., 2007; Miller, 2000). Similar results were obtained in the context of pathologic ageing, indicating a P50 amplitude increase in patients with Alzheimer's disease (Green et al., 2015; Morrison, Rabipour, Knoefel, Sheppard, & Taler, 2018). Although the current study focused on healthy ageing, evidence from these studies suggests that sensitivity differences observed in younger and older adults may be underpinned by similar mechanisms, thus they might possibly be of quantitative nature. Moreover, the P200 and P300 peak latencies were globally delayed for deviant tones in older adults, an effect which was also found by Golob et al. (2007). It has been suggested that the P300 may serve as an index of cognitive ageing, where P300 latencies may reflect neural speed and P300 amplitudes neural power (van Dinteren, Arns, Jongsma, & Kessels, 2014). Moreover, an overall decreased P300 amplitude was observed in the elderly group. Hence, our results are generally in line with previous findings, where with increasing age, P300 target amplitudes decreased and latencies increased (Bourisly, 2016; Fjell & Walhovd, 2001; van Dinteren et al., 2014).

We expected to find interactions of ERP amplitudes and latencies by formal and temporal structure, per age group. Firstly, following the manipulation of temporal structure (i.e., isochronous versus random auditory sequences) the P50 amplitude differed between isochronous and random sequences in the younger adult group, but not in the elderly. This effect of temporal structure in younger participants could also be linked to sensory gating, suggesting less efficient temporal sensory gating for random sequences, in comparison to temporal regular ones. Therefore, the results support the role of the P50 as a marker for temporal predictability only for younger adults (Schwartze et al., 2013), while they highlight less efficient inhibitory processing for older adults. For the P200, increases in amplitude for the isochronous sequence as opposed to the random sequence were observed for standard tones in older but not in younger adults. This could also be interpreted as support for less efficient sensory gating in the elderly for isochronous sequences. Previously, similar findings were observed when investigating pitch discrimination with different foreperiods, thus manipulating temporal predictability (Herbst & Obleser, 2017).

Secondly, effects related to formal structure (i.e., standard versus deviant tones) per age group were more complex than for temporal structure in the P50 and N100 components. For the P50 latency, the processing of standard and deviant tones in the younger group differed significantly, while this was not the case in the older group. Moreover, N100 amplitude values indicated differences in formal structure in both groups similarly to reports by Schwartze, Rothermich et al. (2011). This suggests that formal structure similarly influences the mean N100 amplitude in both groups, while formal structure is distinguishable between groups regarding the P50 latency. Also, the previously mentioned P300 interactions indicate an expected response to deviance in the younger and in the older group but at different ROIs, but in anterior and parietal regions for both groups. Deviants across isochronous and random contexts exhibited larger responses in the younger as opposed to the older group, which is again, in line with the known literature (Bourisly, 2016; Fjell & Walhovd, 2001; van Dinteren et al., 2014).

Moreover, the anteriorisation of the P300 was shown in shortened latencies in anterior regions as compared to parietal regions in the older group. In addition, increased amplitudes for anterior regions were found in older adults and increased amplitudes for parietal regions in younger adults for P300 amplitudes. The anteriorisation of the P300 is a well-known effect occurring when ageing (Fallgatter, Mueller, & Strik, 1999).

To summarize, our results suggest an effect of age for P300 latency and differential processing mechanisms for the P300 amplitude responses when comparing younger with older adults. Regarding temporal structure, our results suggest differential processing mechanisms for P50 amplitude, in addition to the overall age-related amplitude increases for P50 and latency delays for N100, P200 and P300.

5. Conclusion

The present study highlights age effects on neural correlates of temporal and formal predictability. These findings provide robust evidence in support of our hypothesis that the P50 may serve as a marker of temporal predictability in younger adults. Our results further suggest that P200 amplitudes increased for the isochronous sequence as opposed to the random sequence for standard tones in older adults, while the opposite pattern was observed in younger adults. In conclusion, temporal sensory gating was less efficient in the elderly group. This could in turn influence predictive adaptation behavior in the ageing population, which is based on extracting temporally predictable events in our environment. Thus, processing the information transmitted by the initial example of the parking assistant might underlie different or less sensitive temporal predictability mechanisms in younger and older adults. To underline the importance of our results also with respect to pathological ageing, this study may serve as first step to establish a baseline, when investigating patients with neurodegenerative diseases. One may speculate that patients diagnosed with Alzheimer's or Parkinson's disease display an even increased temporal sensory gating impairment.

Future studies, examining age effects for neural signatures of temporal predictability, should try to disentangle whether the observed age-related differences for temporal structure are based on quantitative or qualitative nature (i.e., the same mechanism, but less sensitive or two different kinds of mechanisms).

Funding

SDB was supported by the Natural Sciences and Engineering Research Council of Canada (NSERC) with a Discovery grant RGPIN-2019-05453. Pia Brinkmann was supported by the Doctorate Scholarship of the German Academic Scholarship Foundation (Studienstiftung des Deutschen Volkes).

Declaration of Competing Interest

The authors report no declarations of interest.

References

Allman, M. J., & Meck, W. H. (2011). Pathophysiological distortions in time perception and timed performance. *Brain, 135*(3), 656–677.

Baess, P., Jacobsen, T., & Schröger, E. (2008). Suppression of the auditory N1 event-related potential component with unpredictable self-initiated tones: Evidence for internal forward models with dynamic stimulation. *International Journal of Psychophysiology, 70*(2), 137–143.

Bak, N., Glenthoj, B. Y., Rostrup, E., Larsson, H. B., & Oranje, B. (2011). Source localization of sensory gating: A combined EEG and fMRI study in healthy volunteers. *Neuroimage, 54*(4), 2711–2718.

Benoit, C.-E., Dalla Bella, S., Farrugia, N., Obrig, H., Mainka, S., & Kotz, S. A. (2014). Musically cued gait-training improves both perceptual and motor timing in Parkinson's disease. *Frontiers in Human Neuroscience, 8*, 494.

Bourisly, A. K. (2016). Effects of aging on P300 between late younger-age and early middle-age adulthood: An electroencephalogram event-related potential study. *NeuroReport, 27*(14), 999–1003.

Breska, A., & Ivry, R. B. (2018). Double dissociation of single-interval and rhythmic temporal prediction in cerebellar degeneration and Parkinson's disease. *Proceedings of the National Academy of Sciences, 115*(48), 12283–12288.

Canolty, R. T., & Knight, R. T. (2010). The functional role of cross-frequency coupling. *Trends in Cognitive Sciences, 14*(11), 506–515.

Carroll, C. A., Boggs, J., O'Donnell, B. F., Shekhar, A., & Hetrick, W. P. (2008). Temporal processing dysfunction in schizophrenia. *Brain and Cognition, 67*(2), 150–161.

Cunnington, R., Iansek, R., Bradshaw, J. L., & Phillips, J. G. (1995). Movement-related potentials in Parkinson's disease: Presence and predictability of temporal and spatial cues. *Brain, 118*(4), 935–950.

Dalla Bella, S., Benoit, C.-E., Farrugia, N., Keller, P. E., Obrig, H., Mainka, S., & Kotz, S. A. (2017). Gait improvement via rhythmic stimulation in Parkinson's disease is linked to rhythmic skills. *Scientific Reports, 7*, 42005.

Dankner, Y., Shalev, L., Carrasco, M., & Yuval-Greenberg, S. (2017). Prestimulus inhibition of saccades in adults with and without attention-deficit/hyperactivity disorder as an index of temporal expectations. *Psychological Science, 28*(7), 835–850.

Delorme, A., & Makeig, S. (2004). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods, 134*(1), 9–21.

Fallgatter, A., Mueller, T. J., & Strik, W. (1999). Age-related changes in the brain electrical correlates of response control. *Clinical Neurophysiology, 110*(5), 833–838.
Fjell, A. M., & Walhovd, K. B. (2001). P300 and neuropsychological tests as measures of aging: Scalp topography and cognitive changes. *Brain Topography, 14*(1), 25–40.
Fraisse, P. (1984). Perception and estimation of time. *Annual Review of Psychology, 35*(1), 1–37.
Golob, E. J., Irimajiri, R., & Starr, A. (2007). Auditory cortical activity in amnestic mild cognitive impairment: Relationship to subtype and conversion to dementia. *Brain, 130*(3), 740–752.
Green, D. L., Payne, L., Polikar, R., Moberg, P. J., Wolk, D. A., & Kounios, J. (2015). P50: A candidate ERP biomarker of prodromal Alzheimer′ s disease. *Brain Research, 1624*, 390–397.
Hart, H., Marquand, A. F., Smith, A., Cubillo, A., Simmons, A., Brammer, M., & Rubia, K. (2014). Predictive neurofunctional markers of attention-deficit/hyperactivity disorder based on pattern classification of temporal processing. *Journal of the American Academy of Child & Adolescent Psychiatry, 53*(5), 569-578. e561.
Henry, M. J., Herrmann, B., Kunke, D., & Obleser, J. (2017). Aging affects the balance of neural entrainment and top-down neural modulation in the listening brain. *Nature Communications, 8*, 15801.
Herbst, S. K., & Obleser, J. (2017). Implicit variations of temporal predictability: Shaping the neural oscillatory and behavioural response. *Neuropsychologia, 101*, 141–152.
Ivry, R. B., & Keele, S. W. (1989). Timing functions of the cerebellum. *Journal of Cognitive Neuroscience, 1*(2), 136–152.
Jones, M. R. (1976). Time, our lost dimension: Toward a new theory of perception, attention, and memory. *Psychological Review, 83*(5), 323.
Jones, M. R. (2018). *Time will tell: A theory of dynamic attending*. Oxford University Press.
Knolle, F., Schröger, E., Baess, P., & Kotz, S. A. (2012). The cerebellum generates motor-to-auditory predictions: ERP lesion evidence. *Journal of Cognitive Neuroscience, 24*(3), 698–706.
Knolle, F., Schwartze, M., Schröger, E., & Kotz, S. A. (2019). Auditory predictions and prediction errors in response to self-initiated vowels. *bioRxiv*, Article 671990.
Korzyukov, O., Pflieger, M. E., Wagner, M., Bowyer, S. M., Rosburg, T., Sundaresan, K., & Boutros, N. N. (2007). Generators of the intracranial P50 response in auditory sensory gating. *Neuroimage, 35*(2), 814–826.
Kotz, S. A., Ravignani, A., & Fitch, W. (2018). The evolution of rhythm processing. *Trends in Cognitive Sciences, 22*(10), 896–910.
Kotz, S. A., Stockert, A., & Schwartze, M. (2014). Cerebellum, temporal predictability and the updating of a mental model. *Philosophical Transactions of the Royal Society B: Biological Sciences, 369*(1658), Article 20130403.
Lakatos, P., Chen, C.-M., O'Connell, M. N., Mills, A., & Schroeder, C. E. (2007). Neuronal oscillations and multisensory interaction in primary auditory cortex. *Neuron, 53*(2), 279–292.
Large, E. W. (2008). Resonating to musical rhythm: Theory and experiment. *The psychology of time* (pp. 189–232).
Large, E. W., & Jones, M. R. (1999). The dynamics of attending: How people track time-varying events. *Psychological Review, 106*(1), 119.
Large, E. W., & Kolen, J. F. (1994). Resonance and the perception of musical meter. *Connection Science, 6*(2), 177–208.
Linden, D. E. (2005). The P300: where in the brain is it produced and what does it tell us? *The Neuroscientist, 11*(6), 563–576.
Lopez-Calderon, J., & Luck, S. J. (2014). ERPLAB: An open-source toolbox for the analysis of event-related potentials. *Frontiers in Human Neuroscience, 8*, 213.
Luck, S. J. (2014). *An introduction to the event-related potential technique*. MIT press.
McAuley, J. D., Jones, M. R., Holub, S., Johnston, H. M., & Miller, N. S. (2006). The time of our lives: Life span development of timing and event tracking. *Journal of Experimental Psychology: General, 135*(3), 348.
Miller, E. K. (2000). The prefontral cortex and cognitive control. *Nature Reviews Neuroscience, 1*(1), 59.
Miyakoshi, M. (2018). *Makoto's preprocessing pipeline*.
Morrison, C., Rabipour, S., Knoefel, F., Sheppard, C., & Taler, V. (2018). Auditory event-related potentials in mild cognitive impairment and Alzheimer's disease. *Current Alzheimer Research, 15*(8), 702–715.
Mullen. (2012). *CleanLine EEGLAB plugin*. San Diego, CA: Neuroimaging Informatics Toolsand Resources Clearinghouse (NITRC).
Mullen, K., Chi, O., Kerth, M., & Cauwenberghs. (2015). Real-time neuroimaging and cognitive monitoring using wearable dry EEG. *IEEE Transactions on Biomedical Engineering, 62*(11), 2553–2567.
Näätänen, R., & Picton, T. (1987). The N1 wave of the human electric and magnetic response to sound: A review and an analysis of the component structure. *Psychophysiology, 24*(4), 375–425.
Nobre, & van Ede, F. (2018). Anticipated moments: Temporal structure in attention. *Nature Reviews Neuroscience, 19*(1), 34.
Nobre, Correa, A., & Coull, J. T. (2007). The hazards of time. *Current Opinion in Neurobiology, 17*(4), 465–470.
Nowak, K., Oron, A., Szymaszek, A., Leminen, M., Näätänen, R., & Szelag, E. (2016). Electrophysiological indicators of the age-related deterioration in the sensitivity to auditory duration deviance. *Frontiers in Aging Neuroscience, 8*, 2.
Patterson, J. V., Hetrick, W. P., Boutros, N. N., Jin, Y., Sandman, C., Stern, H., … Bunney, W. E., Jr. (2008). P50 sensory gating ratios in schizophrenics and controls: A review and data analysis. *Psychiatry Research, 158*(2), 226–247.
Polich, J., & Criado, J. R. (2006). Neuropsychology and neuropharmacology of P3a and P3b. *International Journal of Psychophysiology, 60*(2), 172–185.
Puyjarinet, F., Bégel, V., Gény, C., Driss, V., Cuartero, M.-C., Kotz, S. A., & Dalla Bella, S. (2019). Heightened orofacial, manual, and gait variability in Parkinson's disease results from a general rhythmic impairment. *NPJ Parkinson's Disease, 5*(1), 1–7.
Rasco, L., Skinner, R. D., & Garcia-Rill, E. (2000). Effect of age on sensory gating of the sleep state-dependent P1/P50 midlatency auditory evoked potential. *Sleep Research Online, 3*(3), 97–105.
Sauvé, S. A., Bolt, E. L., Fleming, D., & Zendel, B. R. (2019). The impact of aging on neurophysiological entrainment to a metronome. *NeuroReport, 30*(10), 730–734.
Schafer, E. W., & Marcus, M. M. (1973). Self-stimulation alters human sensory brain responses. *Science, 181*(4095), 175–177.
Schiff, S., Valenti, P., Andrea, P., Lot, M., Bisiacchi, P., Gatta, A., & Amodio, P. (2008). The effect of aging on auditory components of event-related brain potentials. *Clinical Neurophysiology, 119*(8), 1795–1802.
Schwartze, M., Farrugia, N., & Kotz, S. A. (2013). Dissociation of formal and temporal predictability in early auditory evoked potentials. *Neuropsychologia, 51*(2), 320–325.
Schwartze, M., Keller, P. E., Patel, A. D., & Kotz, S. A. (2011). The impact of basal ganglia lesions on sensorimotor synchronization, spontaneous motor tempo, and the detection of tempo changes. *Behavioural Brain Research, 216*(2), 685–691.
Schwartze, M., Rothermich, K., Schmidt-Kassow, M., & Kotz, S. A. (2011). Temporal regularity effects on pre-attentive and attentive processing of deviance. *Biological Psychology, 87*(1), 146–151.
Sharbrough, F. (1991). American Electroencephalographic Society guidelines for standard electrode position nomenclature. *Journal of Clinical Neurophysiology, 8*, 200–202.
Smith, D. A., Boutors, N. N., & Schwartzopf, S. B. (1994). Reliability of P50 auditory event-related potential indices of sensory gating. *Psychophysiology, 31*(5), 495–502.
Squires, N. K., Squires, K. C., & Hillyard, S. A. (1975). Two varieties of long-latency positive waves evoked by unpredictable auditory stimuli in man. *Electroencephalography and Clinical Neurophysiology, 38*(4), 387–401.
Tomé, D., Barbosa, F., Nowak, K., & Marques-Teixeira, J. (2015). The development of the N1 and N2 components in auditory oddball paradigms: A systematic review with narrative analysis and suggested normative values. *Journal of Neural Transmission, 122*(3), 375–391.
van Dinteren, R., Arns, M., Jongsma, M. L., & Kessels, R. P. (2014). P300 development across the lifespan: A systematic review and meta-analysis. *PloS One, 9*(2), Article e87347.
Vanneste, S., Pouthas, V., & Wearden, J. H. (2001). Temporal control of rhythmic performance: A comparison between younger and older adults. *Experimental Aging Research, 27*(1), 83–102.