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Age-Related Decline in Neural Synchrony and the FFR

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In

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for the degree of

Doctor of Audiology

Department of Communication Sciences and Disorders

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FACULTY COMMITTEE:

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DEDICATION

I would like to dedicate this dissertation to my partner, Jacob. Throughout the last several years, you have been an unshakable source of support and a wealth of kindness and compassion in the midst of some truly unprecedented times. Your encouragement has been instrumental to my success and, at times, my sanity. Words could never be enough to thank you for all of the late nights and long days spent studying with me, two-hour trips to see me every weekend, and moving across the country to tackle my fourth year together. Your heart, patience, and generosity are my constant inspiration.

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Finally, I must thank all the members of the Harrisonburg community who took the time to complete the several hours of data collection necessary in order to participate in this study. Without them, this dissertation would not have been possible.

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Abstract

It is a known phenomenon that speech understanding in background noise declines with advancing age. Although there is ample evidence of behavioral measures declining with age, there is less physiologic evidence. This study hypothesizes that the FFR will be degraded with advancing age, consistent with poorer phase locking. This is hypothesized to be present even in people with audiograms within normal limits. A second hypothesis is that middle-aged adults will have degraded neural representation as frequency increases, compared to a younger normal hearing group which will have better high frequency neural representation than the middle-aged group. Subjects were divided into two age groups: young (21-30 years old, n = 17, average age 23) and middle-aged (41-50 years old, n = 5, average age 44) adults. Each subject underwent twelve conditions of the FFR. Four frequencies were recorded (500, 750, 1,000, and 1,125 Hz). Each frequency was recorded in a left ear, right ear, and binaural condition. When comparing the data of young normal participants with that of middle-aged participants, it was seen that amplitudes were largest in younger participants. Additionally, amplitudes were biggest in low frequencies, and amplitudes were smallest in higher frequencies across both age groups. The largest amplitudes were seen in the binaural conditions. In general, larger stimulus-to-response correlations were observed in the younger group. Smaller correlations were observed in the middle-aged group. Results of this study could be used in patient counseling, and in the formulation of more tailored and informed treatment plans (particularly in aged individuals).

CHAPTER 1

REVIEW OF THE LITERATURE

Introduction

The Frequency-Following Response (FFR) relies on sustained, phase-locked activity to the carrier frequency of the stimulus to show the integrity of neurons throughout the brainstem- primarily the inferior colliculus. Although there is ample evidence of the decline in behavioral measures with aging, there is less evidence regarding physiological measures (especially those utilizing phase locking measures). In this study, it is hypothesized that the FFR will be degraded with advancing age, consistent with poorer neural synchrony/phase locking. A second hypothesis examined in this study is that the age-effects will be more pronounced in the higher frequencies. In other words, middle-aged adults will have degraded neural representation as frequency increases, compared to a younger normal hearing group which will have better neural representation than the older group.

Binaural Processing

Benefits of Binaural Listening

Humans, ordinarily, are born with two ears. Listening with two ears, also known as binaural listening, has many benefits. One of the most striking benefits of binaural listening is binaural summation. Binaural summation is the phenomenon of perceiving an increase in signal volume when listening with both ears, as opposed to just one ear at a time (Balkany & Zeitler, 2013). Although both ears are utilized in listening, sounds in the environment are not always processed equally in both ears. Two important cues in binaural listening are interaural time and intensity differences. Interaural time differences (ITDs) relate to low frequency sounds. Due to the length of the wavelengths of these low frequency sounds, sounds will reach the ears at two different points in time (different phases). Interaural phase differences may be interpreted by the listener as a sound being heard from a different location around the head. These are often tested by interaural phase difference (IPD) psychoacoustic testing. Interaural level/intensity differences (ILDs/IIDs) refer to high frequency sounds. Since high frequency sounds have shorter wavelengths, these sounds will essentially be absorbed by the head and will thus be heard at different intensities between the ears. When the central auditory system processes interaural time and intensity differences in the horizontal plane, it is able to comprehend the signal with a more positive signal-to-noise ratio. This is called binaural squelch (Balkany & Zeitler, 2013). Another important function of binaural processing is in localization. Through the utilization of both ears (when attending to sounds in the vertical and horizontal planes), humans are able to more effectively locate a sound in the space around them. Binaural listening also makes it easier for humans to locate a signal in the midst of noise. For example, when speech and noise are spatially separated, the signal-to-noise ratio is often different between the two ears due to the shape and orientation of the head. An improvement of 4-7 dB can be achieved through the utilization of the ear with the more favorable signal-to-noise ratio. This is called the head shadow effect.

Aging and Binaural Processing

Although many of the benefits of binaural listening still exist in aging populations, older age groups may have added difficulties regarding speech perception.

Aging comes with a plethora of audiological complications. To name a few, older individuals may experience difficulties separating speech from background noise, and difficulties localizing sound in the environment. The current study is most concerned with the “hidden” problem of degraded speech processing in the midst of an audiogram suggesting normal hearing sensitivity. Evidence suggests that a degradation in temporal processing (at least at the level of the auditory cortex), measured as physiological sensitivity to interaural phase differences, begins as early as mid-life (Ross et al., 2007). Ross et al. (2007) also noted that this degradation in binaural processing was frequency-dependent, with middle-aged and older age groups showing more degradation in the higher frequencies as compared to lower frequencies, when compared to a younger group. It has also been found that middle-aged and older individuals do not detect interaural phase differences between ears as effectively as younger individuals, which suggests poorer processing of temporal fine structure in middle-aged and older populations (Grose & Mamo, 2010). This was especially pronounced in the higher frequencies, suggesting higher frequencies are less discriminable in these older age groups. This lends support to the notion that neural synchrony, at least as reflected in psychophysical measurements, declines with age.

Evidence also suggests that vertical and horizontal localization abilities become less precise with age, even when the sounds are presented at sufficiently audible listening levels in these older individuals (Dobreva et al., 2011). However, it is difficult to distinguish localization impairments due to central aging processes from degradations resulting from peripheral aging processes. Furthermore, the audiometric thresholds of the older participants in the aforementioned study (Dobreva et al., 2011) were still elevated when compared to the younger groups, which could have contributed to the results.

Evidence has suggested that even in adults with audiograms within normal limits, the brainstems ability to phase lock and use temporal encoding for important dynamic speech cues is degraded (Clinard & Cotter, 2015). This is evident even in the lower frequencies. In addition, formant discrimination can diminish with age (Harkrider et al., 2006), which can impact speech perception and understanding. Extended high frequency loss could be predictive of speech-in-noise difficulties and central processing of auditory information as well.

It has been suggested that there is a relationship between age and loss of ganglion cells (Schuknecht & Gacek, 1993). This age-related loss in ganglion cells is greatest near the base of the cochlea, which tends to affect high-frequency hearing thresholds. Although this can lead to an elevated pure-tone average (PTA) in some aged individuals, it can also lead to poor speech discrimination scores. However, it is possible for some individuals, particularly later in life, to show deficits in speech understanding while still presenting with an audiogram and PTA within normal limits.

Spiral ganglion cell bodies (of the primary auditory neurons that they communicate with) can be damaged, and not show these deficits until later in life (Liberman & Kujawa, 2017). Additionally, cochlear nerve synapses can be damaged, while hair cells still remain functional. As behavioral audiograms typically only measure 250-8,000 Hz pure tones in quiet, reflecting a subjective measure of auditory function in a specific, controlled environment, it is obvious that several areas of auditory function (such as speech understanding in noisy listening environments) are not measured in this prevalent auditory test. The behavioral audiogram may be more sensitive to hair cell loss than neural degradation (Liberman & Kujawa, 2017). This offers one example of a scenario in which a behavioral audiogram may show results within normal limits, but the underlying auditory structures are covertly still damaged. Thus, this relates to patient perception of perceived auditory underperformance, which may not be reflected in the limited test results of an audiogram within normal limits. This phenomenon of patients presenting with functional hair cells and degraded synapses/neural function is often referred to as “hidden hearing loss”. Considering this, speech in noise measures are often beneficial in counseling and treating patients who have auditory complaints and a comorbid audiogram within normal limits. When considering speech in noise measures in the aged population in particular, many deficits often come to light (even in the presence of a normal audiogram).

Finally, neural synchrony refers to the ability of a person’s neurons to fire synchronously in response to a signal. Neural synchrony has been shown to decline with age. Some potential reasons for poorer synchrony include differences in nerve fiber diameter and a decrease in the quantity of auditory nerve fibers in aged individuals (Harris & Dubno, 2017).

Phase Locked Neural Activity in Humans

One way to physiologically assess phase-locking and thus neural synchrony in humans is through the Frequency-Following Response (FFR). The Frequency-Following Response has generators throughout the brainstem, but the primary generator (when recorded from the scalp) is the inferior colliculus. The Frequency-Following Response is a sustained response that reflects neural phase locking to the carrier frequency of a stimulus. The number and morphology of FFR peaks is stimulus dependent (Krishnan, 2006). So, as in the present study, if a FFR were to be recorded from a toneburst, the FFR tracing would show a sinusoidal response (shifted later in latency) that mimics the periodicity of the toneburst stimulus. The FFR response has properties similar to the cochlear microphonic, however, it is neural in nature.

To record this evoked potential in humans, a stimulus is presented either monaurally or binaurally, and auditory neurons synchronize to reproduce the waveform of the signal. Unlike many evoked potentials, the FFR is not an onset response. Instead, it is a sustained response that mimics the waveform of the stimulus. The FFR can only be reliably recorded up to approximately 1,500-2,000 Hz when scalp-recorded in humans (Krishnan, 2006). However, obtaining a high fidelity FFR at these upper frequencies is rare. Keeping this in mind, FFRs are characteristically most robust when elicited by lower frequencies, as this is where phase-locking is most efficient. The frequency range at which different auditory nuclei can phase lock gets lower and lower as we ascend the brainstem.

Phase locking can be described as neurons showing a preferred phase in a sinusoid at which to fire. Thus, action potentials will fire locked to a particular phase of a stimulus. In aged individuals, phase locking may be more variable. Whereas in younger auditory systems action potentials typically fire in a less variable (more synchronized) way, in older auditory systems there may be more temporal jitter. Temporal jitter relates to the amount of variance in time there is of a particular neural event. So, temporal jitter in neural firing in aged auditory systems would be expected to affect phase-locking, especially in the high frequencies (Clinard et al., 2010). Aging could also cause an impairment in maintaining sustained neural firing (Anderson & Karawani, 2020).

Variables Contributing to an Altered FFR

When considering the inclusion and exclusion criteria for this study, certain variables that contribute to an altered FFR needed to be taken into account. Musicians (those who practice their instrument at least two to three hours per week) have been found to have more developed and robust FFRs (Rodrigues et al., 2019). Musicians and vocalists can show improved auditory processing and recognition abilities (Bhat J & Krishna, 2021, Rodrigues et al., 2019). When Wong et al. (2007) recorded FFRs in musicians and non-musicians, they found that compared to non-musicians, musicians encode the fundamental frequency (of certain tone contours) more effectively. This suggests finer tuning and thus improved responses arising from musically trained individuals' auditory brainstems. In addition, a person's language experience, particularly the ability to speak tonal languages, can lead to improved auditory processing capabilities as compared to those who are native in a single, non-tonal language (such as English) (Krishnan et al., 2010).

While certain factors, such as musical training and proficiency in tonal languages, may enhance a frequency-following response, there are also certain factors that may lead to a degraded FFR. Firstly, those with middle ear pathologies will likely show a degraded FFR. This is due to the ineffective sound transmission pathway that would be a result of a pathology and/or abnormality in the outer or middle ear spaces. Middle ear pathologies and/or abnormalities (as identified by abnormal otoscopy or tympanometry) in individuals could thus lead to ineffective processing of the FFR stimulus in reaching the auditory nerve which would confound the results of the testing.

Evidence has suggested that the frequency-following response may become weaker with age as well, and this weakness may be apparent particularly in the higher frequencies closer to 1,000 Hz (Clinard et al., 2010). The ability to discriminate between different frequencies, as measured by frequency discrimination difference limens, became poorer in the studied aged individuals as well. These two tests target differing areas of auditory function, however, both showed a decline in older age groups.

Auditory nerve fibers that have been damaged (thus, affecting the spiking of action potentials by these fibers) would likely lead to a degraded FFR as well. However, research in this area is limited. Clinical testing is also limited in isolating pathologies of auditory nerve fibers. As we know, damage to auditory nerve fibers and the synapses between inner hair cells and auditory nerve fibers can exist in tandem with an audiogram showing results within normal limits.

Binaural Interaction Component

The binaural interaction component an electrophysiologic tool used to examine binaural function. It can be described as the difference between the sum of each monaural condition’s amplitude and latency at a particular frequency, and the binaural condition’s amplitude and latency at that frequency. Binaural interaction has historically been used as a tool to assess evoked potentials arising from the brainstem, as well as in middle and long-latency responses (McPherson & Starr, 1995). BIC studies using the ABR are most commonly completed, but studies have explored the usage of the BIC in potentials such as the middle-latency response (MLR) as well (Fowler, 2004).

In ABR studies, the BIC is associated with the neural generators of waves IV-VI (Fowler, 2004). Often, it has been observed that when assessing the binaural and summed monaural conditions' amplitudes in brainstem evoked potentials in both animals and humans, a larger value can be observed through the summed monaural responses (Laumen et al., 2016).

Examined in a comprehensive review, the ABR BIC has been found be to generated across frequencies (Fowler, 2004). The BIC has been assessed in middle-latency responses as well, and results showed even higher ratios (at 500 and 4,000 Hz) than ABR BIC studies using the same frequencies. This suggests a prevalent influence of thalamocortical areas on the BIC and binaural processing (even more of an influence than brainstem areas). Ratios were also higher at lower frequencies than higher frequencies, showing the influence of low frequency activity on binaural processing in these auditory areas.

The effects of age on the BIC, especially in the thalamocortical areas, show inconsistent results in older populations. In the presence or absence of hearing loss, older individuals have been found to have longer ABR-BIC latencies than younger individuals. However, when examining the BIC using the MLR, results of aged vs. young individuals have been quite variable (Fowler, 2004). More research is needed examining the BIC in thalamocortical areas in order to clarify what exactly determines this variability in both animals and humans.

Declines in binaural function can lead to increased difficulties separating speech from background noise. For this reason, the BIC can be used as a tool in assessing binaural functioning in individuals across the lifespan, which could be predictive of auditory complaints such as understanding speech in the midst of background noise, regardless of hearing acuity. Studies examining the BIC using the FFR are very sparse. There is a gap in the literature in examining age-related differences using BIC arising from auditory areas beyond the brainstem. This research would be valuable to have, especially when considering the relationship between the ability of neuron to phase lock to auditory stimuli and binaural processing ability.

FFR studies using the BIC

In the scenario of recording the FFR, it may not be useful to compare waveforms as is traditionally done in BIC studies, specifically in studies utilizing the ABR. Since the FFR is a sustained response, and not an onset response, comparing waveforms is hardly of relevance. Instead, it may be more useful to compare the spectra in examining the BIC of the FFR.

The most prevalently studied evoked potential used when examining the binaural interaction component has historically been the ABR. However, the FFR has also been used to examine the binaural interaction component in addressing various factors. The binaural interaction component has been examined in individuals with hearing thresholds <20 dBHL using both the FFR and ABR in order to examine the effects of frequency, intensity, and rate manipulation on the measurement of the BIC (Parthasarathy & Moushegian, 1993). The FFR-BIC has also been analyzed in conjunction with differing interaural intensity difference cues, which showed the amplitude of the FFR-BIC diminishing as interaural intensity differences were increased over a range of 30 dB (Krishnan & McDaniel, 1998). The FFR-BIC has also been studied (in normal hearing individuals) in order to assess the effect of interaural time difference manipulation on the binaural response (Ballachanda & Moushegian, 2000). Binaural FFR recordings have been shown to have higher amplitudes than monaural recordings, which differs from the results that have historically arisen from ABR studies utilizing the BIC.

Although the history of the FFR-BIC has contributed meaningful findings regarding the manipulation of frequency, rate, intensity, and ITD and IID cues on the response, it can be seen that there is a lack of literature examining the FFR-BIC in regards to aging. This would be valuable information to have, especially when considering the plethora of factors that affect binaural processing as humans age.

Purposes

The FFR can be used as an objective measure of stimulus processing, which can offer information relating to how speech is processed (especially when supplemented with behavioral measures). This relates to bottom-up processing, because if the neural representation of sound is degraded, then higher levels of the ascending brainstem have less high-fidelity information to encode and process. This would then relate to speech perception and listening to speech in noise. This study hopes to gain insight into frequency-related degradation of neural synchrony in aging populations through an objective physiological response. Hypotheses for the current study included:

1) The FFR will be degraded with advancing age, consistent with poorer neural synchrony/phase locking.
2) Age-effects will be more pronounced in the higher frequencies.

CHAPTER 2

MATERIALS AND METHODS

Subjects

Subjects were divided into two age groups: young (21-30 years old, n = 17, average age 23) and middle-aged (41-50 years old, n = 5, average age 44) adults. To participate in this study, subjects needed to have hearing thresholds within normal limits (<=25 dB HL, 250 Hz-8,000 Hz). Exclusion criteria included significant prior musicianship, bilingual/tonal language capabilities, significant head or neck injury, mood or sleep-altering prescription medications, middle ear disorders, and/or hearing loss. Informed consent was received from each participant before data collection began. Each subject received a hearing evaluation (comprised of otoscopy, tympanometry, and a pure-tone air and bone conduction audiogram (250-8,000 Hz)). Cash cards were given to all participants, and they were paid twenty dollars per hour for their time. Written consent to participate in the study was given by all participants.

Stimuli

Each subject underwent twelve conditions of the FFR. Four frequencies were recorded (500, 750, 1,000, and 1,125 Hz). Each frequency was recorded in a left ear, right ear, and binaural condition. Each condition was randomized across participants in the order it was obtained. Tonebursts with a 300 ms duration, a rise time of 75 ms, a plateau of 200 ms, and a fall time of 25 ms were used as stimuli. The rise/fall times were gated with a raised cosine ramp. All conditions were presented at 80 dB SPL. Shielded insert earphones (manufactured by Intelligent Hearing Systems) with double-length tubing were used to deliver the stimuli. A five-minute break was taken in between each condition to control for adaptation.

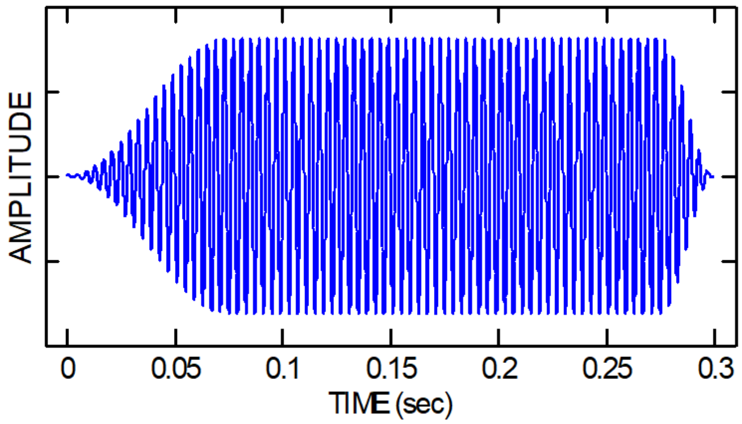


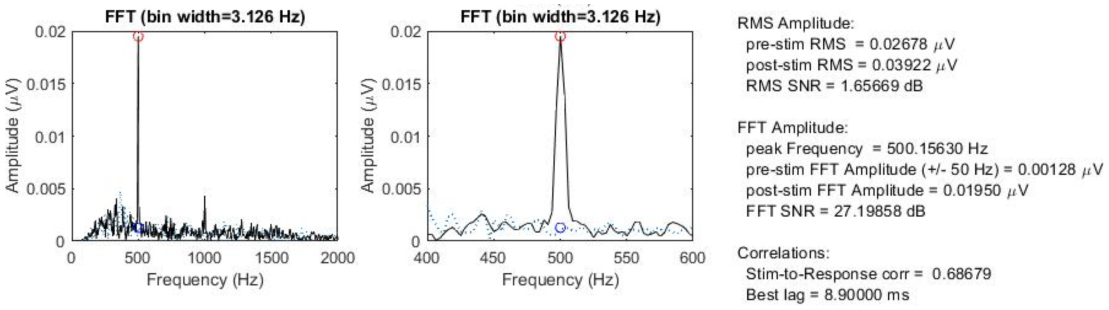
Figure 1: *An example stimulus waveform for the 500 Hz condition*

Physiology Recordings and Procedures

The FFR was recorded using the Neuroscan Synamps RT. The Neuroscan Stim 2 was used for stimulation. A three-channel electrode montage (utilizing silver chloride electrodes) was used as follows: Fpz for ground, Cz (inverting), nape of neck, A1 and A2 (non-inverting). Electrode impedances were documented to be below 5 kΩ and inter-electrode impedances were within 2 kΩ before recording began. Participants were reclined in a reclining armchair and were instructed to relax or fall asleep, if possible. All recordings were completed in a double-walled, sound-proof booth. Stimulus onset asynchrony was 633.33 ms; inter-stimulus interval was 333 ms. The online filters were 100–3000 Hz, the analysis time window was -320 to 320 ms, and the analog-to-digital sampling rate was 20 kHz. Artifact rejection was set to ensure all sweeps exceeding ±30 µV were discarded. At least 1,030 accepted sweeps were collected for each condition.

Physiology Analysis

Offline FFR analyses were performed in Matlab 2019 (included measures of amplitude, signal-to-noise ratios, and stimulus-to-response cross correlations). Amplitude and signal-to-noise measurements were derived from FFTs, which simultaneously show the magnitude of the response in the midst of the noise levels. Stimulus-to-response cross correlations compare the stimulus waveform to the response seen recorded from the FFR. A higher stimulus-to-response cross correlation could indicate more efficient phase locking at a particular frequency. All audiograms and test conditions were organized and synthesized in Excel for each participant.



```
RMS Amplitude:
  pre-stim RMS  = 0.02678 µV
  post-stim RMS = 0.03922 µV
  RMS SNR = 1.65669 dB

FFT Amplitude:
  peak Frequency  = 500.15630 Hz
  pre-stim FFT Amplitude (+/- 50 Hz) = 0.00128 µV
  post-stim FFT Amplitude = 0.01950 µV
  FFT SNR = 27.19858 dB

Correlations:
  Stim-to-Response corr =  0.68679
  Best lag = 8.90000 ms
```

Figure 2: *FFT showing FFT and RMS amplitudes, as well as stimulus-to-response correlations*

Statistical Approach

Repeated measures ANOVAs were completed for the two age groups. The repeated measures ANOVAs were completed with three dependent variables: FFR amplitude, binaural amplitude difference, and stimulus-to-response correlations. Factors were group (between subject on two levels, young and middle-aged), frequency (within subjects on four levels; 500, 750, 1000, and 1125 Hz) and ear condition (within subjects on three levels: average monaural, summed monaural, and binaural). Effect size was measured using partial eta squared with small, medium, and large effect sizes defined as 0.0099, 0.0588, and 0.1279, respectively (Cohen, 1988).

CHAPTER 3

RESULTS

Amplitude

When comparing the data of young normal participants with that of middle-aged participants, it can be seen that amplitudes were largest in younger participants (Figure 3). Additionally, amplitudes were biggest in low frequencies, and amplitudes were smallest in higher frequencies. The largest amplitudes were seen in the binaural conditions. A repeated measures ANOVA with factors of group (between subjects: younger, middle-aged), frequency (4 levels: 500, 750, 1000, and 1125 Hz), and ear (4 levels: left, right, binaural, summed monaural) was performed. The main effect of group was not significant ($F_{(1,20)} = 0.223$, $p = .642$). The main effect of frequency was significant ($F_{(1.96,39.17)} = 27.438$, $p < .001$, partial eta squared = .578). The main effect of ear was also significant ($F_{(2.047,40.9)} = 25.725$, $p < .001$, partial eta squared = .563). Ear x group and ear x frequency x group interactions were not significant ($p > .05$). However, the ear x frequency interaction was significant (p <.001) and was likely driven by the larger 500 Hz amplitude in the binaural condition (Figure 3).

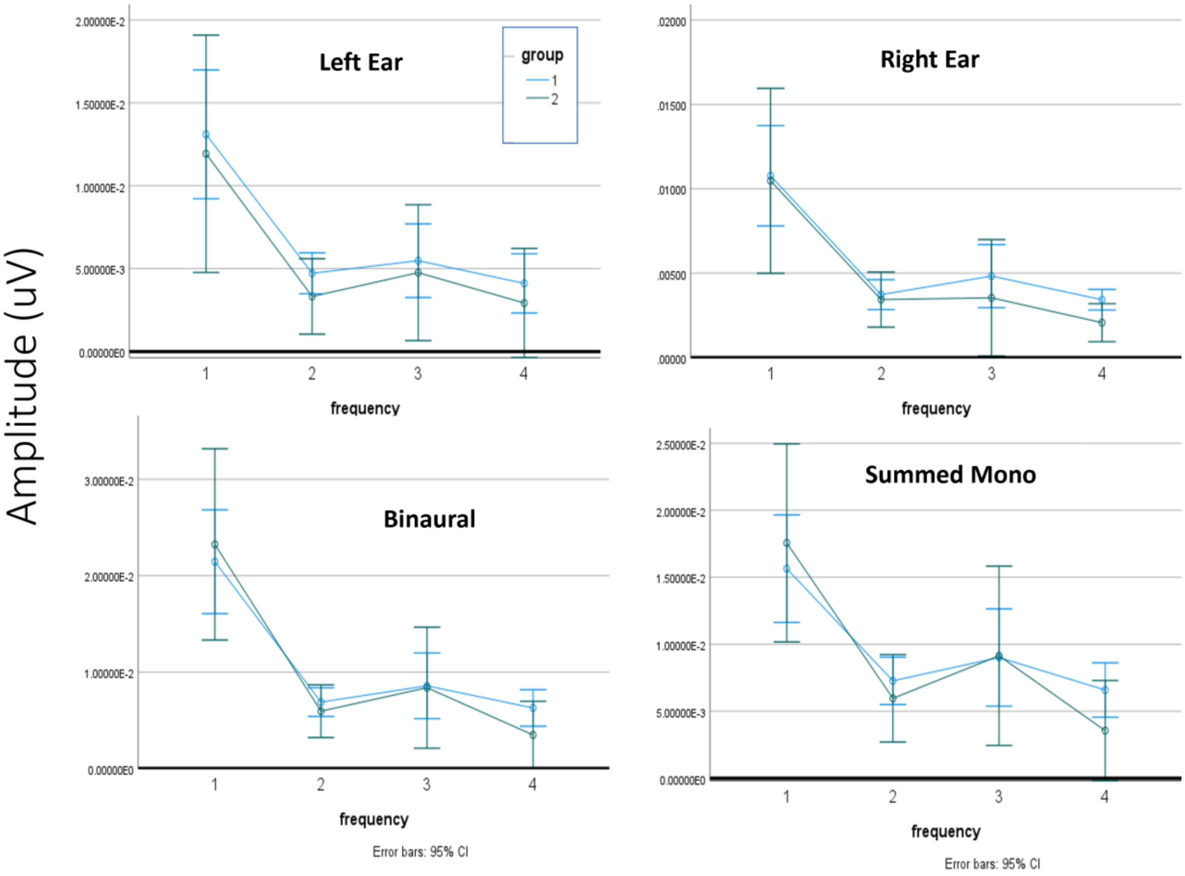


Figure 3. *Error bar plots of FFR amplitude. Each panel is a different ear condition. Within each panel data from young (group 1) and middle-aged (group 2) ears are plotted. Middle-aged amplitudes were poorer than younger amplitudes, and monaural amplitudes were lower than binaural and summed monaural amplitudes. Y-axes are not scaled equally across panels. Frequency plotted as follows: 1=500 Hz, 2=750 Hz, 3=1,000 Hz, 4=1,125 Hz).*

Stimulus-to-Response Correlation

In general, the biggest correlations were observed in the younger group. The largest possible stimulus-to-response correlation is a perfect 1.0, while no correlation seen would be shown by a 0.0. Smaller correlations were observed in older populations. The main effect of group was not significant ($F_{(1,18)} = 0.007$, $p = .936$). The main effect of frequency was significant ($F_{(3, 54)} = 15.840$, $p < .001$, partial eta squared = .468). The main effect of ear condition was also significant ($F_{(1.831, 32.950)} = 39.305$, $p < .001$, partial eta squared = .686). Two- and three-way interactions were not significant ($p > .05$).

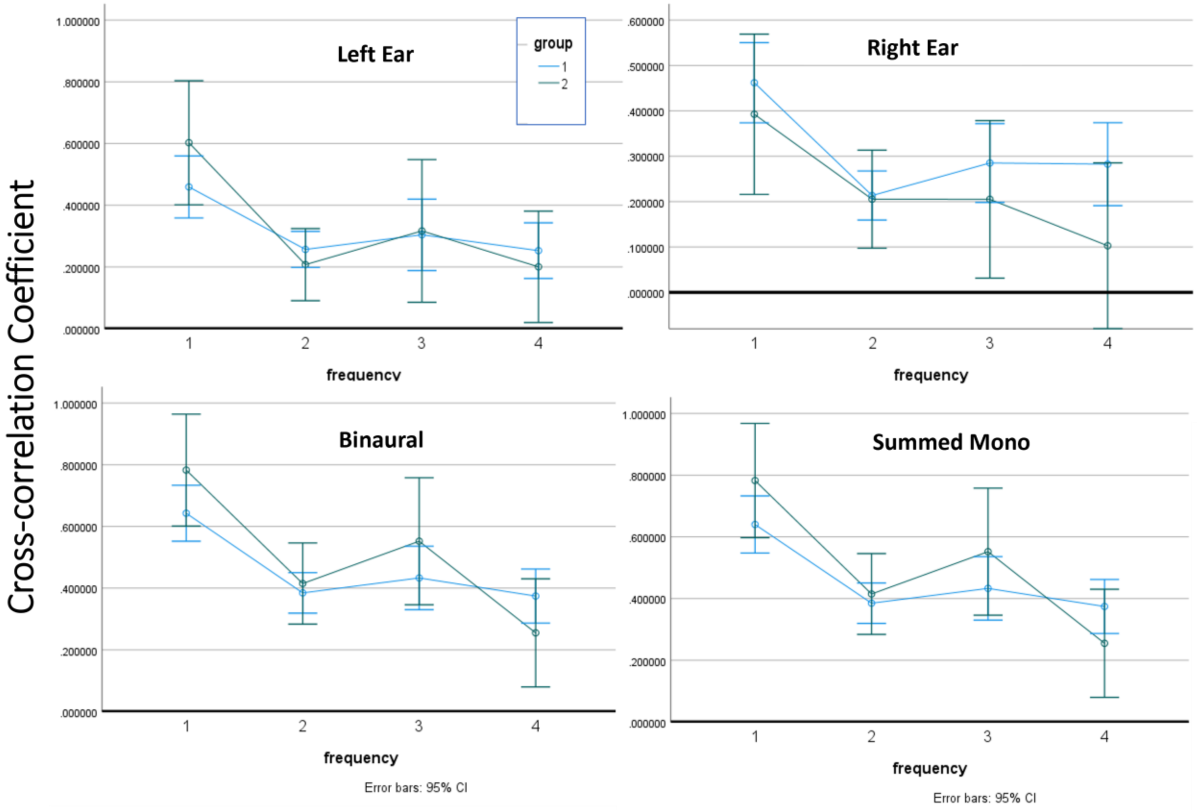


Figure 4. *Error bar plots of FFR stimulus-to-response correlations. Each panel is a different ear condition. Within each panel data from young (group 1) and middle-aged (group 2) ears are plotted. Middle-aged amplitudes were poorer than younger amplitudes, and monaural amplitudes were lower than binaural and summed monaural amplitudes. Y-axes are not scaled equally across all four panels. Frequency plotted as follows: 1=500 Hz, 2=750 Hz, 3=1,000 Hz, 4=1,125 Hz).*

Power Analysis Results

A power analysis was performed in G-Power (version 3.1) to assess the sample size that would be needed in order to achieve significance. When considering the pilot data (Heckler, 2015), a power analysis revealed that a sample size of 100 (n=100) would have been needed in order to find a significant age effect. In the present study, a sample size of 26 (n=26) is needed in order to achieve significance. As the data collection for this study is ongoing, and this document has analyzed only a portion of the future total data to be achieved, this sample size will be hopefully achieved (and thus significance obtained) by the conclusion of the data collection period of the study.

CHAPTER 4

DISCUSSION

Introduction

This study aimed to better understand age-related declines in neural synchrony, in an attempt to better serve aging patient populations. The results of this study can hopefully lead to more effective and informed intervention plans and counseling for this patient population, as well as contributing to the knowledge base documenting objective changes that occur in the aging auditory system.

Age-related perceptual declines have been well-documented with behavioral measures of binaural processing (Grose & Mamo, 2010, Ross et al., 2007). This study attempted to serve as a physiological correlate for the same frequency range (500-1,125 Hz).

FFR Amplitude

FFR amplitude decreased as frequency increased across both age groups. The FFR elicited by the 500 Hz toneburst yielded the largest amplitudes of all frequencies, compared to 750, 1,000, and 1,125 Hz, across all age groups and conditions. In contrast, the FFR elicited by the 1,125 Hz toneburst yielded the smallest amplitude across all age groups and conditions. Clinard et al. (2010) observed similar findings of amplitude decreasing with an increase of stimulus frequency, so these findings were expected to be seen. It is possible that the consistency of these results points to degradations in neural synchrony in the aged auditory brainstem, which would be consistent with these findings. These results can be compared to those obtained by Ross et al. (2007), which indicated an age-dependent reduction in the upper frequency limit of the carrier at which a P1-N1-P2 change complex was evident. The amplitudes of the change response also diminished with increasing frequency (Ross et al., 2007), similar to the results seen in the current study. As the FFR is a following response that can indicate the brainstem's ability to phase lock to certain stimuli, the P1-N1-P2 change response can be thought of as a physiological reflection of discriminatory processes occurring in the auditory system. Both of these responses (the FFR and P1-N1-P2 change response) can be useful tools in researching how aging may affect the central auditory system's ability to objectively process sound.

The monaural FFR conditions were obtained from both the right and left ears. For the summed monaural condition, these two responses (the left and right monaural conditions) were added together and analyzed as a sum. In contrast, the binaural condition was obtained through the stimulus being presented to both ears simultaneously. It can be seen from the results obtained that the summed monaural and the binaural condition elicited similar amplitude responses, however, the summed monaural amplitudes are slightly higher than the binaural amplitudes. Krishnan & McDaniel (1998) found that when they used a 500 Hz toneburst to elicit the FFR, they found that summed monaural amplitudes were larger than binaural amplitudes. While similar results were not necessarily seen in the currently presented data, a contributing factor to the overall results of the present study was likely the small sample size. However, age effects were still more pronounced (shown by decreased amplitude) in the higher frequencies, as compared to the young group. Ross et al. (2007) and Grose & Mamo (2010)'s results supported these findings, as they also showed degradation in the higher frequencies in older age groups.

Stimulus-to-Response Correlation

The stimulus-to-response correlation illustrates how closely the response was replicated from the stimulus at a particular frequency. A perfectly similar response waveform to the stimulus waveform would result in a correlation of 1.0. In contrast, a response waveform that is perfectly dissimilar from the stimulus waveform would result in a correlation of 0. So, the closer the number is to 1.0, the better the stimulus-to-response correlation is, and the closer the FFR response mimics the stimulus waveform.

Monaural (left ear and right ear) stimulus-to-response correlations were smaller than in the binaural and summed monaural conditions. Stimulus-to-response cross-correlations were largest at 500 Hz in both the young and middle-aged groups, meaning that the response waveform most closely followed the stimulus waveform at this frequency as compared to the other tested frequencies (750, 1,000 and 1,1,25 Hz). As phase-locking is more efficient in lower frequencies, these results were reasonably expected to be seen.

In general, the young age group had higher stimulus-to-response correlations. In contrast, the middle-aged group had poorer stimulus-to-response correlations. This can be assumed to be attributed to weaker phase-locking abilities in the middle-aged age group and is particularly evident in the highest frequency tested (1,125 Hz).

Clinical Relevance

Although the FFR may not be translated into a clinical tool, the findings of this study can hopefully inspire better counseling and intervention plans in older age-groups.

In patients with normal audiograms who still struggle understanding speech (or speech in noise), auditory training could be a tool more utilized clinically for these age groups. Implementing auditory training in older age groups who struggle with speech perception, particularly in noise, could be beneficial and may improve speech perception in noise, auditory short term memory, and the speed of neural processing (Anderson et al., 2013).

Additionally, better counseling and education can be given to older populations who do not suffer from hearing loss but are experiencing listening difficulties. Validating patients that research suggests even when audiometric thresholds are within normal limits, a degradation of neural synchrony is being seen in older age groups that may affect aspects of processing, can give them a more thorough answer rather than sending them off with test results that simply say, “normal”.

This is another piece of information, in addition to research exploring behavioral deficits with aging, that can contribute to our knowledge of real-world listening difficulties in older populations and hopefully inspire further research in this area.

Future Directions

Reduced phase-locking capabilities in aging adults could be a result of peripheral auditory nerve degeneration (Märcher-Rørsted et al., 2022) or central deficits (Clinard & Cotter, 2015). Märcher-Rørsted et al. (2022) used auditory nerve modeling to examine the possibility of comorbid peripheral neural degeneration with age-related changes in recorded FFRs in normal hearing listeners. They found that through computational modeling of the peripheral auditory nerve, it can be suggested that there is a relationship between age-related degradations in the FFR and age-related auditory nerve fiber loss.

The age-related changes seen in the FFRs are presumed to be due to a reduction of phase locking capability (and thus reduced neural synchrony) in the aged human brainstem. The addition of the evidence by Märcher-Rørsted et al. (2022) points to an increased role of the peripheral auditory system in conjunction with central processes such as those observed through the FFR. Thus, FFRs elicited by low frequency stimuli may potentially be useful in future applications as a marker of peripheral nerve degeneration, particularly in older individuals.

Although evidence has suggested the relationship between reduced neural synchrony and aging in the peripheral and central auditory system, there is less evidence on how these changes may relate to binaural processing. Cross-examining perceptual results from interaural phase differences with physiological results from the FFR utilizing the same frequency stimuli can give a different perspective as to how older age groups are processing different frequency stimuli. Concurrent research is examining the frequency-following response, as well as interaural phase differences to the same frequency stimuli, and speech-in-noise measurements. Together, these objective and subjective measures can offer a more rounded view of not only the participants' subjective experiences and abilities, but also a deeper understanding of the ability of the auditory system itself to attend to these stimuli.

In the future, this research could be expanded upon by examining the effects of noise exposure on the studied individuals. It has been well documented that noise can have detrimental effects on the cochlea, and studies have suggested that noise can even speed up cochlear degeneration (synaptopathy) in aged individuals (Fernandez et al., 2015, Liberman & Kujawa, 2017). Due to studies such as this one utilizing participants with audiometric thresholds within normal limits, the possibility of participants experiencing any degree of "hidden hearing loss" due to prior noise exposure is entirely possible, even if it is not reflected by their pure-tone hearing thresholds. It may be of value to examine how the results of the study may differ should the participants' noise exposure histories be factored into the results. This may be expanded upon in future studies in this topic area.

Finally, further research in this area utilizing the FFR to assess deficits in aging is needed. As the FFR reflects the auditory system's ability to phase lock (thus showing the integrity of neural synchrony in the brainstem) to differing stimuli, it can be used as an objective tool in future studies to assess degradation of temporal processing across the lifespan.

Conclusions

Results of this study showed that FFRs were highest in amplitude and had the highest stimulus-to-response correlations in the lower frequencies across age groups. Age effects were more pronounced in the higher frequencies. This is supported by existing evidence (Clinard et al., 2010, Grose & Mamo, 2010, Ross et al., 2007), showing age-related degradation in both objective and subjective discrimination abilities, particularly in higher stimulus frequencies.

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