The impact of aging on neurophysiological entrainment to a metronome

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In music, entrainment to the beat allows listeners to make predictions about upcoming events. Previous work has shown that neural oscillations will entrain to the beat of the music or rhythmic stimuli. Despite the fact that aging is known to impact both auditory and cognitive processing, little is known about how aging affects neural entrainment to rhythmic stimuli. In this study, younger and older participants listened to isochronous sequences at a slower and faster rate while EEG data was recorded. Steady-state evoked potentials had amplitude peaks at the stimulus rate and its harmonics. Steady-state evoked potentials at the stimulus rate and the first harmonic was attenuated in older adults compared to younger adults. Additionally, no amplitude difference was found for the second and third harmonics in older adults, while there was a decrease in amplitude in younger adults. This age-related decline in the entrainment specificity of the brain responses to the stimulus rate, suggests that aging may decrease the ability to entrain to stimuli in the environment, and further suggests that older adults may be less able to inhibit neural entrainment that is not directly related to the incoming stimulus. *NeuroReport* 30:730–734 Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

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Introduction

Neural entrainment is an automatic process where neural oscillations synchronize with environmental events [1]. There have been few studies on neural entrainment in older adults. Henry *et al.* [2] reported that neural entrainment to a target frequency was reduced in older adults, but only when they were engaged in a task that required them to attend to the stimulus. In this study they used continuous tones that were frequency-modulated at 2.8 Hz, corresponding to the frequency range of speech sound envelopes. An earlier study that focused only on neural responses to frequency-modulated complex tones during passive listening found that the strength of neural entrainment was larger in older adults for frequencies above 8 Hz [3]. In both studies, there was a continuous auditory stimulation modulated at a frequency similar to speech rhythms. There is also evidence of age effects in automatic (P1-N1-P2 [4]) and attentive (P3, CNV [5]) components of evoked responses. Specifically, that the P1-N1-P2 is enhanced while P3 and CNV latencies increase by ~20 ms per decade in older adults.

In music, entrainment is a core component of rhythm perception and rhythms can be established by modulating the amplitude of a stimulus, such as a drum hit. The impact of aging on neural entrainment to rhythmic stimuli at similar rates to what is found in music has been little explored. Exploring the neurophysiology of music in older adults is important because emerging research on tonal structure suggests that music perception may be less impacted by aging compared to other domains of auditory processing like speech perception [6–10].

The ability to perceive musical beat is necessary to make predictions about upcoming events in music [11]. When listening to music, listeners align with the beat, the perception of a periodicity which is often but not necessarily, present in the signal itself [12]. The resonance theory proposes that the synchronicity of neural populations oscillating at the frequency of the beat is a core component of beat perception [12]. Recent support for this theory comes from Nozaradan *et al.* [13], where steady-state evoked-potentials (SS-EPs) were recorded for listeners hearing a sound pattern containing a 2.4 Hz beat. The SS-EPs showed amplitude peaks at 2.4 Hz, as well as at either 1.2 Hz for listeners imagining a binary meter and at 0.8 and 1.6 Hz for listeners imagining a ternary meter, where meter refers to beat groupings. This was repeated for syncopated rhythms [14] and with movement synchronization [15], providing support for the resonance theory.

This study investigated neural entrainment to amplitude-modulated tones at a slower (2.5 Hz) and faster (5 Hz) rate in older and younger adults. It was expected that these stimuli would evoke an SS-EP at the stimulus rate and harmonics of that rate. In younger adults, inhibitory processes automatically suppress the activation of irrelevant information at the neurophysiological level, and in the case of SS-EPs, this suggests that the amplitude of the SS-EPs should decrease in the higher harmonics of the stimulus frequency. The inhibition theory of aging [16] posits that aging results in a decrease in

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Table 1 Participant demographics

	Age	Formal education (years)[a]	Pure-tone average (dB HL)[b]
Younger adults	20.3 (1.84)	14.6 (2.23)	6.2 (5.07)
Older adults	63.4 (3.68)	12.87 (3.46)	13.28 (9.03)

$P < 0.001$; SD in brackets.
[a]Older versus younger: $t(28) = 1.6$, $P = 0.12$; SD in brackets.
[b]Binaural average of pure-tone threshold at 500, 1000 and 2000 Hz; older versus younger: $t(28) = 40.55$,

automatic inhibitory control. Age-related decline in inhibitory control leads to hyper activation of brain regions, making it difficult to differentiate between relevant and irrelevant information. In the current context, the inhibition theory suggests that oscillatory activity at harmonics of the stimulus frequency would be less dampened in older adults. This could lead to a weaker encoding of the stimulus frequency so that there is less differentiation between neural oscillatory activity at the stimulus frequency and its harmonics in older adults compared to younger adults. On the other hand, a rhythm perception study in older adults [17] asked participants to identify familiar melodies that were either slowed down, and sped up until recognized, or sped up and slowed down until they were recognized. They found that older adults performed as well as younger adults when identifying the slow-to-fast melodies but performed worse when identifying the fast-to-slow melodies. The authors interpreted this finding as being related to cognitive slowing [18], which posits difficulty encoding fast incoming information. This theory suggests that neural entrainment to isochronous rhythms should be impacted by age for faster but not slower rhythms. Thus, an age effect in both tempi conditions would support an inhibition theory of aging while an age effect in the fast tempo condition alone would support a cognitive slowing theory of aging.

Materials and methods

Participants

Twenty-nine participants were recruited for the study and provided written informed consent in accordance with the Interdisciplinary Committee on Ethics in Human Research at the Memorial University of Newfoundland. Participants were divided into two age groups: 15 older adults (60–73 years; 10 female) and 14 younger adults (18–25 years; seven female). All participants self-reported being healthy, right-handed and free of any cognitive deficit. All participants were nonmusicians although some had music training in childhood. Hearing abilities were assessed using pure-tone audiometry (PTA). As expected, older adults had significantly higher hearing thresholds than younger adults (Table 1). All participants received a small cash honorarium for their participation. Table 1 summarizes participant demographics.

Stimuli and task

Stimuli were 250 Hz tones generated in Audacity (version 2.1.3; *https://www.audacityteam.org/copyright/*), presented at 75 dB SPL with 10 ms onset and offset ramps. Tones were presented isochronously in two tempo conditions, with order counterbalanced across participants. In the Fast condition, tones were 100 ms long, and had an inter-stimulus interval of 100 ms (inter-stimulus onset interval of 200 ms to 5 Hz), and in the slow condition tones were 200 ms long and had an inter-stimulus interval of 200 ms (inter-stimulus onset interval of 400 ms to 2.5 Hz). These tempi match two of Nozaradan *et al.*'s [15]. Each condition lasted 504 s. Stimuli were presented using E-Prime 3.0 (Psychology Software Tools, Sharpsburg, Pennsylvania, USA) and Etymonic ER-3A insert headphones. Participants were seated in a double-walled, electrically shielded sound-attenuating booth, and were invited to watch a self-selected silent (subtitled) movie. The use of silent movies has been shown to be an effective way of maintaining alertness, without impacting the neurophysiology of the auditory response [19].

Recording and processing of neuroelectric activity

Neuroelectric brain activity was digitized at a sampling rate of 1024 Hz from 128 electrodes using the radial layout system, with a high pass filter set at 0.1 Hz using a Biosemi ActiveTwo system (Biosemi Inc., Amsterdam, The Netherlands). Six additional electrodes were placed bilaterally at mastoid, inferior ocular, and lateral ocular sites.

Data were analysed using the Letswave signal [20] processing toolbox for Matlab (MathWorks, Natick, Massachusetts, USA). Eye blinks and eye movements were identified for each participant using an independent component analysis and the signal was referenced to an average reference. Each condition was divided into 10 48 s blocks and then averaged into a single 48 s event-related potential (ERP), yielding two ERPs (fast, slow). The first 24 s of each condition was excluded from the analysis to allow time for neuronal entrainment. A fast Fourier transform was applied to both ERPs to calculate the SS-EP. The SS-EP was baseline corrected using a signal-to-noise ratio baseline analysis. This function expresses the amplitude of a frequency spectra relative to the amplitude of the spectra obtained from 10 adjacent frequency bins. For more information see Nozaradan *et al.* [13].

For each tempo (fast, slow) the spectral amplitudes at targeted frequency bins were extracted from a montage of frontocentral electrodes (A1 [Cz], C1, C2, C11, C12, C21 [Fz], C22, C23, C24, C25, D1, D2), selected based on signal distribution (Fig. 2) consistent with previous work [14,15]. These targeted steady-state frequencies (SSFrq) included the stimulus rate (slow: 2.5 Hz; fast

5 Hz) and the first three harmonics (H1–H3) of the stimulus rate frequency (slow: 5, 7.5, and 10 Hz; fast: 10, 15, and 20 Hz). Frequency bins were 0.1 Hz wide, corresponding to each SSFrq plus or minus 0.05 Hz, accounting for possible individual differences in entrainment between participants and trials. To summarize, each data point consisted of a spectral amplitude value (μV) for a given SSFrq, electrode, tempo and participant.

Analysis

A mixed design analysis of variance was calculated in SPSS (version 21) and included tempo (slow, fast) and SSFrq (SF, H1, H2, H3) as within-subject factors, age group (older, younger) as a between-subject factor (Fig. 1) and PTA average (average of threshold at 500, 1000 and 2000 Hz) as a covariate. This covariate was included in order to account for any reduced SSFrq amplitude that might be due to higher PTA thresholds in older adults. Alpha was set at 0.05, however, we also considered effects significant where the effect size (η^2) was greater than 0.1, and the P value was below 0.1. This effect size would be considered a medium to large size based on Cohen's guidelines [21]. Bonferroni correction was applied in follow-up tests.

Results

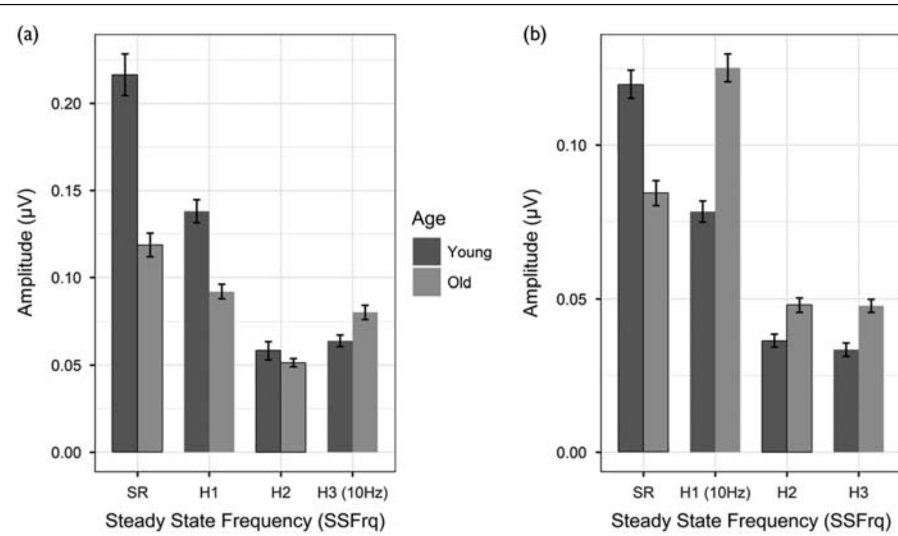
The overall effects of tempo and SSFrq were both significant [$F(1, 26)=4.71$, $P=0.039$, $\eta^2=0.15$ and $F(3, 78)=16.64$, $P<0.001$, $\eta^2=0.39$, respectively], where SSFrq amplitude is larger in the slow tempo as compared to the fast tempo, and SF > H1, H1 > H2 and H2 = H3. The overall effect of age group was not significant [$F(1, 26)=0.98$, $P=0.75$, $\eta^2=0.004$], however, the tempo and SSFrq factors both interacted with age group [$F(1, 26)=5.70$, $P=0.025$, $\eta^2=0.18$ and $F(3, 78)=4.75$, $P=0.004$, $\eta^2=0.15$, respectively]. First, pairwise comparisons in younger adults revealed greater oscillatory power in the slow tempo compared to the fast tempo ($P=0.009$). This effect was similar but reduced in older adults ($P=0.034$). Second, for younger adults, there was a reduction in SSFrq amplitude between SF and H1 ($P=0.006$) and between H1 and H2 ($P<0.001$). There was no difference between H2 and H3 ($P=0.87$). For older adults, the pattern differed. There was no difference in SSFrq amplitude between SF and H1 ($P=0.62$); a reduction between H1 and H2 ($P<0.001$) and an increase between H2 and H3 ($P=0.049$).

Discussion

Overall, neural entrainment at target frequencies closest to the stimulus rates tested (2.5 and 5 Hz) was weaker in older adults compared to younger adults, while no age difference was observed at higher harmonics. In younger adults, amplitude decreased from stimulus rate to the highest harmonic while in older adults, there was no such selectivity of the stimulus rate.

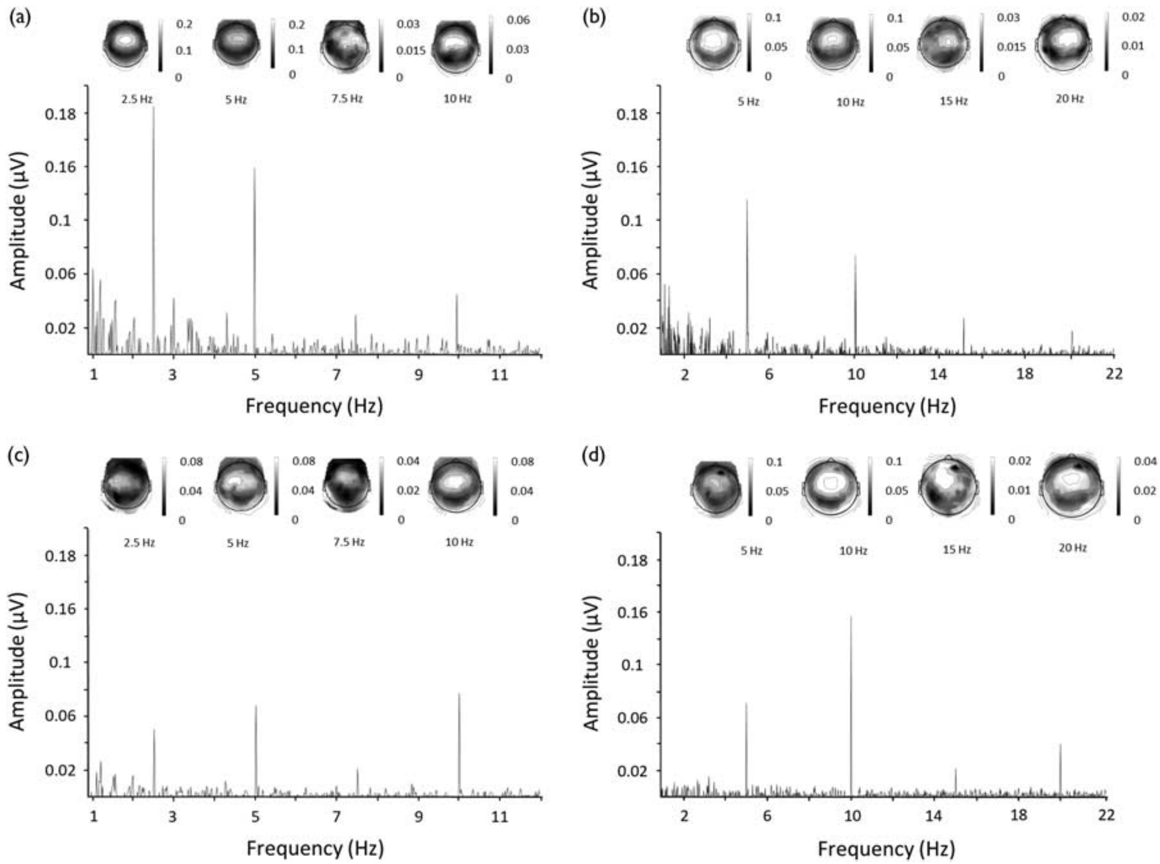
This pattern of results suggests that the automatic processing of auditory temporal regularities in the environment is both reduced and less specific to the stimulus in older adults, regardless of tempo. This is consistent with an inhibition theory of aging [16], where the automatic inhibition of irrelevant information is poorer in older adults. In the context of neural entrainment, this equates less dampening of oscillatory activity at the stimulus rate frequency's harmonics and weaker encoding of the stimulus rate frequency itself. Our results demonstrate this pattern, where older adults display a flatter peak profile than younger adults (Figs 1 and 2). On the other hand, a cognitive slowing theory of aging would suggest an age effect at a fast tempo but not at a slow tempo, which is not supported by our data.

Fig. 1



Mean peak spectral amplitude for stimulus rate (SR) and first three harmonics (H1–H3) for younger and older listeners at slow (2.5 Hz; a) and fast (5 Hz; b) tempi. 10 Hz peaks are identified on the *x*-axis. Error bars represent SEM.

Fig. 2



Amplitude of frequencies at electrode Cz for young (a, c) and old (b, d) adults, ranging from 0.9 to 12 Hz for slow (a, b) and from 0.9 to 22 Hz for fast (c, d) tempi along with topographic maps corresponding to each extracted stimulus rate and its harmonics.

It is worth noting previously observed age effects in automatic auditory evoked responses, where older adults demonstrate larger amplitudes at each peak in the P1-N1-P2 complex [4]. The oscillations of this complex correspond to a rate of 10 Hz, the third harmonic of this study's slow tempo and the first harmonic of the fast tempo. An increase in amplitude at 10 Hz is indeed observed in this study, particularly in older adults in the fast tempo, with a less pronounced difference also observable in the slow tempo.

This pattern of results suggests that neural entrainment to amplitude modulation may be impacted by aging. If aging reduces the neural differentiation between the modulation frequency and harmonics of that frequency, then identifying and synchronizing to a stimulus like a musical beat may be more difficult for older adults, where information about higher harmonics, the musical equivalent of beat subdivisions, are poorly dampened. As musical beat gives rise to meter, an important aspect of musical structure [22], a misinterpretation of the beat level could also affect meter perception. Alternatively, it is possible that attention-dependant processes may be able to overcome this encoding deficit. It has been shown in speech perception that older adults are better able to make use of contextual cues in order to understand speech in difficult listening situations [23]. Accordingly, in active beat finding studies using more realistic music stimuli, older adults may be able to compensate for the encoding deficit by using acquired knowledge of musical structure to identify the beat in music.

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Conflicts of interest

There are no conflicts of interest.

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