

Université de Montréal

Interaural Differences in Sensory Processing at Lower Levels of the Auditory System and their Association with the Right Ear Advantage for Dichotic Listening and Speech Perception in Noise Among Older Adults: An Exploratory Study

Par Alejandro Ianiszewski Gómez

Faculté des études supérieures et postdoctorales

Faculté de médecine

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Cette thèse intitule :

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Présentée par :

Alejandro Ianiszewski Gómez

a été évaluée par un jury composé des personnes suivantes :

Victoria Duda, président-rapporteur
Adrian Fuente, directeur de recherche
Jean-Pierre Gagné, co-directeur
Sylvie Hébert, membre du jury
Eliane Schochat, examinateur externe
Bouthaina Jemel, représentant du doyen de la FES

Résumé

Un biais fonctionnel entre les oreilles droites et gauches a été largement documenté, avec un avantage de l'oreille droite (AOD) dans les tâches perceptives, en particulier celles utilisant le traitement verbal. Les sons complexes tels que la parole sont perçus plus facilement dans l'oreille droite (OD) que dans l'oreille gauche (OG) pour les tâches d'écoute dichotique (ED) ainsi que pour les tâches de perception de la parole dans le bruit (PDB). Des études sur les tâches d'ED ont démontré que le vieillissement est associé à une réduction globale des performances des deux oreilles, avec un déficit de performance plus important pour les stimuli présentés à l'OG par rapport à ceux présentés à l'OD entraînant une augmentation de l'AOD. Ce déficit à l'OG pourrait être le résultat d'une baisse de l'efficacité du transfert inter hémisphérique d'informations auditives via le corps calleux due au vieillissement ou de changements liés au vieillissement dans les fonctions cognitives. Cependant, des preuves chez les jeunes adultes ayant une audition normale suggèrent que les différences interaurales (DI) dans le traitement sensoriel au niveau des parties inférieures du système auditif pourraient également expliquer l'ampleur de l'AOD pour les tâches d'ED. L'objectif principal de cette thèse est d'étudier si les DI dans le traitement sensoriel aux niveaux inférieurs du système auditif sont associés à l'ampleur de l'AOD chez les personnes âgées. De plus, ce projet vise également à déterminer si les DI dans le traitement sensoriel au niveau des parties inférieures du système auditif sont associées aux processus de perception de la PDB chez les personnes âgées. Pour ce faire, 70 personnes âgées ont participé à cette étude. Tous les participants ont été évalués avec une batterie complète de tests auditifs examinant les seuils de sons purs, les émissions otoacoustiques évoquées transitoires avec et sans stimulation acoustique contralatérale, la réponse auditive du tronc cérébral et la performance sur les tâches d'ED et de perception de la PDB. Afin de contrôler la fonction cognitive, les habiletés cognitives telles que la vitesse de

traitement, la flexibilité cognitive et la mémoire de travail ont également été évaluées. Les DI dans le traitement sensoriel aux niveaux inférieurs du système auditif ont été dérivées en calculant la différence entre l'OD et l'OG pour chacune des mesures auditives. Des modèles de régression bivariées et multivariées ont été réalisés en intégrant les variables d'habiletés cognitives dans les modèles de régression. Les résultats ont révélé que la DI pour les seuils de sons purs et la DI pour les émissions otoacoustiques évoquées transitoires avec suppression étaient associés significativement à l'ampleur de l'AOD chez les personnes âgées. De même, la DI pour les émissions otoacoustiques évoquées transitoires et la DI pour la réponse auditive du tronc cérébral expliquent la performance de la perception de la PDB chez les personnes âgées. De plus, les résultats ont révélé que les habiletés cognitives contribuent de manière significative à l'ampleur de l'AOD ainsi que pour la performance de la perception de la PDB chez les personnes âgées. Dans l'ensemble, la présente thèse fournit des données qui suggèrent que les DI dans le traitement sensoriel au niveau des parties inférieures du système auditif explique en partie l'ampleur de l'AOD pour les tâches d'ED ainsi que les problèmes de perception de la PDB chez les personnes âgées.

Mots-clés : Differences sensorielles interaurales, Écoute dichotique, Avantage de l'oreille droite, Vieillissement, Parole dans le bruit.

Abstract

A functional bias between the right and left ears has been widely documented, with a right-ear advantage (REA) in perceptual tasks, particularly those employing verbal processing. Complex sounds such as speech are more accurately perceived in the right ear (RE) compared to the left ear (LE) for dichotic listening (DL) and speech perception in noise (SIN) tasks. Although previous studies have shown that aging is associated with an overall decline in DL performance in both ears among older adults, the left ear (LE) performance often decreases more dramatically relative to the right ear (RE) performance, causing an increased REA for speech stimuli. This greater LE deficit may be the result of age-related changes in (A) cognitive functions; (B) functions of the right hemisphere (RH); and /or (C) the efficiency of interhemispheric transfer of auditory information via the corpus callosum. However, evidence in normal hearing young adults suggest that interaural difference (ID) in sensory processing at lower portions of the auditory system might also explain the magnitude of the REA for DL. The main aim of this thesis is to investigate whether ID in sensory processing at lower levels of the auditory system are associated with the magnitude of the REA for DL among older adults. In addition, this project aimed to investigate whether ID in sensory processing at lower levels of the auditory system is associated with SIN performance in older adults. A total of 70 older adults participated in this study. To assess sensory processing at lower levels of the auditory system, hearing thresholds, transient evoked otoacoustic emission (TEOAE), contralateral suppression of TEOAE, a proxy measure of medial olivocochlear (MOC) activation and click-and-speech auditory brainstem response to speech stimuli were measured in both ears separately. The ID in sensory processing was derived by calculating the difference between the right and left ears for each auditory measure. The mobile device app version for iPhone of the Bergen Dichotic Listening test, the *iDichotic*, was used to evaluate DL. In addition, SIN

performance was evaluated with the hearing-in-noise test (HINT). With the aim to control for cognitive function, cognitive abilities such as speed of processing, cognitive flexibility and working memory were also evaluated. Bivariate and multivariate regression models were performed, and cognitive measures were accounted for in the regression models. Results revealed that ID in pure-tone thresholds and ID in MOC-induced TEOAE suppression were significantly associated with the magnitude of the REA for DL among older adults. Similarly, ID in TEOAE and ID in speech-ABR measures explained SIN performance in older adults. In addition, results revealed that cognitive measures significantly contributed to the magnitude of the REA for DL and SIN performance in older adults. The present thesis provides evidence indicating that ID in sensory processing at lower levels of the auditory system partially explain the magnitude of the REA for DL as well as SIN performance among older adults.

Keywords: Interaural sensory differences, Dichotic listening, Right ear advantage, Aging, Speech perception in noise.

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List of Acronyms and Abbreviations

ABR: Auditory brainstem response
Click-ABR: Auditory brainstem response to click sounds
CV: Consonant-vowel syllable
dB: Decibel
dB HL: decibel hearing level
DL: Dichotic listening
F0: Fundamental frequency
FFR: Frequency following response
HINT: Hearing in noise test
HINT LE: Hearing in noise test left ear
HINT NF: Hearing in noise test noise front
HINT RE: Hearing in noise test right ear
Hz: Hertz
ID: Interaural difference
ISO: International organization for standardization
kHz: Kilo hertz
LE: Left ear
LH: Left hemisphere
LI: Laterality index
MOC: Medial olivocochlear
MoCA: Montreal Cognitive Assessment
RE: Right ear
REA: Right ear advantage
RH: Right Hemisphere
RMS: Root mean square
RST: Reading span test
SIN: Speech perception in noise
SNR: Signal to noise ratio
Speech-ABR: Auditory brainstem response to speech sounds
SPL: Sound pressure level
TEOAE: Transient evoked otoacoustic emissions
TMT: Trail making test
TMT-A: Trail making test part A
TMT-B: Trail making test part B
 μ V: Microvolts

To My Beloved Mother

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Chapter 1- Introduction

1.1 Overview

A functional bias between the right and left ears has been widely documented, with a right-ear advantage (REA) in perceptual tasks, particularly those employing verbal processing. For example, complex sounds such as speech are more accurately perceived in the right ear (RE) compared to the left ear (LE) for dichotic listening (DL) tasks (Kimura, 1961, 1967). Dichotic stimulation involves the simultaneous presentation of two different and competing auditory stimuli (Hugdahl & Helland, 2013). Although previous studies have shown that aging is associated with an overall decline in DL performance in both ears among older adults, the LE performance often decreases more dramatically relative to the RE performance, causing an increased REA for speech stimuli (Jerger et al., 1994; Roup et al., 2006; Kam and Keith, 2010; Roup, 2011; Hirnstein et al., 2013; Westerhausen et al., 2015). This increased REA for speech stimuli (i.e., greater LE deficit) has been significantly correlated with speech perception in noise (SIN) difficulties in older adults (Lavie et al., 2013; Mukari et al., 2020). While several theories explaining changes in DL performance among older adults have suggested a more cortical basis to account for the increased magnitude of the REA (e.g., Dolcos et al., 2002; Goldstein & Braun, 1974; Goldstein & Shelly, 1981; Gootjes et al., 2006; Hugdahl et al., 2009), there is converging evidence in young adults (e.g., Emmerich et al. 1988; Hu and Lau, 2017; Markevych et al., 2011) suggesting that interaural differences (ID) at lower levels of the auditory system might also explain changes in the magnitude of the REA for DL. In older adults however, such an association has not been investigated. This thesis will provide new evidence expanding our understanding about ID in sensory processing at lower portions of the auditory system and their link with perceptual processes, such as DL and SIN performance among older adults.

1.2 The dichotic listening paradigm

Dichotic listening (DL) is a non-invasive technique used to assess central auditory processing among other functions (Broadbent, 1954, 1958; Kimura, 1961, 1967; Martin & Jerger, 2005; Roup et al., 2006; Hugdahl et al., 2009). DL literally means listening to two different sounds in which one auditory stimulus is presented to the RE, and a second different stimulus is simultaneously presented to the LE (Hugdahl et al., 2008). The simultaneous presentation of two different sounds in DL tasks creates competition stressing the auditory system to accurately process each stimulus (Lavie et al., 2013). In addition, depending on the type of auditory stimulus used during DL stimulation, an “ear advantage” occurs, with the stimulus presented to one ear perceived as more dominant relative to the other ear (Rimol et al., 2006). Typically, healthy individuals are faster and more accurate in reporting speech stimuli (e.g., such as consonant–vowel (CV) pairs, digits, words, and sentences) presented to the RE than the LE (Kimura, 1961, 1967). As previously mentioned in the above section, a REA results in DL tasks whereby verbal stimuli are used (Bryden, 1988; Bryden et al., 1983; Wilson & Leigh, 1996). As opposed, when non-speech stimuli are used (e.g., such as music, tone contours and complex tones), material presented to the LE is generally more accurately reported than the material presented to the RE (i.e., a LE advantage) (Colbourn & Lishman, 1979; Gordon, 1980; Sidtis, 1981). The REA for speech stimuli in healthy individuals has been taken as evidence for left hemisphere (LH) lateralization for speech (Kimura, 1961, 1967; Bryden, 1988), while The LE advantage has been linked to a RH activation dominance for non-speech stimuli (Tervaniemi et al., 1999).

The DL paradigm may also differ in number of stimulus per trial, type of response, and instructions (see Westerhausen, 2019 for a more detailed description). For example, performance is usually measured under two different instruction conditions. First, the nonforced or divided attention (free

recall) instruction paradigm, whereby the participant must report either the one stimulus they heard best or exhaustively recall as many stimuli as they heard from both ears (Hugdahl, 2003). Second, the forced-attention or directed-attention paradigm, whereby the participant must exclusively attend to one ear (forced-right or forced-left conditions) and report only the stimulus presented to that ear (Hugdahl & Andersson, 1986). The performance of each ear, indicated by the number of correctly recalled stimuli per ear, is then associated to each other by calculating a laterality index (see Bruder, 1991 for a review of different laterality indices), whereby positive values represent a REA while negative values indicate a left ear advantage. This research project will focus exclusively on the REA for speech stimuli.

In the present study the iPhone version of the Bergen Dichotic Listening test (Hugdahl & Andersson, 1986), the iDichotic (Bless et al., 2013), was used to assess DL. This DL test employs stimuli that combine the six plosive consonants (i.e., /b/, /d/, /g/, /p/, /t/, /k/) with a vowel (usually /a/) to syllables (Hugdahl et al., 2009; Westerhausen et al., 2015). The CV-syllables are paired with each other yielding 36 dichotic pairs, including the homonymic pairs which are mostly excluded in the statistical analyses. The iDichotic was chosen because it presents only a single pair of syllables on each trial as well as requiring only one response per trial (Westerhausen et al., 2015). Therefore, this DL test minimizes the impact of higher cognitive functions on the laterality estimate compared to the strings of stimuli (e.g., digits, sentences) used in other DL paradigms (Westerhausen, 2019).

1.3 Theoretical models of the REA for DL

The REA for speech stimuli in DL has been explained by two models which somehow can be complemented. First, the structural model proposed by Kimura, (1967), which underlies more

automatic or “bottom-up” (stimulus-driven) processing biases. The structural model posits that the REA for speech stimuli results from the functional-anatomic organization of the neural auditory pathways from the auditory periphery to more central auditory structures, as well as the hemispheric specialization for language functions (Kimura, 1961a, b). Specifically, the structural model assumes that the auditory input travelling throughout the auditory pathway, ends in the primary auditory cortex of both the contra-and the ipsilateral cerebral hemispheres. However, since contralateral projections are stronger and more preponderant, auditory information is strongly represented in the hemisphere opposite to the side/ear of stimulus presentation. Moreover, auditory information ascending through the weaker ipsilateral projections are supposedly suppressed or blocked during dichotic stimulation (Kimura, 1967), thereby ensuring more effective conduction along the crossed pathways. Also, the structural model assumes, at least in right-handed individuals, that the LH is specialized for language and speech perception processing, and that information arriving from the LE/RH pathway must cross the corpus callosum (callosal relay model) to reach the language-dominant hemisphere (Sparks and Geschwind, 1968). Thus, the RE stimulus would be immediately transferred to the LH resulting in faster and more accurate processing, while the LE stimulus would be delayed or attenuated due to the additional callosal relay stage (Westerhausen & Hugdahl, 2008).

In summary, according to the structural model (Kimura, 1967), the REA for speech stimuli would be the result of: 1) fixed asymmetries in the ascending auditory pathway due to stronger contralateral neural projections from the RE to the language-dominant LH of the brain; and 2) a relatively small deficit in the LE performance in normal right-handed listeners related to a delay and/or attenuation of information during the additional callosal relay stage (Kimura, 1961; Westerhausen & Hugdahl, 2008). Complementing with the structural model, Hiscock and

Kinsbourne (2011) suggested that ID in sensory processing at lower levels of the auditory system (i.e., periphery and low brainstem) might also account for the magnitude of the REA in DL tasks. This assumption was based on the accumulative evidence suggesting enhanced peripheral (i.e., better hearing sensitivity and higher transient evoked otoacoustic emission response) and subcortical (i.e., shorter latencies and higher amplitudes for the auditory brainstem response to click sounds) auditory processing in the RE relative to the LE in children and young adults (e.g., Eldredge & Salamy, 1996; Kannan & Lipscomb, 1974; Khalfa et al., 1998; McFadden, 1993; Philibert et al., 1998; Sininger et al., 1998; Sininger & Cone-Wesson, 2004, 2006). This research project will investigate whether ID in sensory processing occurring at lower levels of the auditory system (i.e., peripheral, and subcortical) may account for the increased magnitude of the REA for DL exhibited by older adults.

An alternative explanation proposed by Kinsbourne (1970), known as the attentional model (Kinsbourne, 1970), implicates more controlled or “top-down” (instruction-driven) factors (Hugdahl, 2003) to account for the magnitude of the REA for speech stimuli in DL. Kinsbourne argued that perception during DL tasks were likely to depend less on bottom-up processing and more on selective attention. Kinsbourne claimed that interaural asymmetries, or difference in auditory processing between the left and right ears in DL, occurred from a cognitive or attentional bias towards the hemispace contralateral to the engaged cerebral hemisphere (Jerger & Martin, 2006). In other words, he posited that the simple act of anticipation of verbal stimuli would preferentially pre-activate the LH setting up a priming advantage for subsequent processing (Kinsbourne, 1970; Westerhausen & Hugdahl, 2008). The REA for speech stimuli in DL would then arise from a) priming the LH to anticipate speech, which in turn would result in an attentional

bias favoring the processing of the RE input, and/or b) partly suppressing the LE input due to this RE/LH anticipation (i.e., advantage) for speech processing.

The attentional model has been strongly supported by findings demonstrating that the magnitude of the REA for speech stimuli changes due to the manipulation of attention (e.g., Bryden & Murray, 1985; Hugdahl & Andersson, 1986; Hugdahl et al., 2009; see also Hiscock and Kinsbourne (2011) for a review). By comparing the results between the nonforced and the forced attention paradigms (Forced-right and forced-left conditions), both Bryden et al. (1983) and Foundas et al. (2006) showed a stronger REA during the forced attention paradigm compared to the nonforced paradigm. Bryden et al. (1983) suggested that an increase in interaural asymmetry in DL performance depended on the interaction between auditory perception and cognitive processes. In line with this, Hugdahl et al. (2009) claimed that attending to the right or left ears during DL tasks produced different degrees of cognitive conflict and cognitive control strategies. When attention is forced to the RE, bottom-up (stimulus-driven) and top-down (instruction-driven) influences on the REA would work in synchrony both leading to an increased REA. In contrast, during the forced-left condition, bottom-up and top-down influences are in conflict and may thus decrease the number of correct right ear reports (i.e., decreasing the REA). In addition, the forced-left condition would induce a cognitive conflict between bottom-up and top-down factors, requiring the allocation of cognitive control resources to resolve the conflict (Hugdahl & Westerhausen, 2016). Consequently, an attentional bias to either the RE or LE would evoke two different cognitive processes, a non-executive attention in the forced-right condition, and an executive control in the forced-left condition because of the presence of a strong interfering stimulus-driven tendency (Hugdahl et al., 2009) As a result, focusing attention to the RE typically increases the magnitude of the REA for

speech stimuli, while focusing attention to the LE decreases the magnitude of the REA or even result in a LE advantage (Hugdahl et al., 2008; Westerhausen & Hugdahl, 2008).

Thus, considering that cognitive control also contributes to the magnitude of the REA for speech stimuli in DL (Andersson et al. 2008; Hirnstein et al., 2013; Takio et al., 2009), in this doctoral research, cognitive measures will be accounted as covariates during statistical analysis with the aim to determine whether ID in sensory processing at lower levels of the auditory system independently contribute to the magnitude of the REA in DL.

1.4 Age-related peripheral and central auditory effects on the REA for DL among older adults

The DL paradigm has been shown to be a sensitive measure for auditory processing disorders attributed to frank neurological lesions of the central auditory system such as brainstem lesions (Musiek, 1983), and temporal lobe lesions (Musiek et al., 2011; Weihing & Atcherson, 2014). In these populations interaural asymmetries (i.e., REA) in DL performance become more pronounced. DL has also been used to measure age-related changes in auditory processing abilities in older adults (Jerger & Martin, 2006; Roup et al., 2006). A substantial increase in the magnitude of the REA for DL has also been demonstrated in older adults. Although DL performance apparently declines in both ears with increasing age (Hugdahl et al., 2001), the LE performance often decreases more dramatically relative to the RE performance (i.e., increased REA) (Bellis & Wilber, 2001; Fischer et al., 2017; Hirnstein et al., 2013; Jerger et al., 1994; Roup et al., 2006; Roup, 2011; Westerhausen et al., 2015). For example, Kam and Keith (2010) found that when different digits were dichotically presented using a free recall paradigm, the mean REA in older adults was 16.08% while young adults obtained a rather small mean REA of 0.08%. Similarly, Jerger et al. (1994)

investigated age-related changes in the magnitude of the REA using the dichotic sentence identification test (Fifer et al., 1983) in both free-and-directed recall paradigms. The results revealed that the REA was significantly different in all age groups except for the youngest group. The magnitude of the REA increased systematically from an average of 1.5% in the youngest group up to a 40% in the oldest group despite relatively symmetrical hearing loss in the older listeners. These results were similar for both free-and-directed recall paradigms. According to the authors, the enlarged magnitude of the REA for DL observed in older adults was the result of a greater deficit in the LE performance attributed to an age-related auditory processing decline (Jerger et al., 1994).

The presence of an age-related decline in peripheral hearing is the most likely factor contributing to differences in overall DL performance between the young and older groups (Fischer et al., 2017; Jerger et al., 1991; Humes et al., 1996). However, the asymmetrical decline in DL performance between both ears, which leads to a larger the magnitude of the REA among older adults, is not likely to be attributed to age-related declines in peripheral hearing (Bellis & Wilber, 2001; Gootjes et al., 2007; Roup et al, 2006; Strouse & Wilson, 1999). On the one hand, previous studies (e.g., Hälgren et al., 2001; Kam & Keith, 2010) have not revealed a significant association between pure-tone thresholds and the magnitude of the REA for DL, suggesting that age-related changes in audibility may not account for the larger REA observed in older adults. On the other hand, some studies (e.g., Bellis & Wilber, 2001; Gootjes et al., 2004, 2007; Martin & Jerger, 2005) have concluded that the increased magnitude of the REA among older adults does not seem to be explained by differences in peripheral hearing sensitivity between ears as older adults who have participated in previous studies normally exhibit bilateral symmetric hearing.

Remarkably, none of the above-mentioned studies have investigated whether ID in audibility contributes to the increased magnitude of the REA for DL among older adults. Jerger et al. (1994) however, found that ID in pure-tone thresholds accounted for only 5 % of the variance for the interaural asymmetry (i.e., REA) in DL performance in the dichotic sentence identification test (Fifer et al., 1983). Jerger et al. used sentences which have relatively more semantic and lexical content as opposed to other speech stimuli such as digits or CV syllables (Findlen & Roup, 2011). Thus, the potential effect of ID in audibility in the magnitude of the REA may have been obscured by older adults' ability to make use of semantic and lexical content conveyed by the sentences (Findlen & Roup, 2016). Therefore, by minimizing the relevance of lexical content, using speech material such as CV syllables, this research project will provide new insights regarding the possible contribution of ID in audibility in the magnitude of the REA for DL among older adults with age-appropriate hearing.

Changes in the REA's magnitude due to a greater deficit in the LE performance have been partly attributed to age-related declines in central auditory processing (Jerger & Martin, 2006). As previously mentioned, the structural model of DL (Kimura, 1961) explains the REA for speech stimuli because of a) prewired asymmetries in the ascending auditory pathway due to stronger contralateral neural projections from the RE to the language-dominant LH of the brain (Kimura, 1961), and b) a relatively small deficit in the LE performance in normal right-handed listeners related to a delay and/or attenuation of information during the additional callosal relay stage (Kimura, 1961). Following Kimura's model, several theories have been proposed to explain the increased REA in older adults. On the one hand, the RH dysfunction theory (Goldstein & Shelly, 1981) proposes that the RH would be more vulnerable to the effects of age relative to the LH, causing a stronger decline in the functions of the RH (Dolcos et al., 2002). Therefore, a greater

deficit of the LE in DL could result from an age-related decline of the RH's ability to process the LE stimuli before it reaches the LH auditory/speech areas for final processing (Gootjes et al., 2004; Westerhausen et al., 2015).

On the other hand, the corpus callosum deficit theory (Goldstein & Braun, 1974) proposes that age-related structural changes in the corpus callosum deteriorates (i.e., delay or weaken) interhemispheric transfer of verbal auditory stimuli from the LE to the LH, further accentuating the LE deficit in DL and thus, increasing the magnitude of the REA among older adults. There is converging evidence suggesting that callosal lesions yield large interaural asymmetries in DL tasks with decreased LE performance relative to the RE (Gadea et al., 2002; Pollmann et al., 2002; Springer & Gazzaniga, 1975; Weihing & Atcherson, 2014). Age-related changes in the corpus callosum have also been found in older adults (Allen et al., 1991; Doraiswamy et al., 1991). These changes may likely affect the efficiency of interhemispheric transfer across the corpus callosum (Sullivan et al., 2002; Fling et al., 2011) and therefore, reduce LE performance in DL tasks. Gootjes et al. (2006) found that corpus callosum size correlated with an increased interaural asymmetry in DL performance in older adults. Specifically, decreased size in the posterior callosal subarea (isthmus and splenium) was significantly associated with an increased magnitude of the REA in older adults (Gootjes et al., 2006). Thus, an increased magnitude of the REA for DL among older adults might also be attributed to compromised interhemispheric connections via the corpus callosum.

In summary, based on the above-mentioned theories, changes in the REA's magnitude due to a greater LE deficit may be attributed to a selective age-related decline of RH functions and/or an age-related decline of corpus callosum functioning resulting in reduced interhemispheric

interaction. While these theories of DL performance in older adults suggest a more cortical (structural and functional) basis to account for the increased magnitude of the REA, it remains unclear whether sensory processing at lower portions (i.e., peripheral and subcortical) of the auditory system might also explain the enlarged REA observed in this population. This research project will attempt to answer this question.

1.5 Age-related cognitive effects on the REA for DL among older adults

Age-related declines in cognitive functions might also be linked to a greater decline in the LE performance in DL, likely exerting an effect on the magnitude of the REA among older adults (Jerger et al., 1991; Hällgren et al., 2001; Humes et al., 2006; Andersson et al., 2008; Hugdahl et al., 2009; Hommet et al., 2010). For example, Bellis and Wilber (2001) found that speed of mental processing, as measured by the Cross-Out subtest of the Woodcock-Johnson Psycho-Educational Test Battery, was negatively correlated with the REA of the 2-paired dichotic digit test. Specifically, as speed of mental processing decreased with age, the magnitude of the REA in DL increased. Similarly, Hällgren et al. (2001) found that speed of mental processing and working memory were significantly correlated with the results of the DL test when focusing to the LE, but not when focusing to the RE in the directed recall condition. These results suggest that older adults require increased cognitive involvement to focus attention, store and correctly report the speech stimuli coming from the LE during DL (Hällgren et al., 2001).

In addition, an age-related decline in the LE performance in DL has also been linked with reduced cognitive control (Hugdahl et al., 2009) and reduced inhibitory control (Hommet et al., 2010). As described by Hugdahl (2000, 2003), during the forced-left condition, when attention must be focused to the LE, stimulus-driven processing and instruction-driven processing have opposite

effects: the former is in favor of the RE while the latter is in favor of the LE. Thus, individuals must overcome stimulus-driven processing in favor of instruction-driven processing. In general, older adults show less inhibitory cognitive control to counteract (i.e., suppress) a bottom-up or stimulus-driven RE response tendency and to focus attention to the LE during the forced-left condition (Andersson et al., 2008; Takio et al., 2009; Thomsen et al., 2004). This difficulty to overcome the stimulus driven processing in favor of instruction driven processing might strongly depend on executive inhibitory functions, which have been found to decrease in older adults (Chao & Knight, 1997; Kramer et al., 1994; MacPherson et al., 2002). This might explain the increased difference in performance of the attended ear between the forced-right and forced-left condition in older adults (Gootjes et al., 2007; Hugdahl et al., 2009; Westerhausen et al., 2015). Overall, changes in the magnitude of the REA for DL might also be explained by a greater LE deficit in DL performance attributed to age-related declines in cognitive functions.

However, it appears that age-related declines in cognitive functions cannot fully account for the increased magnitude of the REA in DL among older adults. In a recent study, which investigated the effects of age on the magnitude of the REA in DL, Westerhausen et al. (2015) utilized a nonforced and single consonant-vowel stimulus pair DL paradigm (Hugdahl & Anderson, 1986). The rationale to select this DL paradigm was that it minimized a) the influence of higher cognitive functions, such as working memory by only including one dichotic stimulus pair as well as requiring only one response per trial, and b) the relevance of cognitive-control processes by not requiring stimulus localization and response-selection processes (Westerhausen et al., 2015). The main result showed that the magnitude of the REA was stable throughout the young and middle adult lifespan (20 to 59 years), but significantly increased in older adults above 60 years. Such an

increase in the REA's magnitude starting at 60 years was mainly driven by an age-related deficit in the LE performance.

According to Westerhausen et al., this selective age-related LE deficit likely occurred at an early, pre-attentional bottom-up stage of processing, since top-down cognitive-control process and working memory load were minimized by the DL paradigm used. The authors hypothesized that this greater LE deficit resulted from an age-related decline in the LE auditory pathway, delaying or weakening the trajectory of LE stimuli starting from the cochlea to the LH in older adults (Westerhausen et al., 2015).

As previously stated, reduced interhemispheric transfer function of the corpus callosum (Gootjes et al., 2006) and/or declines in the functions of the RH due to increasing age (Goldstein & Shelly, 1981; Dolcos et al., 2002) might affect LE performance in DL among older adults. Yet, as a logical extension of the hypothesis proposed by Westerhausen et al. an age-related decline in the LE but not in the RE auditory pathway may also suggest an increase in ID in sensory processing occurring at lower (i.e., peripheral and brainstem) portions of the auditory system. Accordingly, increased ID in sensory processing at earliest stages of the auditory system might also account for the increased magnitude of the REA for DL among older adults. This research project will investigate this hypothesis.

1.6 Speech perception in noise and its link with DL performance among older adults?

Understanding speech in challenging acoustic environments is difficult for everyone, particularly for older adults which are more vulnerable to the effects of background noise compared to their younger counterparts (Ben-David et al., 2012; Gates & Mills, 2005; Gordon-Salant, 2005). SIN

difficulties are a common complaint among older listeners in the clinical setting (Tremblay et al., 2003; Yueh et al., 2003), which often complicates the rehabilitation process, leading to social isolation and/or decreased quality of life (Heine and Browning, 2002). With widespread population aging (Vincent & Velkoff, 2010), it is essential to understand the age-related changes associated with SIN performance along with the underlying biology that contributes to these problems.

According to Chandrasekaran and Kraus (2010), SIN can be understood as a “*complex task involving the abilities to extract key features in the signal while suppressing irrelevant details, temporarily store this information while ignoring noise, process a stream from a single source amid numerous other sources (e.g., a speaker’s voice), and use linguistic context to ‘fill in’ details lost in the noise*” (p.297). Successful understanding of speech in the presence of background noise depends on cognitive abilities along with sound processing at peripheral, subcortical, and cortical levels (Humes et al., 2012). Consistent with the Working Group on Speech Understanding and Aging Committee on Hearing, Bioacoustics, and Biomechanics (CHABA, 1988), SIN abilities among older adults decreases if one of the above-mentioned aspects declines. Correlational studies indicate that age-related decline in peripheral hearing may be considered as the primary underlying factor contributing to SIN difficulties experienced by older adults (Humes, 1996; Humes et al., 1994; Humes and Roberts, 1990). However, these difficulties may still be present in older listeners even in the absence of hearing impairment (Dubno et al., 2002b; Humes, 1996), suggesting that age-related declines that go beyond sound detection abilities might also contribute to impaired SIN among older listeners (Anderson et al, 2011).

Cognition plays an important role in older adult’s SIN performance (Anderson et al. 2012; 2013). Age-related declines in cognitive abilities, such as working memory, attention, and processing

speed may increase older adult's difficulties to understand speech in noise (Schneider et al., 2010; Füllgrabe et al., 2015; Gordon-Salant & Cole, 2016). Moore et al. (2014) studied the association between cognitive functions (e.g., processing speed and memory) and SIN performance in adults between 40 to 60 years. Results revealed that SIN ability declined exponentially with age starting at 50 years, and that such a decline was more considerable among participants with lower cognitive abilities. Both advancing age and reduced cognitive ability were independently associated with increased difficulties to understand speech in the presence of background noise (Moore et al., 2014). These results suggest that older adults may require more cognitive resources, putting higher demands on top-down processing to interpret the speech signal in the presence of background noise (Gosselin & Gagné, 2011; Schoof & Rosen, 2014). For example, when the audibility of the speech signal is reduced due to background noise, older adults will allocate more working memory resources trying to comprehend the impoverished incoming speech signal (Gordon-Salant & Cole, 2016).

In addition, older adults usually experience age-related changes in auditory processing such as exhibiting a deterioration in dichotic listening (DL) abilities (Roup et al., 2006; Strouse et al., 2001). DL may be considered as a challenging listening situation whereby the listener is required to cope with the simultaneous presentation of two different and competing auditory stimuli to the right and left ears (Hugdahl & Helland, 2013). Older adults often exhibit an overall decline in DL scores relative to young adults, which indicates reduced capacity to segregate and/or integrate information during binaural competing situations (Martin & Jerger, 2005; Moncrieff et al., 2013). Moreover, older adults usually exhibit an increased REA for speech processing as compared to young adults (Jerger et al., 1994; Kam & Keith, 2010; Roup et al., 2006). However, such a substantial increase in the magnitude of the REA among older adults seems to be the result of a

greater LE deficit in DL performance (Jerger et al., 1994; Bellis & Wilber, 2001; Roup et al., 2006; Kam & Keith, 2010). It has been suggested that this marked interaural imbalance (i.e., greater LE deficit) observed in verbal DL tasks might have a considerable impact on older adults' ability to use binaural information effectively, which could ultimately interfere with their capacity to understand speech in the presence of background noise (Jerger et al., 1994, 1995; Carter et al., 2001). In fact, DL performance has been significantly associated with increased difficulties understanding speech in noise among older adults (Lavie et al., 2013, Mukari et al., 2020). Specifically, an increased REA (i.e., greater LE deficit) for DL has been significantly associated with worse SIN performance, as measured with the hearing-in-noise test (HINT; Nilsson et al., 1994), among older listeners (Mukari et al., 2020). Moreover, reduced performance in the LE have been significantly associated with higher signal-to-noise ratios required to identify words in the presence of background noise in older adults (Lavie et al., 2013).

Previous studies have suggested that a greater LE deficit in DL performance, which substantially increases the magnitude of the REA among older adults, may be partly attributed to a selective age-related decline of the right hemisphere (RH) functions and/or an age-related decline of corpus callosum functioning resulting in reduced interhemispheric interaction (Goldstein & Shelly, 1981; Dolcos et al., 2002; Gootjes et al., 2006). More recently, it has been shown that asymmetries (hereafter interaural differences (ID)) in sensory processing occurring at lower (i.e., peripheral and brainstem) levels of the auditory system might also contribute to the increased magnitude of the REA (i.e., greater LE deficit) for DL (Emmerich et al., 1988; Markevych et al., 2011; Hu & Lau, 2017). In older adults however, this association has not been investigated. As mentioned above, DL and SIN performance appears to be significantly associated among older adults (Lavie et al., 2013; Mukari et al., 2020), which suggests that some of the underlying auditory processing

mechanisms for both skills might be overlapping (Martin and Jerger, 2005; Walden & Walden, 2005; Bhatt & Wang, 2019). Therefore, if ID in peripheral and subcortical auditory processing are indeed associated with the increased magnitude of the REA for DL among older adults, they might also be associated with SIN performance. This project will investigate whether ID in sensory processing at lower levels of the auditory system contribute to the increased REA for DL and SIN difficulties among older adults.

The current study utilized the Hearing-in-Noise Test (HINT, Nilsson et al., 1994) which is an efficient and reliable method to assess speech intelligibility in noise (Soli & Wong, 2008). The reason to use the HINT was two-fold: first, the HINT has been adapted for the adult Canadian Francophone population (Vaillancourt et al., 2005) and it has been previously used to assess SIN in challenging acoustic situations among older adults (Dubno et al., 2002a; Kim et al., 2006); Second, the HINT evaluates speech intelligibility in different listening conditions that differ only in the location of the noise source: sentences and noise presented in front; noise presented to the RE with sentences presented in the front; and noise presented to the LE with sentences presented in the front (Nilsson et al., 1994).

1.7 ID in sensory processing at lower levels of the auditory system in young and older adults

Evidence of ID in peripheral and subcortical auditory processing have been well documented in young adults. At a peripheral level, when evaluated using measures such as behavioral hearing thresholds, better (lower) hearing thresholds have been observed in the RE compared to the LE in young adults (McFadden, 1993; McFadden & Mishra, 1993). Similar results have been found with transient evoked otoacoustic emissions (TEOAE), which are sounds that arise following an

acoustic stimulation that correspond to the active mechanical function of the outer hair cells of the organ of Corti (Brownell, 1990). Young adults show significantly larger TEOAE response amplitudes (dB SNR) in the RE than the LE (McFadden, 1993; McFadden & Mishra, 1993; Khalfa & Collet, 1996; McFadden et al., 1996; Khalfa et al., 1997). Further evidence for the existence of a left/right difference in the functioning of the human peripheral auditory system comes from studies demonstrating stronger auditory efferent activity in the RE than the LE (Khalfa & Collet, 1996; Khalfa et al., 1998; Philibert et al., 1998; Bidelman & Bhagat, 2015).

At a subcortical level, similar amplitudes, and neural response latencies between RE and LE presentation have been shown in young adults for the ABR when it is elicited by click stimuli. However, for speech-like stimuli (e.g., /da/syllable), temporal and frequency-related components of speech (i.e., first, and high-frequency formants) seem to be preferentially encoded by the RE compared to the LE (Ahadi et al., 2014; Hornickel et al., 2009; Sinha & Basavaraj, 2010), suggesting that at a preattentive, sensory stage of auditory processing, acoustic elements of speech are asymmetrically processed between the right and left auditory pathways in young adults. Overall, the evidence supports the existence of enhanced peripheral and subcortical auditory processing in the RE compared the LE in younger population.

Remarkably, little is known about ID in sensory processing at lower level of the auditory system in older adults. At a peripheral level, better (lower) hearing thresholds in the RE compared to the LE have been demonstrated in older adults (e.g., Glorig, 1958; Gates et al., 1990; Gates et al., 1991; Cruickshanks et al., 1998). However, evidence indicating right/left TEOAE response differences in older adults is rather inconclusive. To the best of our knowledge, there are only two studies showing opposite findings of TEOAE differences between the right and left ears in older adults.

Tadros et al. (2005) found that older adults with normal hearing thresholds showed significantly larger TEOAE response amplitudes in the RE compared with the LE. Whereas Profant et al. (2015) found no significant TEOAE amplitude differences between right and left ears among older adults. Based on this evidence, the pattern of TEOAE lateralization among older adults may not be clearly identified. Similar results can be observed regarding TEOAE suppression. There is only one published study indicating no significant differences in MOC-induced TEOAE suppression between the right and the left ears among older adults (Tadros et al., 2005). Taking all this evidence into account, further research is therefore required to conclude whether older adults exhibit a pattern of lateralization for TEOAE and MOC-induced TEOAE suppression between both ears like young adults.

At a subcortical level, studies of click-ABR reveal that monaural RE and LE presentation yield similar amplitude and latency neural response at the brainstem level in older adults (Vander Werff & Burns, 2011; Van Yper et al., 2016). These results are like the results found in young adults suggesting the absence of ID in subcortical processing for click stimuli (e.g., Rowe, 1978; Lauter & Karzon, 1990; Hornickel et al., 2009; Sinha & Basavaraj, 2010; Vander Werff & Burns, 2011; Peng et al., 2016). Regarding speech-like stimuli, findings of subcortical laterality of speech encoding have only been reported by Vander Werff & Burns (2011). Specifically, faster temporal encoding for RE presentation compared to LE presentation was found for the transient component A of the speech-ABR. ID in subcortical processing for other speech-ABR components were not found. These results partially agree with the above-mentioned results found in young adults showing ID in subcortical processing for transient (like older adults), sustained and frequency components of speech stimuli. Taking this scant evidence into account, it remains thus unclear

whether older adults exhibit a clear pattern of subcortical laterality of speech encoding as young adults do. Further research in a larger group of older adults is necessary to solve this issue.

As mentioned early, it has been suggested that the auditory structures/pathways subserving LE input are somehow more affected by aging than the structures/pathways subserving RE input (e.g., Gates et al., 1990; Gates & Cooper, 1991; Jerger et al., 1994; Weihing & Musiek, 2014; Westerhausen et al., 2015). Thus, it may be possible that a greater age-related decline in the LE relative to the RE pathway increases ID in peripheral and subcortical auditory processing among older adults. This research project will investigate ID in peripheral and subcortical auditory processing to further understand whether sensory differences along the auditory pathway (i.e., peripheral and brainstem) between the RE and LE are modified with age.

1.8 ID in sensory processing at lower levels of the auditory system and their link with the REA for DL

A few studies carried out in young adults provide some evidence supporting an association between ID in sensory processing at lower levels of the auditory system and the magnitude of the REA for DL tasks. Emmerich et al. (1988) investigated the relationship between interaural audibility differences and the REA for DL. Results showed that the REA was significantly correlated with the mean ID in audibility for 1000Hz, 2000Hz, and 4000Hz. Also, Markevych et al. (2011) found in young adults with normal hearing a significant correlation between ID for the suppressed TEOAE with contralateral acoustic stimulation and the REA in a DL test with CV-stimuli. Specifically, as the ID for the suppressed TEOAE became more negative (i.e., TEOAEs in the LE were less suppressed by noise from the RE), the LE performance in DL decreased, leading to a larger REA. In addition, Hu and Lau (2017) examined the association between ID in click-ABR

and DL. Findings indicated a significant correlation between ID in central conduction time (interpeak I-V) and DL performance. Specifically, as the ID in central conduction time became more positive (i.e., faster central conduction time in the RE), the magnitude of the REA for DL increased among young adults (Hu & Lau, 2017). It should be mentioned however, that ID in sensory processing at lower levels of the auditory system (i.e., audibility, TEOAE suppression and click-ABR neural timing) were significantly correlated with the REA for DL albeit the fact that there were no statistically significant differences between the RE and the LE (Emmerich et al., 1998; Markevych et al., 2011; Hu & Lau, 2017). These results suggest that small differences (which are not statistically significant) at preattentive bottom-up sensory stages (i.e., peripheral and brainstem) of auditory processing between the RE and the LE could impact an individual's ability to process speech during competing acoustic situations such as DL.

In older adults, the association between the magnitude of the REA for DL and ID in sensory processing at lower levels of the auditory system has not been investigated. However, considering the results in young adults and the view that ID in peripheral and subcortical processing could likely increase due to a weaker LE auditory pathway, it may be possible that an increase magnitude of ID in sensory processing at lower levels of the auditory system partly contributes to the increased magnitude of the REA for DL in older adults. From a neuroscientific perspective, this information is important because the source of variability accounting for the substantial increase in interaural asymmetry in DL performance among older adults, which ranges between 10% and 30% (Jerger et al., 1994; Bellis & Wilber, 2001; Strouse & Wilson, 1999, 2001; Roup et al., 2006, 2011; Kam and Keith, 2010) has been mostly attributed to declines in cognitive functions (e.g., working memory, attention) and reduced callosal thickness. Thus, results from the present research may help explain some of the performance variability in DL experienced by aging adults. In addition, considering

that DL performance (i.e., greater LE deficit) has been significantly associated with increased difficulties understanding speech in noise among older adults (Lavie et al., 2013, Mukari et al., 2018), it may be thus possible that an increased ID in peripheral and subcortical processing due to an age-related decline in the LE auditory pathway may partly explain SIN difficulties among older adults.

Chapter 2- Aims of the research

Existing evidence suggests that the source of the increased magnitude of the REA for DL with advancing age may originate mainly from a greater LE deficit caused either: (A) by an age-related decline in cognitive abilities, such as working memory, attention, processing speed, and inhibitory control (Bellis & Wilber, 2001; Hällgren et al., 2001; Hommet et al., 2010); (B) by an age-related decline of corpus callosum functioning resulting in reduced interhemispheric interaction (Gootjes et al., 2006); and/or (C) by an age-related decline in the functions of the RH (Goldstein & Shelly, 1981; Dolcos et al., 2002). Current evidence in normal hearing young adults suggest that ID in sensory processing at lower portions of the auditory system (i.e., periphery and brainstem) might also explain the magnitude of the REA for DL. This association has not been investigated among older adults. The main objective of this thesis is to investigate whether the magnitude of ID in sensory processing at lower levels of the auditory system are associated with the magnitude of the REA for DL among older adults. In addition, considering that a greater LE deficit may increase speech perception difficulties in the presence of background noise (Jerger et al., 1995; Carter et al., 2001; Moncrieff et al., 2013; Lavie et al., 2013), this project will also investigate if the magnitude of ID in sensory processing at lower levels of the auditory system are associated with SIN performance in older adults. However, considering that the pattern of peripheral and subcortical lateralization among older adults is still unclear, additional research is foremost required to understand whether older adults demonstrate sensory differences at early stages of auditory processing between the RE and LE. To this end, the following specific objectives were addressed in the current study:

1. The first objective was to investigate ID in sensory processing at lower levels of the auditory system in older adults. More precisely, this study aimed to determine whether older adults exhibit differences in peripheral and subcortical processing between the right and left ears. This objective was addressed in a cross-sectional manner within the articles. Particularly, the focus of the first article was to investigate possible subcortical processing differences between right and left ear presentation in older adults. Differences in subcortical processing for click and speech stimuli between the right and left auditory pathways have been widely documented in young adults (e.g., Levine & McGaffigan, 1983; Levine et al., 1988; Sininger et al., 1998; Hornickel et al., 2009; Sinha & Basavaraj, 2010; Ahadi et al., 2014). However, it remains unclear whether the pattern observed in younger samples (i.e., symmetric responses for click stimuli and asymmetric responses for speech-like stimuli at the brainstem level between RE and LE input) changes among older adults. In addition, the second article devote a part of the research to investigate ID in peripheral auditory processing among older adults. At a peripheral level, better hearing sensitivity in the RE compared to the LE has been demonstrated among older adults (e.g., Glorig, 1958; Gates et al., 1990; Gates et al., 1991; Cruickshanks et al., 1998). However, further research is therefore required to conclude whether older adults exhibit a clear pattern of lateralization for TEOAE and MOC-induced TEOAE suppression between both ears like young adults. Several studies have suggested that the auditory structures/pathways subserving LE input are more affected by aging than the structures/pathways subserving RE input (e.g., Gates et al., 1990; Gates & Cooper, 1991; Jerger et al., 1994; Weihing & Musiek, 2014; Westerhausen et al., 2015). Therefore, if older adults do exhibit ID in peripheral and subcortical auditory processing, it may be hypothesized that these ID will be larger than those among young adults.

2. The second objective was to investigate whether the magnitude of ID in sensory processing at lower levels of the auditory system was associated with the increased magnitude of REA for DL among older adults. Converging evidence in normal hearing young adults (e.g., Emmerich et al. 1988; Markevych et al., 2011; Hu and Lau, 2017) indicates that ID in sensory processing at lower portions of the auditory pathways partly explain the magnitude of the REA for DL. In older adults however, the association between the REA in DL and ID in sensory processing at lower levels of the auditory system has not been investigated. Taking the above-mentioned studies conducted in young adults into account and the evidence that the LE pathway becomes even weaker in older adults, it may be hypothesized that the magnitude of the ID in sensory processing at lower portions of the auditory system explains in part the increased magnitude of the REA in DL observed in older adults. The second article test this hypothesis by examining whether ID in peripheral (i.e., hearing thresholds, TEOAE response, and MOC suppression of TEOAE) and subcortical (i.e., speech-ABR neural timing encoding) processing account for the increased REA's magnitude for DL in older adults.

3. The third objective was to investigate whether the magnitude of ID in sensory processing at lower levels of the auditory system was associated with SIN performance among older adult listeners. Several authors have suggested that aging causes a greater decline in the LE auditory pathway than the RE pathway. A greater age-related decline in the LE than the RE auditory pathway suggests that older adults may exhibit an increased ID in sensory processing at lower levels of the auditory system and with this, SIN difficulties may likely increase among older adults. Thus, it may be hypothesized that the magnitude of ID in sensory processing at lower levels of the auditory system explains, at least in part, SIN performance among older adults. The third article

addresses this subject by exploring if ID in peripheral and subcortical processing explain speech perception performance under three different simulated noise conditions.

Chapter 3- General methodology

The research protocol was reviewed and approved by the ethics committee of the Centre de recherche de l'Institut universitaire de gériatrie de Montréal (CER VN 17-18-15). Signed consent forms were obtained from all participants, and monetary compensation was given for their participation.

3.1 Participants

A total of 70 older adults (35 women and 35 men) between the ages of 61 and 90 years (mean \pm Standard Deviation (SD) = 71.47 ± 6.12) participated in the study. Participants were recruited from the registry of research participants from the Institut Universitaire de Gériatrie de Montréal (IUGM) as well as via posts and word of mouth. Inclusion criteria for all participants comprised: 1) Quebec-French as first language; 2) right-hand dominance determined by the Edinburgh Handedness Inventory (Oldfield, 1971); 3) no history of middle-ear infections, neurologic conditions, or major chronic health conditions; 4) normal global cognitive function determined by the Montreal Cognitive Assessment (MoCA; Nasreddine et al, 2005); 5) no visible alterations of the ear canal or tympanic membrane under otoscopic examination; 6) bilateral type-A (normal) results for tympanometry (Jerger, 1970); 7) bilateral pure-tone thresholds not exceeding the 25th percentile of the distribution of hearing thresholds obtained from an otologically screened population of similar age and sex (ISO 7029-2000); and 8) symmetric hearing defined as an interaural pure-tone threshold difference of no more than 10 dB at two or less audiometric frequencies between 250 and 8000 Hz.

3.2 Procedures

3.2.1 Participant selection

Each participant was individually scheduled for an appointment at the audiology laboratory located at l'école d'orthophonie et audiologie de l'Université de Montréal. The session started with an oral explanation about the research aims and procedures to be used. Participants were invited to ask for clarification in case something was not clear. Also, an informed consent form was provided. All participants were asked to read the form and sign it if they agree to proceed with the interview and auditory assessment. None of the subjects refused to proceed. Once the research aims and assessment procedures were clear the Edinburgh Handedness Inventory (Oldfield, 1971) was used to evaluate hand-dominance. This inventory is a ten-item questionnaire designed to assess handedness by self-report of the preferred hand for carrying out common activities. The questionnaire was utilized with the aim to include only right-handed dominant participants in the study due to the greater variability in dichotic speech recognition performance associated with left-handed individuals (Wilson & Leigh, 1996). Then, the Montreal Cognitive Assessment (MoCA; Nasreddine et al, 2005) was used to rule out mild cognitive impairment. The MoCA is a screening tool for cognitive impairment that covers major cognitive domains such as episodic memory, language, attention, orientation, visuospatial ability, and executive functions, while remaining brief and easy to administer. All participants achieved a normal MoCA score of ≥ 26 (out of 30 points). The average MoCA score was 28.7 (SD = 1.12) suggesting no cognitive impairment (Nasreddine et al., 2005).

Following the procedures, bilateral otoscopy and tympanometry were carried out. Only participants with an absence of visible pathologic alteration of the ear canal and normal type A tympanometric

results (tympanic peak pressure between -100 and $+50$ daPa and static compliance ≥ 0.2 mL, Jerger, 1970) were included in the sample. Bilateral type A tympanograms were obtained in all participants with a Zodiac 901 tympanometer (Madsen, GN Otometrics, Denmark). Then, a standard comprehensive audiometric evaluation was performed to determine if participants had age-appropriate peripheral hearing. Bilateral pure-tone audiometry was conducted with an Interacoustics AC40 clinical audiometer (Interacoustics A/S, Middelfart, Denmark) using ER-3A insert earphones (Etymotic Research, Elk Grove Village, IL, USA). Audiometry along with other hearing tests (mentioned in the section below) were conducted in a double-walled sound treated room meeting ANSI S3.1-1999 for ambient sound pressure levels. All participants included in the study presented with pure-tone thresholds at the tested frequencies (i.e., 250, 500, 1000, 2000, 3000, 4000, 6000 and 8000 Hz) that did not exceed the 25th percentile of the distribution of hearing thresholds obtained from an otologically screened population of similar age and sex (ISO 7029-2000). As mentioned in the inclusion criteria, only participants with symmetric hearing levels between both ears were included in the sample. Bilateral pure-tone thresholds were stored and further used for statistical analyses as a measure of the function of the peripheral auditory system. Word recognition in quiet was measured using prerecorded 25-item word lists spoken in Quebec French. The word lists were presented at 40 dB SL above the pure-tone average of 500, 1000, and 2000Hz. The mean word recognition score was 98.29% on the RE and 97.76% on the LE, with at least 92% accuracy in each ear for all participants.

3.2.2 Data collection

All selected participants were then evaluated with a comprehensive battery of hearing tests investigating TOEAEs, click and speech ABR, DL and SIN performance. In addition, all participants were assessed for cognitive function. To reduce fatigue, data for all participants were

collected over two sessions. Participant selection (see above section 2.1.1) and behavioral tasks (i.e., DL and SIN tasks) were administered in session I and were completed within two hours. Cognitive tests in addition to electroacoustic and electrophysiological assessment of the auditory system were conducted in session II. This session lasted approximately two hours and thirty minutes. The second session was completed within four weeks after the first session in all participants.

First session

After each participant was selected for the study, a DL test in French was used to evaluate DL ability. The iPhone version of the Bergen Dichotic Listening test (Hugdahl & Andersson, 1986), the *iDichotic* (Bless et al., 2013), was used. The stimuli consisted of six consonant-vowel syllables /ba/, /ga/, /da/, /pa/, /ka/ and /ta/. The full set includes 30 dichotic-stimulus pairs, presenting different syllables to right and left ears (e.g., /ba/-/ka/, /ka/-/ba), as well as 6 homonymic pairs, presenting the same syllable to the right and left ear. The syllables were natural recordings, spoken by a male voice with constant and neutral intonation. Participants were instructed to repeat back in a nonforced and forced attention (forced-right and forced-left) manner. In the nonforced paradigm, participants were instructed to report the syllable that was heard best immediately after each stimulus presentation. In the forced-right and forced-left conditions, participants were required to report the syllable heard from the cued ear (only right or only left), ignoring the stimulus from the contralateral ear. The *iDichotic* test was administered using an iPhone 6, which was connected to the clinical audiometer (Interacoustics AC40). Participants listened to the stimuli through ER-3A insert earphones connected to the above-mentioned audiometer, at a fixed presentation level of 70 dB HL to allow maximum intelligibility of the dichotic stimuli. Before starting the test, the 1-kHz

tone in the device app was used to calibrate the audiometer's volume unit meter with the output intensity of the iPhone for each audiometric channel separately.

Then, the Hearing-in-Noise Test (HINT, Nilsson et al., 1994) with the Canadian French sentence module (Vaillancourt et al. 2005) was used to evaluate speech perception in noise. All stimuli were delivered via ER-3A earphones. Signal-to-noise ratios (SNRs) for 50% speech discrimination were calculated. For each condition, a set of 20 sentences was presented in the presence of noise, spectrally matched to the average long-term spectrum of the sentences. The HINT was conducted in three different noise simulated conditions: 1) sentences and noise delivered to the front (HINT NF); 2) noise delivered to the RE with sentences delivered to the front (HINT LE); and 3) noise was delivered to the LE with sentences delivered to the front (HINT RE). Throughout testing, sentences were only played once, and participants were encouraged to repeat the complete sentence and to guess if they were unsure of the sentence heard.

Second session

During the second session, two different cognitive tests were carried out. First, the Trail making test (TMT; Reitan & Wolfson, 1993) which is administered in two parts was conducted. The TMT part A evaluates cognitive speed of processing. This test requires participants to draw a line connecting a series of numbers in sequential order (1–3, etc.). The TMT part B provides information on mental flexibility and executive functions. This test requires participants to draw a line connecting a series of number and letters in alternating, sequential order (1-A-2-B, etc.). Following the TMT, the short French version of the reading span test (RST; Desmette et al., 1995) was used to assess the participant's working memory capacity. Each participant had to read aloud the sentences presented within a set and to remind the sentence-final word. After reading all the

sentences within a set, participants had to recall the final word of each sentence without starting the recall process with the last word of the last sentence read.

Once participants completed the cognitive tests, other auditory tests were conducted. TEOAE provide frequency-specific information about cochlear function and outer hair cell motility (Kemp, 2002). TEOAEs with and without contralateral acoustic stimulation were obtained measured and analyzed for both ears using the SmartTrOAE module (version 5.10, Intelligent Hearing Systems, Miami, FL, USA) connected to an HP ProDesk 600 G2 Mini Desktop computer. Participants were instructed to stay as still as possible and to keep their head straight during TEOAE measurement. TEOAE were expressed in dB signal-to-noise ratio (dB SNR). Then, click and speech ABR were used to objectively explore the ability of the brainstem to accurately encode timing information in older adults (Vander Werff & Burns, 2011; Anderson et al., 2012). Click and speech ABR for right- and left-ear stimulation was elicited and registered using a two-channel Intelligent Hearing System (IHS, Miami, FL, United States) SmartEP module (version 3.95) connected to an HP ProDesk 600 G2 Mini Desktop computer. Electrodes placed at Fz (positive), A1 and A2 (negative), and the forehead (ground) in accordance with the International 10 to 20 system EEG were used for all recordings. For the click-ABR, two recordings were obtained (1024 sweeps each) per ear using 80-dBnHL in alternating polarity at a rate of 21.1/s. For the speech-ABR, two stimulus durations were used: 1) a 5-formant synthesized 40-ms /da/ syllable; and 2) a 6-formant synthesized 170-ms /da/ syllable. Both stimuli were presented separately to the right and left ear at 80 dB SPL in alternating polarity to minimize stimulus artifact. The 40-ms /da/ was presented at a rate of 10.9/s, and two blocks' of 2500 responses were recorded. The 170-ms /da/ was presented at a rate of 4.35/s, and two blocks of 3000 responses were collected and averaged resulting in 6000 response trials for each ear. For TEOAE and ABR testing, participants were seated in a comfortable chair in a quiet

room with lights dimmed. For a detailed description of the audiological and cognitive tests used, see the ‘material and methods’ section for each article presented.

Chapter 4- Article 1

Auditory brainstem response asymmetries in older adults: an exploratory study using click and speech stimuli

Alejandro Ianiszewski-Gómez, Adrian Fuente, Jean-Pierre Gagné

École d'orthophonie et d'audiologie, Faculté de médecine, Université de Montréal, Montréal,
Québec, Canada.

Centre de recherche de l'Institut universitaire de gériatrie de Montréal, Montréal, Québec,
Canada.

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Abstract

Some evidence suggests that young adults exhibit a selective laterality of auditory brainstem response (ABR) elicited with speech stimuli. Little is known about such an auditory laterality in older adults. The aim of this study was to investigate possible asymmetric auditory brainstem processing between right and left ear presentation in older adults. Sixty-two older adults presenting with normal hearing thresholds according to their age and who were native speakers of Quebec French participated in this study. ABR was recorded using click and a 40-ms /da/ syllable. ABR was elicited through monaural right and monaural left stimulation. Latency and amplitude for click- and speech-ABR components were compared between right and left ear presentations. In addition, for the /da/ syllable, a fast Fourier transform analysis of the sustained frequency-following response (FFR) of the vowel was performed along with stimulus-to-response and right-left ear correlation analyses. No significant differences between right and left ear presentation were found for amplitudes and latencies of the click-ABR components. Significantly shorter latencies for right ear presentation as compared to left ear presentation were observed for onset and offset transient components (V, A and O), sustained components (D and E), and voiced transition components (C) of the speech-ABR. In addition, the spectral amplitude of the fundamental frequency (F0) was significantly larger for the left ear presentation than the right ear presentation. Results of this study show that older adults with normal hearing exhibit symmetric encoding for click stimuli at the brainstem level between the right and left ear presentation. However, they present with brainstem asymmetries for the encoding of selective stimulus components of the speech-ABR between the right and left ear presentation. The right ear presentation of a /da/ syllable elicited reduced neural timing for both transient and sustained components compared to the left ear. Conversely, a stronger left ear F0 encoding was observed. These findings suggest that at a preattentive, sensory stage of auditory processing, older adults lateralize speech stimuli similarly to young adults.

Key words: Auditory brainstem response, speech encoding, ear asymmetries, auditory processing.

4.2 Introduction

Subcortical asymmetries between the right and left auditory pathways have been reported in newborns (Eldredge & Salamy, 1996; Sininger & Cone-Wesson, 2006; Sininger et al., 1998) and young adults (Hixson & Mosko, 1978; Hornickel et al., 2009; Lauter & Karzon, 1990; Peng et al., 2016; Rowe, 1978; Sinha & Basavaraj, 2010; Vander Werff & Burns, 2011). Studies conducted in samples of young adults have found that click stimuli seem to produce similar responses (i.e., amplitude and latency) for the auditory brainstem response (ABR) between right and left ear presentation. However, when using speech-like stimuli (e.g., /da/ syllable) an asymmetric pattern characterized by better encoding of both temporal and frequency components of stimuli for right ear presentation has been systematically reported in young adults (e.g., Ahadi et al., 2014; Hornickel et al., 2009; Krishnan et al., 2011; Sinha & Basavaraj, 2010). Therefore, at a preattentive, sensory stage of auditory processing, acoustic elements of speech are asymmetrically processed between the right and left auditory pathways. Some authors have suggested that asymmetric processing of speech-like stimuli at the subcortical level is expected due to hemispheric specialization for speech processing (e.g., Levine & McGaffigan, 1983; Levine et al., 1988). In other words, it has been suggested that hemispheric lateralization is associated with lateralization of the entire auditory pathway (Philibert et al., 1998; Schönwiesner et al., 2007) and thus speech-like stimuli are more efficiently processed when presented to the right ear (Jerger & Martin, 2004; Kimura, 2011).

Several studies have demonstrated that hemispheric lateralization diminishes with age and thus, less differentiation between right and left cortices is likely to be observed in older adults (Bellis et al., 2000; Chen et al., 2013; Goossens et al., 2016). Therefore, if subcortical processing is associated with the pattern of hemispheric lateralization as mentioned above, then it would be

expected that older adults exhibit a loss or reduction of the asymmetric subcortical processing of speech-like stimuli. However, little is known about asymmetric auditory processing at the brainstem level in older adults. Vander Werff and Burns (2011) and Van Yper et al. (2016) found no significant click-ABR latency or amplitude differences between right and left ear presentation in a group of older adults with age-appropriate hearing levels. Similarly, Munro et al. (2007) found comparable results (in latency and amplitude) for click-ABR between right and left ear presentation in a group of older adults with age-related symmetrical high-frequency sensorineural hearing loss. Therefore, these results are like the results found in young adults. With regards to speech-like stimuli, findings of subcortical laterality of speech encoding have only been reported by Vander Werff and Burns (2011). Specifically, faster temporal encoding for right ear (RE) presentation compared to left ear (LE) presentation was found for the transient component A of the speech-ABR. Asymmetric processing for the other speech-ABR components were not found. According to Vander Werff and Burns however, relatively few participants contributed to the significant result. Therefore, mean differences could have been driven by extreme values (in either ear) rather than by an ear laterality effect. As discussed by the authors, this is particularly plausible given the high similarity of each ear's waveform when they were visually inspected. Thus, according to Vander Werff and Burns (2011) a larger group of older adults is necessary to investigate any effects of brainstem laterality for speech encoding. Consequently, it remains unclear whether the pattern observed in young adults (i.e., asymmetric responses for speech-like stimuli at the brainstem level between RE and LE input) is modified in older adults. This piece of information is important because asymmetries in the processing of speech sounds throughout the entire auditory pathway (i.e., from the cochlea to the cortex) appear to be critical for normal speech perception (Bellis et al., 2000). Rapid temporal information, as conveyed in speech sounds, is preferentially processed in the RE/left auditory cortex pathway (Ahadi et al., 2014; Belin et al., 1998; Hornickel et al., 2009;

Krishnan et al., 2011; Sinha and Basavaraj, 2010; Tervaniemi & Hugdahl, 2003), whereas frequency components of sounds have been found to engage the RE/right auditory cortex more strongly than the opposite pathway (Ballachanda et al., 1994; Ballachanda & Moushegian, 2000; Zatorre & Belin, 2001; Zatorre et al., 1992). Thus, a loss of asymmetric processing between the right and left ear pathways may ultimately affect the ability to effectively process acoustic features of speech (Bellis et al., 2000; Chen et al., 2013; Goossens et al., 2016). Therefore, age-related changes in the asymmetric subcortical processing of speech-like stimuli may, at least partially, explain speech perception difficulties that go beyond sound detection problems, widely observed in older adults (Humes et al., 2012). The aim of this study was to investigate auditory brainstem processing asymmetries between right and left ear presentations in healthy older adults. With the aim of controlling for central auditory changes associated with a reduction in audibility, we selected a sample of older adults with hearing thresholds expected according to their age (ISO 7029, 2000)

4.3 Methods and materials

4.3.1 Sample size calculation

The sample size was calculated based on the data reported by Hornickel et al. (2009), who investigated subcortical asymmetry of speech encoding in normal hearing young adults by recording brainstem responses to a 40-ms /da/ syllable, monaurally presented to the right and left ears. The same procedure was applied in this study with a sample of older adults. Hornickel et al. found significant ear asymmetries for temporal and frequency components of a 40-ms /da/ syllable. Ear differences showed small to moderate (0.4-0.5) effect sizes which were estimated using Cohen's d . Thus, to calculate the sample size for the current study, the measure of the effect ($d = 0.4$) reported by Hornickel et al. (2009) was chosen. Considering a statistical power of 80%, a $p <$

0.05 as significant (using a two-tailed test), and a 10% of probable loss, the sample size for this study was set for 60 participants.

4.3.2 Participants

Sixty-two older adults (33 women and 29 men) between the ages of 61 and 90 years (mean and Standard Deviation (DS) = 71.80 and 6.28, respectively) were selected. Participants were recruited from the registry of research participants from the Institut Universitaire de Gériatrie de Montréal (IUGM) as well as via posts and word of mouth. All participants presented with no history of middle-ear infections, neurologic conditions, or major chronic health conditions. They were all right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971) and spoke Quebec French as their first language. All participants reported that they spoke a second language (in most cases English). None of the participants spoke a tonal language and none of them reported past or present musical training. They exhibited no visible alterations of the ear canal or tympanic membrane under otoscopic examination, and all had bilateral type-A results (Jerger, 1970) for tympanometry. Also, bilateral pure-tone audiometry was conducted with an Interacoustics AC40 clinical audiometer (Interacoustics A/S, Middelfart, Denmark) using ER-3A insert earphones (Etymotic Research, Elk Grove Village, IL, USA). All participants presented with pure-tone thresholds at the tested frequencies (i.e., 250, 500, 1000, 2000, 3000, 4000, 6000 and 8000 Hz) without exceeding the 25th percentile of the distribution of hearing thresholds obtained from an otologically screened population of similar age and sex (ISO 7029-2000). Moreover, only participants with symmetric hearing thresholds between both ears were included. This was defined as an interaural pure-tone threshold difference of no more than 10 dB at two or less audiometric frequencies between 250 and 8000 Hz. Finally, participants scored at least 26/30 in the Montreal Cognitive Assessment (MoCA, Nasreddine et al., 2005), suggesting no cognitive impairment.

Signed consent forms were obtained from all participants, and all study procedures were reviewed and approved by the ethics committee of the Centre de recherche de l'Institut universitaire de gériatrie de Montréal. Participants received a monetary compensation for their participation.

4.3.3 Neurophysiologic stimuli and recording parameters

Click-and speech-ABR for RE and LE presentation was elicited and registered using a two-channel Intelligent Hearing System (IHS, Miami, FL, United States) SmartEP module (version 3.95). Electrodes placed at Fz (positive), A1 and A2 (negative), and the forehead (ground) in accordance with the International 10 to 20 system EEG were used for all recordings. Contact impedance was maintained below 5 k Ω , and inter-electrode impedance was maintained below 3 k Ω . Click-ABR was obtained in each ear before recording brainstem responses to the /da/ speech syllable. Stimuli were monaurally presented through unshielded insert earphones (ER-3, Etymotic Research, Elk Grove Village, IL, USA). For the click-ABR, clicks were presented at 80 dB nHL in alternating polarity at a rate of 21.1/sec. Online analysis consisted of artifact rejection at 30 μ V and digital filtering from 100 to 3000 Hz. Two blocks of 1,024 artifact-free samples were acquired for each ear in a recording window set from 0 to 12 ms relative to stimulus onset. The two blocks were then combined to obtain a grand average of 2,048 sweeps for each ear.

Speech-ABR was elicited by a 40-ms synthesized /da/ syllable provided by the IHS SmartEP module. The syllable contained an initial noise burst and voiced formant transition with a fundamental frequency (F0) that linearly increased from 103 to 125 Hz with a voicing that began at 5 ms with an onset release burst during the first 10 ms. The first formant frequency (F1) linearly increased from 220 to 720 Hz, whereas the second formant frequency (F2) decreased from 1700 to 1240 Hz over the duration of the stimulus. The third formant frequency (F3) decreased slightly

from 2580 to 2500 Hz, whereas the fourth (F4) and fifth (F5) formant frequencies remained constant at 3600 and 4500 Hz, respectively (Skoe & Kraus, 2010). Although the stimulus does not contain a steady-state portion, it is psychophysically perceived as a consonant-vowel speech syllable (Johnson et al., 2005). For a detailed description of the synthesized speech stimulus /da/, refer to Johnson et al. (2005), and Kraus & Nicol (2005).

The 40-ms /da/ stimulus was monaurally presented to right and left ears at 80 dB SPL in alternating polarity to minimize stimulus artifact at a rate of 10.9/s. A time window of 71.81 ms (including a 20 ms prestimulus time) and online filter setting of 50–3000 Hz was used for recording. Brainstem responses were then offline bandpass filtered from 70 to 2000 Hz. Trials with artifact exceeding 30 μ V were excluded from the average. A grand average of 5,000 (two subaverages of 2,500 sweeps) artifact-free responses were obtained for each ear. This number of artifact-free responses was chosen because it falls between the epochs' range (1600 to 6400) required to record speech-ABRs with clearly identifiable peaks to the 40-ms /da/ syllable (BinKhamis et al., 2019). For all ABR testing, participants were seated in a comfortable reclining chair in a quiet room with lights dimmed. The order of ear presentation for click and speech-ABR was counterbalanced across participants. Both ears were plugged with the insert earphone during the entire recording session, regardless of which ear was stimulated. Participants were asked to relax with their eyes closed.

4.3.4 Discrete peak measure analysis

For each participant, click-and speech-ABR peaks were manually marked. Peaks I, III, and V of the click-ABR were visually identified for each ear using the average waveform obtained from the two brainstem recordings. Latencies and peak-to-trough amplitudes were obtained for all three

main peaks. For the speech-ABR, measurements of both timing and magnitude were utilized to assess the discrete peaks. Speech-ABR peaks were expected to appear 7-8 after the corresponding stimulus landmark, which is consistent with the neural transmission time from the ear to the midbrain (Krizman & Kraus, 2019). Krizman et al. (2012) peak picking criteria were used to identify the characteristic seven peaks of the response to the 40-ms /da/. Latencies (after stimulus onset) for brainstem transient and sustained peaks were identified using previously described latency values (Skoe et al., 2015). Speech-ABR peaks included the onset (V and A); the onset of voicing (C), which is supposed to encode the transition from the aperiodic stop burst to the periodic (voiced) formant transition (Johnson et al., 2005); the frequency-following response (FFR) [D, E, and F], which corresponds to the voiced portion of the syllable, and offset (O) peaks (Kraus & Nicol, 2005). Interpeak interval differences for the sustained peaks D-E and E-F, which reflect the period of the stimulus fundamental frequency, were also calculated. Latencies and amplitudes of individual peaks for the speech stimuli were further analyzed using an open-source, MATLAB-based toolbox developed and distributed by Erika Skoe, Trent Nicol, and Nina Kraus from the Auditory Neuroscience Laboratory, Northwestern University (Brainstem Toolbox, 2013). Using this toolbox, visually picked peak latencies (after stimulus onset) and corresponding amplitudes previously obtained were automatically adjusted (within ± 2 sampling points) to obtain the absolute minimum and maximum (Hornickel et al., 2009; Skoe & Kraus, 2010; Vander Werff & Burns, 2011)

4.3.5 Sustained measures analysis

Spectral encoding across the FFR region of the 40-ms /da/ neural response was further analyzed using fast Fourier transform (FFT). The FFR region for the 40-ms /da/ response was defined as the time window between 11.4 and 40.6 ms after stimulus onset, which includes peaks C, D, E, and F. Average spectral amplitude was calculated for three frequency ranges: the fundamental frequency (F0 amp: 103–120 Hz), the first formant (F1 amp: 455–720 Hz), and a higher-frequency region corresponding to the seventh-to-eleventh harmonics of stimulus F0 (HF amp: 721–1154 Hz) [7,9,11]. The root mean square (RMS) amplitude for the entire period was also calculated. A cross-correlation technique was used to calculate the stimulus-to-response (SR) correlation for each neural response from right and left ears. In addition, a right-left (RL) ear correlation analysis was also carried out. These techniques quantify to what extent two neural signals are related using standard Pearson's correlation coefficient (r). One signal is displaced in time relative to the other to find the temporal delay (time lag) that one signal must undergo to be maximally correlated with the other (Jerger & Martin, 2004). The SR correlation analysis was performed for the FFR region of the stimulus (40-ms /da/: 13–34 ms). The RL correlation analysis was performed over the entire neural response (onset peak and FFR). Sustained measure analysis was also conducted using the above-mentioned MATLAB-based toolbox 2012 (Skoe et al., 2013).

4.3.6 Statistical analysis

Data were analyzed with statistical software R (Bates et al., 2015; R Core Team, 2020). The data set included a small proportion of missing values (0.9%), which corresponded to peaks that were deemed not replicable or not reliably above the noise floor. Given the within-subject nature of the independent variable (ear), statistical analyses were conducted considering all complete cases per

variable, as opposed to complete cases throughout the whole data set. This granted more power to observe differences, since conducting analyses with only complete cases throughout the data set meant working with a substantially reduced sample (Pigott, 2001) but involved working with different sample sizes across dependent variables. Using Shapiro-Wilk tests, the first step was to determine whether continuous quantitative variables of interest were normally distributed. Then, normally distributed variables were compared (between ears) conducting paired t-tests, while non-normally distributed variables were compared using Wilcoxon signed-rank tests. Cohen's d and Rosenthal's formula (Rosenthal, 1994) $r = Z/\sqrt{N}$ were reported as effect size measures for these tests to better gauge effects. If statistically significant differences were identified between ears, a second analysis was conducted to determine whether those significant differences were influenced by the participants' age and/or the magnitude of hearing sensitivity. The latter was defined as the binaural average of pure-tone thresholds at 250, 500, 1000, 2000, 3000, 4000, 6000 and 8000 Hz (binaural PTA). The binaural PTA is expressed by the following formula: $[(\text{right ear threshold at } 250 + 500 + 1000 + 2000 + 3000 + 4000 + 6000 + 8000 \text{ Hz}) + (\text{left ear threshold at } 250 + 500 + 1000 + 2000 + 3000 + 4000 + 6000 + 8000 \text{ Hz})]/16]$. Then, multiple mixed-effects models were implemented (Restricted Maximum Likelihood method), with each statistically significant speech-ABR component as dependent variable, participants as a random effect, and ear, age, and binaural PTA as predictors. Following the decision made by the authors of the R package used for these analyses (Bates et al., 2015), significance for implemented models' coefficients was based on t-values. Thus, they were significant whenever they exceeded a standard ± 1.96 critical value. Assumptions for all models were inspected, with no major violations detected (Schielzeth et al., 2020)

4.4 Results

4.4.1 Pure-tone audiometry results.

Figure 1 displays the mean and standard errors for pure-tone thresholds for the right and left ears for different age ranges (60–69, 70–79, and 80–89) in the group of participants. No significant differences ($p > 0.05$) between RE and LE pure-tone thresholds were found across the frequency range (250-8000 Hz). In addition, there was no significant difference for the pure-tone average ($p = 0.088$) between ears.

4.4.2 Click-ABR

Mean latency and amplitude values for waves I, III, and V of the click-ABR for both ears are shown in Table 1. No significant differences ($p > 0.05$) between the RE and the LE were observed for the latency or amplitude of peaks I, III, and V. More than half of the participants (57.1%) showed a shorter click-ABR wave V latency for RE stimulation than LE stimulation, whereas 33.9% of participants showed the opposite pattern. Finally, 8.9% of participants did not present with interaural differences for click-ABR wave V latency. Figure 2 depicts the grand average waveform for the click-ABR for RE and LE presentation.

4.4.3 Speech-ABR

4.4.3.1 Detectability

Overall, detectability was robust for all peaks, except for peak C, which was detected for 83.9% of the participants in the RE (52/62 ears) and in 72.6% of the participants in the LE (45/62 ears). For onset and offset peaks (V-A and O, respectively) detectability varied between 93.5 and 100% in the RE and between 90.3 and 100% in the LE. Finally, for the FFR components D, E, and F,

detectability varied between 98.4 and 100% in the RE and between 93.5 and 100% in the LE. Grand average speech-ABR waveforms for RE and LE presentation are shown in Figure 3.

4.4.3.2 Right and left ear differences for peak latencies and amplitudes

Latency and amplitude values for all the main speech-ABR peaks using the 40-ms /da/ syllable for the right and left ears are displayed in Table 2. Note that ear comparisons were carried out using only the data from those participants whose speech-ABR latencies and amplitudes were identified in both the right and the left ears. Significant ear differences in latency were found for the onset peak V ($t_{52} = -2.674$; $p = 0.010$; $d = 0.367$), peak A ($t_{53} = -3.258$; $p = 0.002$; $d = 0.443$) and offset peak O ($t_{61} = -4.326$; $p < 0.001$; $d = 0.549$). Latency for all transient peaks (V, A, and O) in the right ear were significantly shorter than in the left ear. Regarding peak C, the right ear showed a significantly shorter latency than the left ear ($t_{39} = -2.649$; $p = 0.012$; $d = 0.418$). Regarding the FFR components, right ear latencies were also significantly shorter than those for the left ear for components D ($t_{56} = -3.040$; $p = 0.004$; $d = 0.402$) and E ($t_{57} = -3.050$; $p = 0.003$; $d = 0.400$). No significant latency differences ($p > 0.05$) were found between ears for peak F. Similarly, no significant interpeak interval differences ($p > 0.05$) for the sustained peaks D-E and E-F were found. The percentage of participants showing shorter speech-ABR peak latency response for right ear presentation is shown in Table S2. Finally, no significant differences ($p > 0.05$) for peak amplitudes between the right and left ears were found (Table 2).

4.4.3.3 Stimulus-to-response (SR) and right-and left-ear (RL) response correlations

SR and RL correlation values are reported in Table 3. The maximum SR correlation did not differ significantly ($p > 0.05$) between both ears. The associated lag between the stimulus and the response, which is based on the time-shifting necessary to obtain the highest correlation was

delayed by 0.02 ms in the LE as compared to the RE. However, such a delay was not statistically significant ($p > 0.05$). Regarding the RL response correlation, the LE response lagged by 0.01 ms as compared to the RE response relative to the obtained maximum correlation coefficient between both ear responses.

4.4.3.4 Spectral encoding measures

The sustained components of the FFR were also analyzed to investigate possible ear differences in neural phase-locking to the frequency components (Table 3). The overall RMS magnitude for the 40-ms /da/ stimulus was not statistically different ($p > 0.05$) between both ears. The LE showed a significantly larger spectral amplitude for the frequency region around the F0 than the RE ($Z = -2.433$; $p = 0.015$; $r = 0.218$). A 61.3% of participants showed a larger F0 amplitude response for LE presentation, while 38.7% of participants exhibited either symmetric F0 encoding or a larger amplitude response for RE presentation. The spectral magnitudes from the other harmonic components did not show significant differences ($p > 0.05$) between both ears.

4.4.3.5 Effects of age and audibility on ear asymmetries for the speech-ABR

Further analyses were conducted with the seven dependent variables (i.e., speech-ABR peaks V, A, C, D, E, O, and F0 amplitude) which showed statistically significant differences between ears. To control for the influence of age and binaural PTA, several mixed-effects models (REML method) were implemented, always specifying participants as a random effect variable. First, the impact of age and binaural PTA was inspected by constructing single-predictor models, with each variable individually predicting all statistically significant speech-ABR components. None of the models showed a significant impact of either variable on any of the observed dependent variables.

Second, model comparisons were implemented with Likelihood Ratio tests, comparing a baseline model including age and binaural PTA against a model which added ear as predictor. For all dependent variables, the inclusion of ear significantly improved prediction (chi-squared value always $p < 0.05$). Table 4 provides a summary of the full models' results.

4.5 Discussion

What motivated the current study was the question of whether older adults exhibit auditory brainstem processing asymmetries between RE and LE presentation similar to young adults. In a cross-sectional sample of older adults with age-appropriate hearing, our results showed a RE laterality for selective stimulus components of the speech-ABR. Specifically, significantly shorter latencies were found for the onset (V, A) and offset (O) peaks as well as for some sustained components (C, D, and E) of the speech-ABR elicited from RE presentation compared to LE presentation. Moreover, the spectral amplitude of the F0 for the sustained component of the speech-ABR was significantly larger for the left ear than for the right ear presentation. This finding has not been previously reported in either young or older adults. According to our results, none of the above-mentioned findings were modulated either by age or by the magnitude of hearing sensitivity. Shorter latencies and lower spectral amplitude for the frequency region around the F0 in the right ear are consistent with the evidence suggesting that the right ear/left hemisphere pathway is more efficient to process fast temporal modulations, rather than frequency components of sounds (Tervaniemi, 2003; Zatorre, 2001; Zatorre et al., 1992). In fact, we hypothesize that the F0 was preferentially encoded by the left ear pathway in most of the participants as this pathway has direct access to the right hemisphere which has been associated with the processing of suprasegmental features of speech (Ballachanda & Moushegian, 2000; Ballachanda et al., 1994; Johnsrude et al.,

2000; Liégeois-Chauvel et al., 2001; Zatorre, 2001; Zatorre et al., 1992). This hypothesis is further discussed below. The click-ABR showed no significant differences between RE and LE presentation. Overall, latencies for the speech-ABR components found in this sample of older adults were slightly longer than the values reported in young adults (e.g., Ahadi et al., 2014; Hornickel et al., 2009; Sinha and Basavaraj, 2010). However, they were similar to the latency values reported by Vander Werff and Burns (2011) and Skoe et al. (2015) in older adults. Table 4 provides a comparison of the mean latency values for the speech-ABR components, including studies conducted in both young and older adults.

4.5.1 Asymmetries for the click-ABR in older adults

The results from the click-ABR analysis showed symmetrical responses between the RE and LE presentation. These results are consistent with previous research in older adults (Johansen & Lehn, 1984; Munro et al., 2007; Peng et al., 2016; Van Yper et al., 2016; Vander Werff & Burns, 2011). Moreover, the evidence of symmetric auditory brainstem processing for click stimuli revealed in this study is also in accordance with findings reported in young adults (Hixson & Mosko, 1978; Hornickel et al., 2009; Lauter & Karzon, 1990; Peng et al., 2016; Rowe, 1978; Sinha & Basavaraj, 2010; Vander Werff & Burns, 2011). Therefore, the results from this study along with previous research support the hypothesis of symmetric auditory brainstem processing for click stimuli.

4.5.2 Asymmetries for the speech-ABR in older adults

The results for the speech-ABR, as opposed to click-ABR, suggest a rather asymmetric auditory brainstem processing for speech acoustic components in older adults. Therefore, it may be suggested that click and speech stimuli elicited different patterns of auditory brainstem activity in

this sample of older adults. It is possible that asymmetric processing between both auditory pathways in response to speech sounds results from active exposure to the complex acoustic properties conveyed (e.g., phonetic information) in speech. Hearing speech sounds, as opposed to click sounds, lead to the extraction of significant information about encoding of the time-varying aspect of sounds, which may potentially shape the auditory system to react differently when encoding complex (i.e., speech) versus non-complex (i.e., click) sounds (Johnson et al., 2008). Moreover, the degree of asymmetry at the brainstem level seems to change accordingly to the complexity of the acoustic signal that needs to be processed (King et al., 1999). Therefore, pervasive exposure to the complex acoustic sounds and everyday use of speech instead of clicks may reinforce brainstem projections to process more accurately and rapidly the acoustic features of the speech stimulus (Firszt et al., 2006; Hornickel et al., 2009). Supporting evidence for this hypothesis comes from studies conducted in young adults. Several studies have found symmetric processing for click-ABR and asymmetric processing for speech-ABR between RE and LE presentation in young adults (Hornickel et al., 2009; Sinha & Basavaraj, 2010). There is only one study previously published reporting symmetric processing for click-ABR and asymmetric processing for speech-ABR among older adults [9]. Like the findings of this study, Vander Werff and Burns [9] found symmetric processing for click-ABR and an asymmetric processing only for the transient component A of the speech-ABR between right and left ear presentation. Asymmetric processing for the other speech-ABR components were not found. Note that older adults in Vander Werff and Burns' study showed better hearing thresholds than those obtained by the participants in our study. Although the magnitude of hearing sensitivity did not explain our results, it is possible that hearing thresholds could have accounted for the difference in results between Vander Werff and Burns' study (2011) and our current study. This hypothesis should be further explored. Therefore, taking the above-mentioned studies into account we conclude that older adults, like

young adults, exhibit a symmetric auditory brainstem processing for click stimuli but an asymmetric auditory brainstem processing for speech-like stimuli.

Note that the results of the speech-ABR found in this study revealed a different pattern of brainstem lateralization for the temporal and frequency acoustic elements of the speech stimulus. Participants, as a group, showed faster temporal encoding for transient and sustained components for RE presentation and better F0 encoding for LE presentation. Faster neural timing favoring RE presentation is consistent with previous findings in young adults showing shorter RE latencies for speech-ABR transient and sustained components (Ahadi et al., 2014; Hornickel et al., 2009; Sinha & Basavaraj, 2010). Thus, older adults investigated in this study showed a rightward laterality of brainstem auditory processing for temporal components of speech, similar to young adults. These results may be attributed to the RE/left hemisphere pathway specialization for processing complex, rapidly changing acoustic stimuli with a high degree of temporal precision (McGettigan & Scott, 2012; Nicholls et al., 2002; Zatorre & Belin, 2001).

However, in the frequency domain, the F0 spectral amplitude was significantly larger for the LE neural response compared to the RE. This finding is consistent with previous studies showing that frequency components of speech sounds that convey nonlinguistic (suprasegmental) information, such as F0, are more efficiently processed by the LE/right hemisphere pathway than the opposite pathway (Ballachanda et al., 1994; Ballachanda & Moushegian, 2000; Johnsrude et al., 2000; Liégeois-Chauvel et al., 2001; Sidtis, 1982; Zatorre & Belin, 2001; Zatorre et al., 1992). Note that in Indo-European languages, such as English or French, F0 does not convey linguistic and/or semantic information, as opposed to tonal languages, in which variations in F0 produce changes in the meaning of the word and are known as lexical tones (Liu et al., 2010). Therefore, a larger F0

spectral amplitude for LE presentation was expected based on the above-mentioned theoretical model, as none of the participants spoke a tonal language.

Nevertheless, previous studies of young adults have achieved different and rather contradictory results. On one hand, Hornickel et al. (2009) and Ahadi et al. (2014) found symmetric encoding of F0 between RE and LE presentation for the same speech stimulus used in the present study in English speakers and monolingual Persian speakers, respectively. Hornickel et al. (2009) did not report whether the participants spoke a second language. On the other hand, Sinha and Basavaraj (2010), using the same stimulus as the present study's, found that the F0 spectral amplitude in young adults was significantly larger for the RE presentation than the LE presentation. The authors did not report the participants' native language nor whether they were monolinguals or bilinguals. However, as the study was conducted in India, it may be assumed that most of the participants spoke more than one language (Azam et al., 2013; Clingingsmith, 2014; Weinreich, 1957). As mentioned above, our results showed that the older adults in this study, as a group, exhibited a larger F0 for the LE input than the RE input. However, individual data showed that the F0 spectral amplitude was larger for LE presentation in 61.3% of participants, while 37.1% of them exhibited a larger F0 spectral amplitude for RE presentation, and 1.6% showed no lateralization of F0 encoding (i.e., the same F0 spectral amplitude in both ears). Thus, some of our results are like those reported in young adults. Note that as the above-mentioned studies in young adults did not report individual data, it cannot be concluded whether some participants in those studies exhibited an F0 lateralization pattern different than the group mean. Previous researchers (Ahadi et al., 2014; Hornickel et al., 2009; Sinha & Basavaraj, 2010) have suggested that the 40-ms /da/ syllable used in the studies, including the current one, may be too transient to allow a valid pitch encoding, and

thus, LE preference should not be attained. This hypothesis explains the group results for studies carried out in young adults and for around 38% of the participants in the present study.

We cannot fully explain why around 61% of the participants in this study exhibited a preferential F0 spectral amplitude for LE presentation, as compared to previous studies conducted in young adults. We propose three hypotheses for this finding. First, participants who exhibited a larger F0 spectral amplitude for LE presentation may have indeed been able to perceive the brief periodic portion of the stimulus as a tone rather than a transient, enabling them to process F0 as a suprasegmental component of the stimulus. However, to accept this hypothesis, many of the participants in this research should have presented with a distinct characteristic that is not found in the samples of young adults investigated in previous research. Certainly, the age of the participants is an important difference between this sample and the previous samples investigated. Nevertheless, around 37% of the participants in this sample, even if their age was like the remaining 61%, exhibited an F0 spectral amplitude like the findings reported in young adults (e.g., larger for right ear input). Thus, we believe that aging itself cannot account for this particular result. A possible explanation for this finding can be bilingualism. Note that all participants in this study lived in Montreal, which is a bilingual city where people are exposed to English and French at different levels—while some people may solely utilize one language in everyday life with little contact with the other language, others may be exposed to and use both languages on a regular basis. All participants in this study reported that they spoke two languages (in most of the cases, French and English). It has been previously suggested that bilingualism is associated with enhanced neural encoding of speech sounds at the brainstem level (Kraus & Anderson, 2014; Krishnan & Gandour, 2009; Krishnan et al., 2012), and recent data using the FFR have shown that bilingual listeners exhibit better encoding of acoustic features of speech than their monolingual peers

(Krizman et al., 2012; Skoe et al., 2017). Therefore, we hypothesize that enhanced neural encoding for speech sounds induced by bilingualism may have been associated with the capacity to extract F0 as a suprasegmental aspect of the /da/ syllable and thus triggered LE/right hemisphere preferential processing, as discussed above. However, with the current data, we cannot test this hypothesis, as (a) we did not determine the degree of bilingualism in each participant, and (b) previous research in young adults did not report whether participants spoke more than one language. In addition, no previous studies have investigated differences for the encoding of F0 between RE and LE presentation using the FFR comparing monolingual and bilingual speakers. Thus, we cannot determine whether those participants who exhibited larger F0 spectral amplitudes for left ear presentation (i.e., 61% of the sample) differed in terms of their bilingual experience from the other participants. Future studies should be conducted to test this hypothesis. Second, it may be possible that biological variability accounts for the differences observed. For the short speech-like stimulus (/da/), some listeners are simply able to extract F0 as a suprasegmental aspect of the stimulus, and others are not able to do so. This can be explained by the variability we observed in the participants of this study regarding the lateralization of F0. As mentioned above, previous studies have not reported the percentages of listeners with larger right or larger left F0 spectral amplitudes. Therefore, previous results may just represent the group trend without necessarily representing individual results. Thus, further studies in this field need to be carried out with the aim to test this hypothesis. In addition, we suggest that future studies should report the percentage of listeners who exhibit larger F0 amplitudes for the right and left ears. Third, we also consider the possibility of a technical bias due to electrode montage (Hood, 1998). Electrode placement (e.g., Beattie et al., 1986; Dzulkarnain et al., 2008; Dzulkarnain et al., 2014) can affect the amplitude of the auditory brainstem response, biasing enhanced amplitude towards one ear. If this bias occurred, we do not believe that it completely accounted for the larger F0 amplitude in

61.3% of the participants. Finally, it may be possible that each of these hypotheses is not exclusive, and thus, a combination thereof may have triggered these results.

In summary, this study suggests an asymmetric auditory brainstem processing between RE and LE presentation of speech-like stimuli. In this sample of older adults, a distinct pattern characterized by a larger F0 spectral amplitude of the 40-ms /da/ syllable for LE presentation was observed, as opposed to previous studies conducted in young adults. Further research is required to better understand this finding, especially the effect of bilingualism on the capacity of the auditory system to extract and process F0 in short speech-like stimulus.

4.6 Limitations of the study

There were a few caveats that should be considered for future research. First, lifelong experience such as music and bilingualism may enhance neural encoding of complex sound features such as neural timing and frequency encoding (Kraus & Anderson, 2014; Krizman et al., 2012; Parbery-Clark et al., 2012; Skoe et al., 2017; White-Schwoch et al., 2013). Although none of the participants reported past or present musical training, they were all bilingual speakers. Therefore, bilingual experience might have enhanced FFR neural representation of speech components in older adults. Future studies should investigate whether music and bilingualism may modulate the pattern of subcortical laterality of speech encoding among older adults. Second, participants were mainly selected from a registry of participants who are actively involved in research. Therefore, given their profile, they may not represent the general population of older adults. Third, given the difficulty to identify some of the click-and speech-ABR peaks in certain participants, some statistical analyses (e.g., ear comparisons for click-ABR peaks I and III and speech-ABR peak C) were carried out with several observations lower than those established according to the sample size calculation.

Therefore, caution is warranted to interpret the results. Fourth, although our detectability percentage for the different speech-ABR components was rather high, we observed inter-individual variations in the response. Some of the neural responses showed patterns of complex morphology. This may be attributed to background noise contamination or muscle artifact.

4.7 Conclusions

The current study presents data to support brainstem laterality for the encoding of acoustic components of speech in older adults. In addition, no asymmetric brainstem processing for click stimuli was found in the sample of older adults. Overall, both findings suggest that older adults with age-appropriate hearing exhibit a pattern of brainstem laterality of click and speech encoding like young adults. A result that has not previously been reported in either younger or older adults is the larger spectral F0 amplitude (for the 40-ms /da/ syllable) for LE presentation as opposed to RE presentation, which suggests that most of the listeners could perceive the very short periodic component of the stimulus as a tone. Future studies should be conducted to further explore this finding and the variables, such as bilingualism, that may be associated with it. Finally, it should be noted that our findings may not be entirely representative of the older adult population. The characteristics (e.g., audibility, cognition, and spoken language) of the sample may not accurately represent the general population of older adults and may have affected the results of this study. Therefore, caution is warranted in generalizing these results to the general population of older adults.

4. References

- Ahadi, M., Pourbakht, A., Jafari, A. H., & Jalaie, S. (2014). Effects of stimulus presentation mode and subcortical laterality in speech-evoked auditory brainstem responses. *International journal of audiology*, 53(4), 243-249.
- Azam, M., Chin, A., & Prakash, N. (2013). The returns to English-language skills in India. *Economic Development and Cultural Change*, 61(2), 335-367.
- Ballachanda, B. B., & Moushegian, G. (2000). Frequency-Following Response: Effects of Interaural Time and Intensity Differences. *Journal of the American Academy of Audiology*, 11(1).
- Ballachanda, B. B., Rupert, A., & Moushegian, G. (1994). Asymmetric frequency-following responses. *Journal of the American academy of audiology*, 5, 133-133.
- Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting linear mixed-effects models using lme4. *arXiv preprint arXiv:1406.5823*.
- Beattie, R. C., Beguwala, F. E., Mills, D. M., & Boyd, R. L. (1986). Latency and amplitude effects of electrode placement on the early auditory evoked response. *Journal of Speech and Hearing Disorders*, 51(1), 63-70.
- Belin, P., Zilbovicius, M., Crozier, S., Thivard, L., Fontaine, A. A., Masure, M. C., & Samson, Y. (1998). Lateralization of speech and auditory temporal processing. *Journal of cognitive neuroscience*, 10(4), 536-540.
- Bellis, T. J., Nicol, T., & Kraus, N. (2000). Aging affects hemispheric asymmetry in the neural representation of speech sounds. *Journal of Neuroscience*, 20(2), 791-797.
- BinKhamis, G., Léger, A., Bell, S. L., Prendergast, G., O'Driscoll, M., & Kluk, K. (2019). Speech auditory brainstem responses: Effects of background, stimulus duration, consonant–vowel, and number of epochs. *Ear and hearing*, 40(3), 659.
- Chen, X., Liang, Y., Deng, Y., Li, J., Chen, S., Wang, C., & Luo, P. (2013). Age-associated reduction of asymmetry in human central auditory function: a 1H-magnetic resonance spectroscopy study. *Neural plasticity*, 2013.
- Clingingsmith, D. (2014). Industrialization and bilingualism in India. *Journal of Human Resources*, 49(1), 73-109.

Dzulkarnain A, Tengku Zam Zam T, Azed Z, Rahman Zuri M, Sulaiman N. (2014). Effects of electrode position on tone-burst-evoked auditory brainstem responses (ABR) in humans. *Middle East Journal of Scientific Research*. 21: 1180-1187.

Dzulkarnain, A. A., Wilson, W. J., Bradley, A. P., & Petoe, M. (2008). The effects of electrode montage on the amplitude of wave V in the auditory brainstem response to maximum length sequence stimuli. *Audiology and Neurotology*, 13(1), 7-12.

Eldredge, L., & Salamy, A. (1996). Functional auditory development in preterm and full-term infants. *Early human development*, 45(3), 215-228.

Firszt, J. B., Ulmer, J. L., & Gaggl, W. (2006). Differential representation of speech sounds in the human cerebral hemispheres. *The Anatomical Record Part A: Discoveries in Molecular, Cellular, and Evolutionary Biology: An Official Publication of the American Association of Anatomists*, 288(4), 345-357.

Goossens, T., Vercammen, C., Wouters, J., & Wieringen, A. V. (2016). Aging affects neural synchronization to speech-related acoustic modulations. *Frontiers in aging neuroscience*, 8, 133.

Hixson, W. C., & Mosko, J. D. (1979). Normative bilateral brainstem evoked response data for a naval aviation student population: group statistics (No. NAMRL-1262). Naval Aerospace Medical Research Lab Pensacola Fl.

Hornickel, J., Skoe, E., & Kraus, N. (2009). Subcortical laterality of speech encoding. *Audiology and Neurotology*, 14(3), 198-207.

Hood, L. J. (1998). Clinical applications of the auditory brainstem response. *Singular*.

Humes, L. E., Dubno, J. R., Gordon-Salant, S., Lister, J. J., Cacace, A. T., Cruickshanks, K. J., ... & Wingfield, A. (2012). Central presbycusis: a review and evaluation of the evidence. *Journal of the American Academy of Audiology*, 23(8), 635-666.

International Organization for Standardization. (2000) *Acoustics Statistical Distribution of Hearing Thresholds as a Function of Age. ISO 7029*. Geneva: ISO.

Jerger, J. (1970). Clinical experience with impedance audiometry. *Archives of otolaryngology*, 92(4), 311-324.

Jerger, J., & Martin, J. (2004). Hemispheric asymmetry of the right ear advantage in dichotic listening. *Hearing research*, 198(1-2), 125-136.

- Johannsen, H. S., & Lehn, T. (1984). The dependence of early acoustically evoked potentials on age. *Archives of oto-rhino-laryngology*, 240(2), 153-158.
- Johnson, K. L., Nicol, T. G., & Kraus, N. (2005). Brain stem response to speech: a biological marker of auditory processing. *Ear and hearing*, 26(5), 424-434.
- Johnson, K. L., Nicol, T., Zecker, S. G., & Kraus, N. (2008). Developmental plasticity in the human auditory brainstem. *Journal of Neuroscience*, 28(15), 4000-4007.
- Johnsrude, I. S., Penhune, V. B., & Zatorre, R. J. (2000). Functional specificity in the right human auditory cortex for perceiving pitch direction. *Brain*, 123(1), 155-163.
- Kimura, D. (2011). From ear to brain. *Brain and Cognition*, 76(2), 214-217.
- King, C., Nicol, T., McGee, T., & Kraus, N. (1999). Thalamic asymmetry is related to acoustic signal complexity. *Neuroscience letters*, 267(2), 89-92.
- Kraus, N., & Anderson, S. (2014). Bilingualism enhances neural speech encoding. *The Hearing Journal*, 67(7), 40.
- Kraus N, Nicol T. (2005). Brainstem origins for cortical -what-and-where- pathways in the auditory system. *Trends Neuroscience*. 28 (4): 176-181.
- Krishnan, A., & Gandour, J. T. (2009). The role of the auditory brainstem in processing linguistically relevant pitch patterns. *Brain and language*, 110(3), 135-148.
- Krishnan, A., Gandour, J. T., & Bidelman, G. M. (2012). Experience-dependent plasticity in pitch encoding: from brainstem to auditory cortex. *Neuroreport*, 23(8), 498.
- Krishnan, A., Gandour, J. T., Ananthakrishnan, S., Bidelman, G. M., & Smalt, C. J. (2011). Functional ear (a) symmetry in brainstem neural activity relevant to encoding of voice pitch: A precursor for hemispheric specialization? *Brain and language*, 119(3), 226-231.
- Krizman, J., Marian, V., Shook, A., Skoe, E., & Kraus, N. (2012). Subcortical encoding of sound is enhanced in bilinguals and relates to executive function advantages. *Proceedings of the National Academy of Sciences*, 109(20), 7877-7881.
- Krizman, J., Skoe, E., & Kraus, N. (2012). Sex differences in auditory subcortical function. *Clinical Neurophysiology*, 123(3), 590-597.

- Lauter, J. L., & Karzon, R. G. (1990). Individual Differences in Auditory Electric Responses III. A Replication, with Observations of Individual vs. Group Characteristics. *Scandinavian audiology*, 19(2), 67-72.
- Levine, R. A., Liederman, J., & Riley, P. (1988). The brainstem auditory evoked potential asymmetry is replicable and reliable. *Neuropsychologia*, 26(4), 603-614.
- Levine, R. A., & McGaffigan, P. M. (1983). Right-left asymmetries in the human brain stem: auditory evoked potentials. *Electroencephalography and clinical neurophysiology*, 55(5), 532-537.
- Liégeois-Chauvel, C., Giraud, K., Badier, J. M., Marquis, P., & Chauvel, P. (2001). Intracerebral evoked potentials in pitch perception reveal a functional asymmetry of the human auditory cortex. *Annals of the New York Academy of Sciences*, 930(1), 117-132.
- Liu, H., Wang, E. Q., Chen, Z., Liu, P., Larson, C. R., & Huang, D. (2010). Effect of tonal native language on voice fundamental frequency responses to pitch feedback perturbations during sustained vocalizations. *The Journal of the Acoustical Society of America*, 128(6), 3739-3746.
- McGettigan, C., & Scott, S. K. (2012). Cortical asymmetries in speech perception: what's wrong, what's right and what's left? *Trends in cognitive sciences*, 16(5), 269-276
- Munro, K. J., Pisareva, N. Y., Parker, D. J., & Purdy, S. C. (2007). Asymmetry in the auditory brainstem response following experience of monaural amplification. *Neuroreport*, 18(17), 1871-1874.
- Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., ... & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53(4), 695-699.
- Nicholls, M. E., Gora, J., & Stough, C. K. (2002). Hemispheric asymmetries for visual and auditory temporal processing: an evoked potential study. *International journal of psychophysiology*, 44(1), 37-55.
- Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*, 9(1), 97-113.
- Parbery-Clark, A., Anderson, S., Hittner, E., & Kraus, N. (2012). Musical experience offsets age-related delays in neural timing. *Neurobiology of aging*, 33(7), 1483-e1.

- Peng, L., Yu, S. L., Jing, Y., Chen, R. C., & Liang, J. P. (2016). Diffusion tensor imaging of the central auditory system in the elderly. *Lin chuang er bi yan hou tou jing wai ke za zhi= Journal of clinical otorhinolaryngology, head, and neck surgery*, 30(8), 637-640.
- Philibert, B., Veuillet, E., & Collet, L. (1998). Functional asymmetries of crossed and uncrossed medial olivocochlear efferent pathways in humans. *Neuroscience letters*, 253(2), 99-102.
- Pigott, T. D. (2001). A review of methods for missing data. *Educational research and evaluation*, 7(4), 353-383.
- Rosenthal, R., Cooper, H., & Hedges, L. (1994). Parametric measures of effect size. *The handbook of research synthesis*, 621(2), 231-244.
- Rowe III, M. J. (1978). Normal variability of the brain-stem auditory evoked response in young and old adult subjects. *Electroencephalography and Clinical Neurophysiology*, 44(4), 459-470.
- Schielzeth, H., Dingemanse, N. J., Nakagawa, S., Westneat, D. F., Allegate, H., Teplitsky, C., ... & Araya-Ajoy, Y. G. (2020). Robustness of linear mixed-effects models to violations of distributional assumptions. *Methods in Ecology and Evolution*, 11(9), 1141-1152.
- Schönwiesner, M., Krumbholz, K., Rübsamen, R., Fink, G. R., & von Cramon, D. Y. (2007). Hemispheric asymmetry for auditory processing in the human auditory brain stem, thalamus, and cortex. *Cerebral Cortex*, 17(2), 492-499
- Sidtis, J. J. (1982). Predicting brain organization from dichotic listening performance: Cortical and subcortical functional asymmetries contribute to perceptual asymmetries. *Brain and Language*, 17(2), 287-300.
- Sinha, S. K., & Basavaraj, V. (2010). Lateral asymmetry in speech processing at the brainstem: evidence from speech evoked ABR. *Journal of the All India Institute of Speech & Hearing*, 29(1).
- Sininger, Y. S., & Cone-Wesson, B. (2006). Lateral asymmetry in the ABR of neonates: evidence and mechanisms. *Hearing research*, 212(1-2), 203-211.
- Sininger, Y. S., Cone-Wesson, B., & Abdala, C. (1998). Gender distinctions and lateral asymmetry in the low-level auditory brainstem response of the human neonate. *Hearing Research*, 126(1-2), 58-66.
- Skoe, E., Burakiewicz, E., Figueiredo, M., & Hardin, M. (2017). Basic neural processing of sound in adults is influenced by bilingual experience. *Neuroscience*, 349, 278-290.

Skoe, E., & Kraus, N. (2010). Auditory brainstem response to complex sounds: a tutorial. *Ear and hearing*, 31(3), 302.

Skoe, E., Krizman, J., Anderson, S., & Kraus, N. (2015). Stability and plasticity of auditory brainstem function across the lifespan. *Cerebral Cortex*, 25(6), 1415-1426.

Skoe, E., Nicol, T., Kraus, N. (2013). The Brainstem Toolbox. Version 2013. www.brainvolts.northwestern.edu.

Spivak, L. G., & Seitz, M. R. (1988). Response asymmetry and binaural interaction in the auditory brain stem evoked response. *Ear and hearing*, 9(2), 57-64.

Team, R. Core. (2020). R: A language and environment for statistical computing. Vienna: R Foundation for Statistical Computing: 201.

Tervaniemi, M., & Hugdahl, K. (2003). Lateralization of auditory-cortex functions. *Brain research reviews*, 43(3), 231-246.

Van Yper, L. N., Vermeire, K., De Vel, E. F., Beynon, A. J., & Dhooge, I. J. (2016). Age-related changes in binaural interaction at brainstem level. *Ear and hearing*, 37(4), 434-442.

Vander Werff, K. R., & Burns, K. S. (2011). Brain stem responses to speech in younger and older adults. *Ear and hearing*, 32(2), 168-180.

Weinreich, U. (1957). Functional aspects of Indian bilingualism. *Word*, 13(2), 203-233.

White-Schwoch, T., Carr, K. W., Anderson, S., Strait, D. L., & Kraus, N. (2013). Older adults benefit from music training early in life: biological evidence for long-term training-driven plasticity. *Journal of Neuroscience*, 33(45), 17667-17674.

Zatorre, R. J., Evans, A. C., Meyer, E., & Gjedde, A. (1992). Lateralization of phonetic and pitch discrimination in speech processing. *Science*, 256(5058), 846-849.

Zatorre, R. J., & Belin, P. (2001). Spectral and temporal processing in human auditory cortex. *Cerebral cortex*, 11(10), 946-953.

4.9 Tables and figures

Table 1. Mean and standard deviation (SD) of the latency (after stimulus onset) and amplitude values of the click-ABR components for the right and left ears for all participants (n=62).

<i>Measure</i>	<i>Ear</i>				<i>Test</i>			
	<i>Right (SD)</i>	<i>%</i>	<i>Left (SD)</i>	<i>%</i>	<i>t</i>	<i>Z</i>	<i>p-value</i>	<i>Effect size</i>
Latency (ms)								
I (n = 44)	1.80 (0.13)	85.5	1.81 (0.15)	75.8	-0.914		0.366	0.137
III (n = 41)	4.00 (0.13)	72.6	3.99 (0.18)	66.1	0.154		0.878	0.024
V (n = 56)	5.87 (0.26)	93.5	5.91 (0.28)	90.3	-1.331		0.189	0.177
Amplitude (µV)								
I (n = 44)	0.08 (0.06)		0.10 (0.09)			-0.555	0.579	0.059
III (n = 41)	0.17 (0.08)		0.17 (0.10)		-0.914		0.913	0.017
V (n = 56)	0.34 (0.16)		0.29 (0.19)			-1.731	0.083	0.163

% = percentage of detectability; t = paired t-test; Z = Wilcoxon signed-rank test.

Table 2. Mean and standard deviation of latency (after stimulus onset) and amplitude values of the speech-ABR components for the right and left ears for all participants (n = 62)

<i>Measure</i>	<i>Ear</i>				<i>Test</i>			
	<i>Right (SD)</i>	<i>%</i>	<i>Left (SD)</i>	<i>%</i>	<i>t</i>	<i>Z</i>	<i>p-value</i>	<i>Effect size</i>
Latency (ms)								
V (n = 53)	7.00 (0.47)	93.5	7.21 (0.46)	90.3	-2.674		0.010*	0.367
A (n = 54)	8.02 (0.55)	95.2	8.32 (0.67)	90.3	-3.258		0.002**	0.443
C (n = 40)	18.46 (0.72)	83.9	18.87 (0.87)	72.6	-2.649		0.012*	0.418
D (n = 57)	23.80 (0.88)	98.4	24.23 (0.78)	93.5	-3.040		0.004**	0.402
E (n = 58)	31.66 (0.95)	95.2	32.15 (1.11)	96.8	-3.050		0.003**	0.400
F (n = 62)	40.72 (0.92)	100	40.95 (0.89)	100	-1.583		0.119	0.201
O (n = 62)	48.96 (1.22)	100	49.65 (1.13)	100	-4.326		0.000***	0.549
D-E (n = 54)	7.89 (1.02)		7.77 (1.23)		0.538		0.593	0.075
E-F (n = 56)	8.99 (0.95)		8.82 (1.08)		0.996		0.324	0.133
Amplitude (μV)								
V (n = 53)	0.16 (0.14)		0.21 (0.21)		-1.450		0.153	0.197
A (n = 54)	-0.19 (0.15)		-0.23 (0.20)		1.265		0.211	0.168
C (n = 40)	-0.26 (0.22)		-0.24 (0.34)			-0.430	0.667	0.046
D (n = 57)	-0.24 (0.22)		-0.30 (0.26)			-1.526	0.127	0.142
E (n = 58)	-0.19 (0.27)		-0.21 (0.33)			-0.285	0.776	0.027
F (n = 62)	-0.32 (0.31)		-0.36 (0.35)			-0.998	0.318	0.090
O (n = 62)	-0.24 (0.23)		-0.32 (0.33)			-1.588	0.112	0.142

% = percentage of detectability; t = Paired t-test; Z = Wilcoxon signed-rank test. *p < 0.05; **p < 0.01; ***p < 0.001

Table 3. Mean and standard deviation values of (A) spectral magnitude measures, (B) stimulus-to-response correlation for right and left ears and (C) right-left correlation.

<i>Measure</i>	<i>Right ear (SD)</i>	<i>Left ear (SD)</i>	<i>Z</i>	<i>p-value</i>	<i>Effect size</i>
A. Spectral magnitudes (μV)					
RMS	0.48 (0.28)	0.55 (0.31)	-1.932	0.053	0.174
F0	0.34 (0.28)	0.45 (0.35)	-2.433	0.015*	0.218
F1	0.03 (0.01)	0.03 (0.01)	-0.438	0.661	0.039
HF	0.01 (0.003)	0.01 (0.003)	-0.991	0.322	0.088
B. Stimulus-to-response (SR) correlation					
SR corr (r)	0.14 (0.06)	0.12 (0.07)	-1.515	0.130	0.136
SR lag (ms)	7.97 (1.08)	7.99 (1.12)	-0.099	0.921	0.008
C. Right-left (RL) correlation					
Straight correlation (Zero lag)		0.071 (0.25)			
Maximum correlation (r)		0.379 (0.19)			
RL lag (ms)		0.011 (1.18)			

Z = Wilcoxon signed-rank test; RMS = Root mean square; F0 = Fundamental frequency; F1 = First formant; HF = Higher frequency formants. * $p < 0.05$

Table 4. Mixed effects results for all inspected speech-ABR components

	Estimate	SE	t
V (n = 53)			
Age	-0.01	0.01	-1.05
Binaural PTA	-0.01	0.01	-0.94
Ear	-0.20	0.08	-2.62*
A (n = 54)			
Age	-0.00	0.01	-0.09
Binaural PTA	-0.01	0.01	-1.73
Ear	-0.30	0.09	-3.26*
C (n = 40)			
Age	0.02	0.01	1.65
Binaural PTA	0.00	0.01	0.21
Ear	-0.43	0.14	-3.15*
D (n = 57)			
Age	-0.01	0.01	-0.73
Binaural PTA	-0.00	0.01	-0.89
Ear	-0.36	0.14	-2.50*
E (n = 58)			
Age	-0.00	0.01	-0.14
Binaural PTA	0.01	0.01	0.75
Ear	-0.48	0.16	-3.06*
O (n = 62)			
Age	-0.00	0.02	-0.21
Binaural PTA	-0.00	0.02	-0.21
Ear	-0.69	0.16	-4.33*
F0 (n = 62)			
Age	0.00	0.01	-0.54
Binaural PTA	0.00	0.01	0.57
Ear	-0.11	0.05	-2.08*

Coefficients for predictors listed in Estimate column; coefficients are significant (*) whenever their t value is above or below +- 1.96; SE= Standard Error.

Table 5. Comparative Latency mean and standard deviation values for speech-ABR components using a 40-ms speech syllable /da/ in young and older adults.

Measure	Hornickel et al. (2009) *		Sinha & Basavaraj (2010) *		Adahi et al. (2014) *		Vander Werff & Burns (2011) *	Skoe et al. (2015)	Ianiszewski et al. (current study) *	
	(YA)		(YA)		(YA)		(OA)	(OA)	(OA)	
	RE	LE	RE	LE	RE	LE	CE	RE	RE	LE
	(SD)	(SD)	(SD)	(SD)	(SD)	(SD)	(SD)	(SD)	(SD)	(SD)
Latency (ms)										
V	6.64 (0.27)	6.58 (0.25)	6.5 (0.26)	6.54 (0.23)	6.72 (0.39)	6.77 (0.41)	6.70 (0.32)	6.92 (0.38)	7.00 (0.47) *	7.21 (0.46) *
A	7.65 (0.38)	7.61 (0.33)	7.36 (0.37)	7.39 (0.35)	7.73 (0.52) *	7.87 (0.52) *	7.75 (0.37) *	7.89 (0.46)	8.02 (0.55)	8.32 (0.67)
C	NR	NR	NR	NR	18.56 (0.69)	18.72 (0.78)	NR	NR	18.46 (0.72) *	18.87 (0.81) *
D	22.52 (0.58) *	22.68 (0.51) *	22.07 (0.69) *	22.68 (0.58) *	22.87 (0.72)	22.91 (0.72)	23.00 (0.87)	23.05 (0.61)	23.80 (0.88) *	24.23 (0.78) *
E	30.96 (0.38)	31.28 (0.58)	30.58 (0.54) *	30.94 (0.55) *	31.50 (1.08) *	31.78 (1.06) *	31.39 (0.91)	31.37 (0.56)	31.66 (0.95) *	32.15 (1.11) *
F	39.33 (0.43) *	39.65 (0.43) *	39.02 (0.53) *	39.45 (0.45) *	40.26 (1.44)	40.39 (1.32)	39.70 (0.56)	39.68 (0.46)	40.72 (0.92)	40.95 (0.89)
O	48.14 (0.39)	48.37 (0.58)	47.43 (0.96) *	47.90 (0.57) *	48.63 (1.03)	48.75 (1.08)	48.70 (0.41)	48.84 (0.56)	48.96 (1.22) *	49.65 (1.13) *

YA= Young adults; OA= Older adults; RE = Right ear; LE = Left ear; CE = Combined ears, NR = Not reported. * denotes studies and specific peaks where evidence of significant brainstem asymmetries between right and left ear presentation for speech-ABR have been found.

Supplementary Table S1. Percentage and number (n) of participants showing shorter latency response for right ear presentation, left ear presentation, and no interaural latency difference for each speech-ABR peak.

	<i>Right ear</i>	<i>No interaural latency difference</i>	<i>Left ear</i>
Peaks			
V (n = 53)	50.9 (27)	13.2 (7)	35.8 (19)
A (n = 54)	62.9 (34)	5.6 (3)	31.5 (17)
C (n = 40)	60.0 (24)	5.0 (2)	35.0 (14)
D (n = 57)	68.4 (39)	3.5 (2)	28.1 (16)
E (n = 58)	67.2 (39)	3.4 (2)	29.3 (17)
F (n = 62)	59.7 (37)	6.5 (4)	40.3 (25)
O (n = 62)	75.8 (47)	1.6 (1)	22.6 (14)

Figure. 1. Mean pure-tone thresholds in dB HL for the group of older adults. (A) 60-69 years (B) 70-79 years, (C) 80-89 years and (D) grand average, with error bars. Conventional symbols are used to show data from the right and left ears. Grey areas represent expected values according to the 25th percentile of the ISO 7029.

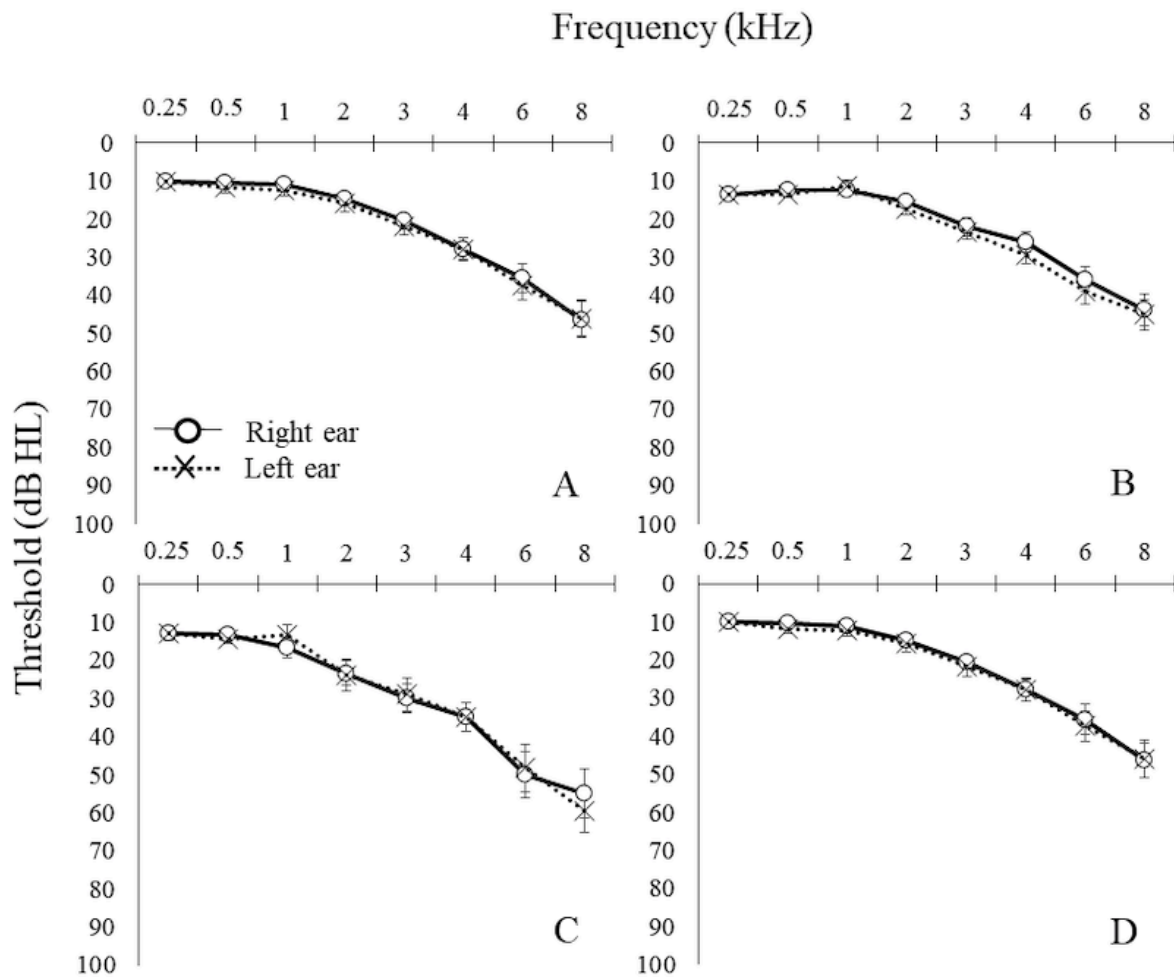


Figure. 2. Grand average waveform for the click-ABR obtained from 62 older adults to right (red line) and left (blue line) ear presentation. The stimulus evoked three prominent peaks labeled as I, III and V.

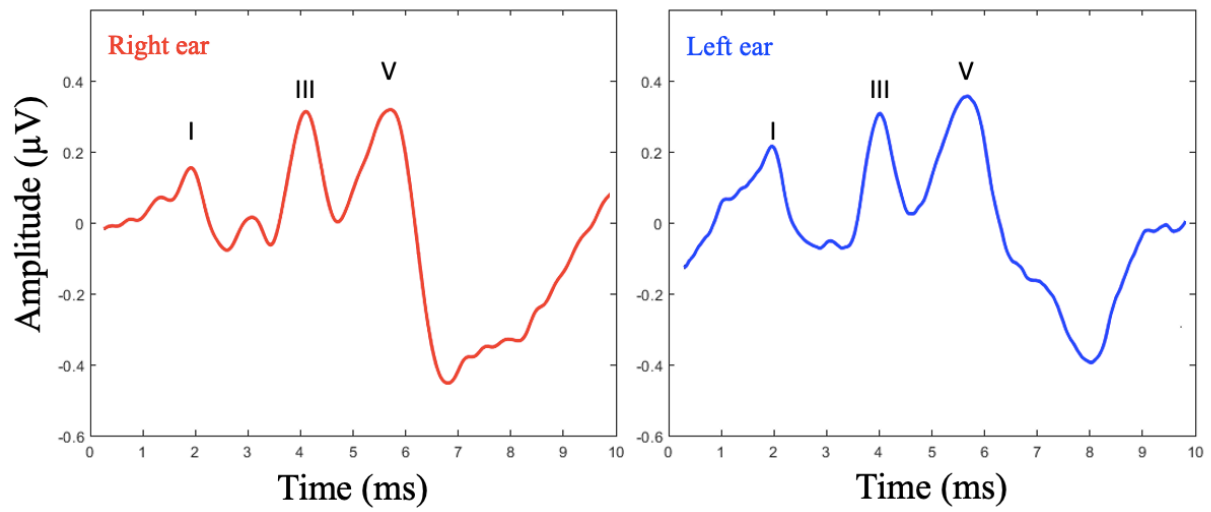
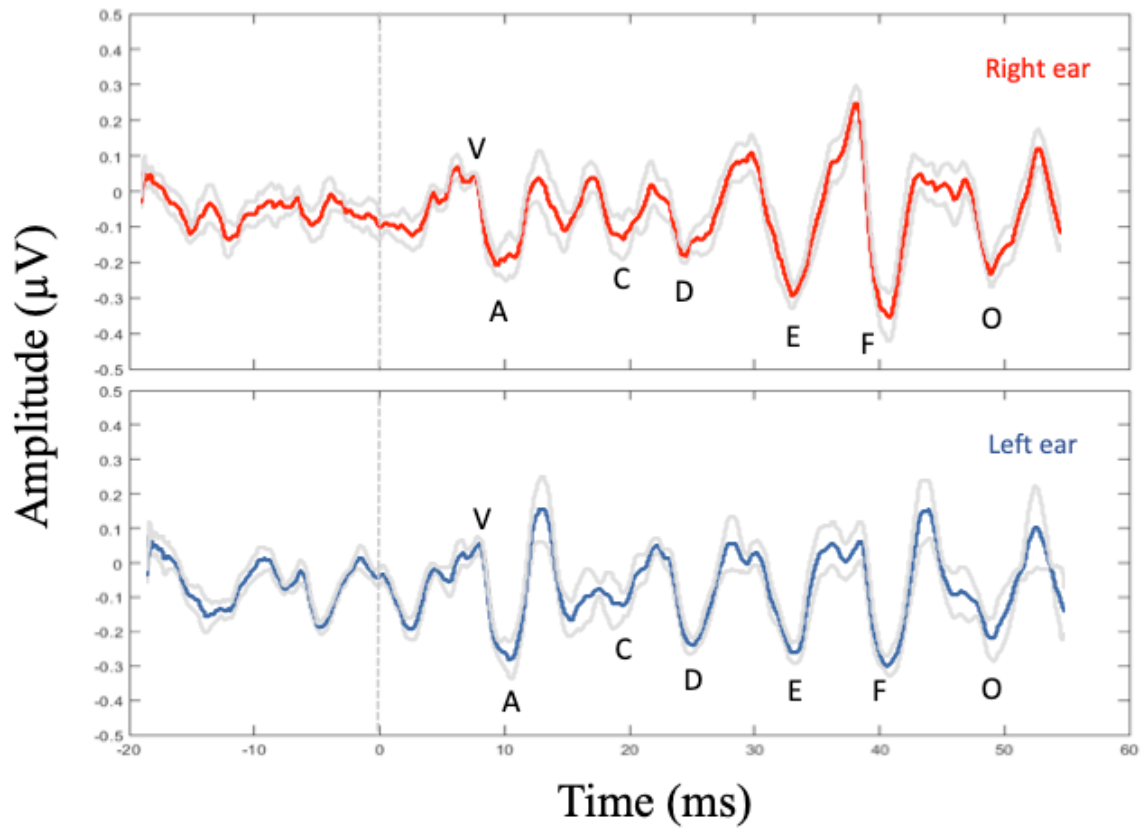


Figure. 3. Grand average waveform for the speech-ABR obtained from 62 older adults to right (red line) and left (blue line) ear presentation of 40-ms speech syllable /da/. The stimulus evoked seven prominent peaks, labeled as V, A, C, D, E, F and O. Grey lines in both panels represent ± 1 SE.



Chapter 5- Article 2

Association Between the Right Ear Advantage in Dichotic Listening and Interaural Differences in Sensory Processing at Lower Levels of the Auditory System in Older Adults

Alejandro Ianiszewski-Gómez, Adrian Fuente, Jean-Pierre Gagné

École d'orthophonie et d'audiologie, Faculté de médecine, Université de Montréal, Montréal,
Québec, Canada.

Centre de recherche de l'Institut universitaire de gériatrie de Montréal, Montréal, Québec,
Canada.

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5.1 Abstract

Current evidence suggests that an enhanced right ear advantage (REA) in dichotic listening (DL) among older adults may originate from age-related structural changes in the corpus callosum and/or age-related decline in cognitive processes. Less is known about the effect of information processing at lower portions of the auditory system on DL performance. The present study investigates whether interaural differences (ID) in sensory processing at lower levels of the auditory system are associated with the magnitude of the REA in DL among older adults. Sixty-eight older adults participated in the study. Participants were assessed with a DL test using nonforced and forced attention paradigms. Hearing sensitivity, transient evoked otoacoustic emission (TEOAE), contralateral suppression of TEOAE, a proxy measure of medial olivocochlear (MOC) activation, and auditory brainstem response to speech stimuli (speech-ABR) were tested in both ears separately. The ID in sensory processing at lower levels of the auditory system was derived by calculating the difference between the right and left ears for each auditory measure. Bivariate and multivariate regression models were performed. One multivariate model for each DL paradigm was independently constructed. Measures of cognitive speed of processing and cognitive flexibility were accounted for in the regression models. For both multivariate regression models, ID in pure-tone thresholds and ID in MOC suppression of TEOAE were significantly associated with the magnitude of the REA for DL among older adults. Cognitive measures of speed of processing and cognitive flexibility also contributed to the magnitude of the REA. These results suggest that ID in sensory processing at lower levels of the auditory system account, at least in part, for the increased magnitude of the REA in DL among older adults.

Key words: Older adults, Right ear advantage, Dichotic listening, Interaural audibility difference, Transient evoked otoacoustic emissions, Contralateral suppression, Speech-ABR.

5.2 Introduction

The Dichotic listening (DL) paradigm involves the simultaneous presentation of different and competing auditory stimuli to the left and right ears (Musiek & Weihing, 2011; Hugdahl & Helland, 2013). Typically, normal young adults are faster and more accurate in reporting verbal stimuli (consonant-vowel (CV) pairs, digits, and words) presented to the right ear (RE) than the left ear (LE) (Kimura, 1961, 1967). Accordingly, a right ear advantage (REA) results in DL tasks whereby verbal stimuli are used (Bryden, 1988; Wilson & Leigh, 1996). The REA in DL may be explained by two neural models. First, the structural model proposed by Kimura (1961) explains the REA as a result of a) prewired asymmetries in the ascending auditory pathway due to stronger contralateral neural projections from the RE to the language-dominant left hemisphere (LH) of the brain (Kimura, 1961), and b) a relatively small deficit in the LE performance in normal right-handed listeners related to a delay and/or attenuation of the LE information during the additional callosal relay stage from the right hemisphere (RH) to the left auditory cortex (Kimura, 1961). Second, the attentional model (Kinsbourne, 1970), suggests that the REA arises from a cognitive or attentional bias towards the hemisphere contralateral to the engaged cerebral hemisphere. In other words, the simple act of anticipation of verbal stimuli might preferentially pre-activate the LH setting up a priming advantage for subsequent processing, which in turn would result in an attentional bias favoring the processing of the RE input (Kinsbourne, 1970; Westerhausen & Hugdahl, 2008).

Several authors have investigated DL in older adults (e.g., Bellis & Wilber, 2001; Roup et al., 2006). Older adults often exhibit an age-related decline in DL, which typically results in worse overall performance together with a pronounced interaural asymmetry (i.e., increased REA) relative to young adults (Jerger et al., 1994; Kam & Keith, 2010). It has been proposed that such a substantial increase in the magnitude of the REA among older adults is the result of a greater LE

deficit in DL performance (Jerger et al., 1994; Bellis & Wilber, 2001; Roup et al., 2006; Kam & Keith, 2010). Consistent with the corpus callosum deficit theory (Goldstein & Braun, 1974), a greater LE deficit in DL among older adults may emerge because of an age-related decline in the efficiency of interhemispheric transfer of verbal auditory stimuli (Jerger et al., 1994; Gootjes et al., 2004; Martin & Jerger, 2005; Jerger & Martin, 2006). Indeed, decreased size of the anterior and posterior callosal subareas (Gootjes et al., 2006) have been associated with an increased REA (i.e., greater LE deficit) in DL among older adults. Thus, age-related structural changes in the corpus callosum might deteriorate (i.e., delay or weaken) interhemispheric transfer of verbal auditory stimuli from the LE to the LH, likely exerting an effect on the magnitude of the REA in DL tasks (Jerger et al., 1994; Gootjes et al., 2004, 2006).

It has also been suggested that a greater LE deficit among older adults may be linked to age-related declines in cognitive functions (Davis et al., 2015). Hällgren et al. (2001) showed that working memory and speed of processing were significantly associated with DL when subjects had to selectively attend to the LE stimuli. These results demonstrate that older adults require an increased cognitive capacity to focus and report from the LE during DL. Moreover, a greater LE deficit has also been linked with reduced cognitive control (Hugdahl et al., 2009) and reduced inhibitory control (Hommet et al., 2010). Anderson et al. (2008) suggested that older adults show reduced top-down modulation capacity to focus attention to the LE stimuli, while simultaneously suppressing the RE stimuli, during DL paradigms that require selective attention. In summary, the source of an increased magnitude of the REA in DL among older adults would originate from an age-related decline of corpus callosum functioning resulting in reduced interhemispheric transfer (Goldstein & Braun, 1974; Gootjes et al., 2006), and/or an age-related decline in cognitive abilities,

such as working memory, attention, processing speed, and inhibitory control (Bellis & Wilber, 2001; Hällgren et al., 2001; Hugdahl et al., 2009; Hommet et al., 2010).

While the above-mentioned evidence of DL performance suggests a more cortical basis to account for the increased magnitude of the REA in older adults (e.g., Goldstein & Braun, 1974; Goldstein & Shelly, 1981; Gootjes et al., 2006; Hugdahl et al., 2009), there is converging evidence in normal hearing young adults (e.g., Emmerich et al. 1987; Markevych et al., 2011; Hu and Lau, 2017) suggesting that interaural difference (ID) in sensory processing at lower portions of the auditory pathways might also explain the magnitude of the REA for DL. Emmerich et al. (1987) showed that the REA was significantly correlated with an ID in audibility. Markevych et al. (2011) found a significant correlation between an ID for the suppressed TEOAE with contralateral acoustic stimulation and the REA in a DL test with CV-stimuli. In addition, Hu and Lau (2017) found a significant correlation between DL performance and ID in central conduction time (interpeak I-V) for the auditory brainstem response (ABR). Taking these findings into account, the current evidence suggests an association between ID in sensory processing occurring at lower levels of the auditory system and the magnitude of the REA in DL in normal hearing young adults.

In older adults however, the association between the REA in DL and the ID in sensory processing at lower levels of the auditory system has not been investigated. Note that several studies have suggested that the LE auditory pathway is more affected by aging compared to the RE pathway and thus, an increased ID in sensory processing is likely to be observed in older adults (Gates et al., 1990; Gates & Cooper, 1991; Jerger et al., 1994; Weihing & Musiek, 2014). Therefore, taking the studies conducted in young adults into account (i.e., an association between the ID in sensory processing and REA in DL) and the evidence that the LE pathway becomes even weaker in older

adults, we hypothesize that the magnitude of the ID in sensory processing at lower portions of the auditory system explains in part the increased magnitude of the REA in DL observed in older adults. From a neuroscientific perspective, this piece of information is important because the source of variability accounting for the substantial increase in interaural asymmetry in DL performance among older adults has been mostly attributed to declines in cognitive functions (e.g., working memory, attention) and reduced callosal thickness. Thus, results from this study may help explain some of the performance variability in DL experienced by aging adults. Moreover, providing evidence that increased interaural asymmetry in DL performance among older adults might also have peripheral and subcortical origins would support the utilization of clinical training programs specifically designed to restore the DL deficit by implementing strategies oriented to improve the processing along the weaker auditory pathway reducing the asymmetry between ears.

Thus, the aim of this exploratory study was to investigate whether the magnitude of ID in sensory processing at lower portions of the auditory system was associated with the increased REA in DL among older adults. Specifically, it was hypothesized that the magnitude of peripheral and subcortical processing differences between the right and left auditory pathways account, at least in part, for the magnitude of the REA in DL. To test this hypothesis, a sample of older adults with normal hearing thresholds according to their age (ISO 7029, 2000) was selected. Also, considering that performance in DL tasks relies on higher cognitive demands (Jerger & Martin, 2006), we selected a DL test (*iDichotic*; Bless et al., 2013) that minimizes the impact of higher cognitive functions such as working memory (i.e., only one dichotic stimulus pair). However, given that DL still requires controlled attention capacity (Hugdahl, 2003; Hugdahl et al., 2003), cognitive measures were accounted as covariates during the regression analyses.

5.3 Material and methods

5.3.1 Participants

A total of 68 older adults (35 women and 33 men) between the ages of 61 and 90 years (mean \pm Standard Deviation (SD) = 71.47 ± 6.12) participated in this study. The participants were enrolled from the registry of research participants of the Centre de recherche de l'Institut universitaire de gériatrie de Montréal as well as via posts and word of mouth. None of the participants reported a history of neurologic, chronic, or middle ear disease. All participants were native speakers of Quebec French and righthanded as determined by the Edinburgh Handedness Inventory (Oldfield, 1971). The mean level of education was 15.66 years (SD = 0.38). All participants scored at least 26/30 in the Montreal Cognitive Assessment (MoCA, Nasreddine et al., 2005). The average MoCA score was 28.7 (SD = 1.16), suggesting no cognitive impairment (Nasreddine et al., 2005).

5.3.2 Audiometric Tests

All participants completed an audiological evaluation performed by a trained audiologist. They exhibited no visible alterations of the ear canal and tympanic membrane under otoscopic examination. Bilateral type A (normal) tympanograms (Jerger, 1970) were obtained in all participants with a Zodiac 901 tympanometer (Madsen, GN Otometrics, Denmark). Ipsilateral acoustic reflexes were obtained at expected values at 500, 1000, and 2000 Hz in both ears in all participants (Wertheimer, 2017). Also, pure-tone audiometry was conducted in both ears with an Interacoustics AC40 clinical audiometer (Interacoustics A/S, Middelfart, Denmark) using ER-3A insert earphones (Etymotic Research, Elk Grove Village, IL, USA). All participants presented with pure-tone thresholds in the frequency range of 250 to 8000 Hz (including 3000 and 6000 Hz) equal to or better than the 25th percentile of an otologically screened population of the same age range

and sex (ISO 7029, 2000). Moreover, only participants with symmetric hearing levels between both ears were included. The latter was defined as an interaural pure-tone thresholds difference of maximally 10 dB HL at two or less audiometric frequencies between 250 and 8000 Hz. For the statistical analysis, the average of pure-tone thresholds for each ear at 250, 500, 1000, 2000, and 3000 Hz was used. This frequency range was selected because it represents the energy range in the CV syllables presented in the study (Hugdahl, 2003).

5.3.3 DL Task

The mobile device app version for iPhone of the Bergen Dichotic Listening test (Hugdahl & Andersson, 1986), the *iDichotic* (Bless et al., 2013), was used to evaluate DL. Stimuli were presented in French. In this procedure, the stimuli consisted of six consonant-vowel syllables /ba/, /ga/, /da/, /pa/, /ka/, and /ta/. The syllables were paired in all 36 possible combinations, with one syllable presented to the LE and the other one presented simultaneously to the RE. As a result, the full set included 30 dichotic-stimulus pairs, presenting different syllables to the right and left ears (e.g., /ba/-/ka/, /pa/-/ta/), as well as 6 homonymic pairs, presenting the same syllable to the right and left ears to secure that the participant was able to identify the syllables. The syllables used for the test were natural recordings, spoken by a male voice with constant and neutral intonation (Hugdahl & Andersson, 1986). Each syllable had a duration of approximately 400-500 ms with a 4-s pause between each presentation of syllable pairs. The *iDichotic* test was administered using an iPhone 6, which was connected to the above-mentioned audiometer. Participants listened to the stimuli through Etymotic ER-3A insert earphones. Before starting the test, the 1-kHz tone in the device app was used to calibrate the audiometer's volume unit meter with the output intensity of the iPhone for each audiometric channel separately.

The test was conducted in a soundproof booth, and the pairs of syllables were delivered at a fixed presentation level of 70 dB HL to allow maximum intelligibility of the dichotic stimuli. Two test paradigms were used in this study: a nonforced attention paradigm and a forced attention paradigm (i.e., forced-right, and forced-left conditions). In the nonforced paradigm, participants were instructed to report the syllable that was heard best immediately after each stimulus presentation. In the forced-right and forced-left conditions, participants were required to report the syllable heard from the cued ear (only right or only left), ignoring the stimulus from the contralateral ear. The nonforced condition was always carried out first, and the forced-right and forced-left conditions were automatically randomized by the *iDichotic* app. The rationale to administer the nonforced condition first was that participants may not “attend to both ears” once they have been previously instructed to attend to a specific ear (Andersson et al., 2008).

For each participant, the number of correctly reported syllables for the right and left ears was obtained and converted into percentages. Also, an individual laterality index (LI) was calculated for all participants. The LI is expressed by the following equation:
$$([correct\ RE\ results - correct\ LE\ results] / [correct\ RE\ results + correct\ LE\ results]) * 100$$
 The LI is an individualized score that integrates DL results from both ears. LI scores can vary between -100 and +100 whereby positive values represent an REA while negative values signify a left ear advantage. Separate LIs were calculated for both nonforced and forced attention paradigms. The LI for the forced attention paradigm was calculated using the attended ear scores from forced-right and forced-left conditions to further control for attention bias (Bryden et al., 1983).

5.3.4 Trail Making Test

The trail making test (TMT) (Reitan & Wolfson, 1993) provides information on the speed of processing, mental flexibility, and executive functions. The test was administered in two parts. In part A, participants were asked to draw a line connecting in ascending order 25 circles numbered from 1 to 25. In part B, participants were required to connect circles containing numbers (from 1 to 13) or letters (from A to L) in an alternating numeric-alphabetical order (1-A-2-B-3-C, etc.). For both parts of the test, participants were instructed to connect the circles as quickly as possible without lifting the pen or pencil from the paper. In the present study, the time taken to complete the test was recorded. If an error occurred, the participant was instructed to correct it, but the clock used to time the test was not stopped. The total time taken to complete the task was considered as the final score. Results from the TMT were used for further analyses of processing speed (TMT-A) and cognitive flexibility, a key executive function involving set shifting (TMT-B) (Sanchez-Cubillos et al., 2009). Set shifting is an executive function that requires individuals to switch their attention between two rules or tasks (Miyake et al., 2000). To emphasize cognitive flexibility (set-shifting ability), a TMT ratio score was also calculated using the following formula: TMT part B - TMT part A/TMT part A (Stuss et al., 2001).

5.3.5 Other Auditory Tests

5.3.5.1 TEOAE Recordings

TEOAEs provide frequency-specific information about cochlear function and outer hair cell motility (Kemp, 2002). TEOAEs were measured using the SmartTrOAE module (version 5.10, Intelligent Hearing Systems, Miami, FL, USA). A probe tip positioned in the participant's ear canal was used to record all otoacoustic emissions. The in-ear probe calibration test was automatically performed by the SmartTrOAE software. TEOAEs were elicited with 75 μ s clicks presented at 80

dB pSPL at the rate of 19.3/s. Responses to a total of 1024 sweeps were averaged. TEOAEs were considered present if the response amplitude exceeded the noise amplitude in at least 3 dB (signal-to-noise ratio [SNR] ≥ 3 dB) at each frequency band from 1000 to 4000 Hz. TEOAE responses were accepted only if the stimulus stability was $\geq 80\%$ and wave reproducibility was $\geq 70\%$ (Hood et al, 1997).

Then, TEOAEs with contralateral acoustic stimulation were measured. Contralateral acoustic stimulation activates the medial olivocochlear (MOC) bundle, which is an efferent neural pathway originating from the periolivary nuclei of the superior olivary complex and terminating on the base of the outer hair cells in the cochlea (Guinan, 2006). Activation of the MOC efferent pathways attenuates (i.e., suppress) the cochlear response to sound by reducing the gain of the outer hair cell response to acoustic stimulation (Siegel & Kim, 1986; Murugasu & Russel, 1996; Guinan, 2018). Without removing the probe tip inserted in the tested ear, a broadband noise (125-8000 Hz) was simultaneously presented to the contralateral ear at a level of 60 dB sound pressure level. This level was selected based on previous work demonstrating that it is an effective activator of the MOC (e.g., Guinan et al., 2003) while minimizing elicitation of the middle-ear muscle reflex. Contralateral acoustic stimulation was presented through the SmartTrOAE software connected with unshielded Etymotic ER-3A insert earphones. The noise was presented for period of 400 ms with an inter-stimulus interval of 20 ms. Responses to a total of 256 sweeps were averaged. TEOAE response amplitude in SNR was registered by the SmartTrOAE for each test condition (with and without contralateral acoustic stimulation) for both ears. Participants were instructed to stay as still as possible and to keep their head straight during measurement. The average in dB SNR of TEOAE responses across frequencies (1000-4000 Hz) with and without contralateral acoustic stimulation

was calculated for each ear separately. Ear-specific MOC-induced TEOAE suppression was determined by subtracting the average of TEOAE responses with contralateral stimulation from the average of TEOAE responses without contralateral acoustic stimulation. For example, MOC-induced TEOAE suppression for the RE was obtained by subtracting TEOAE response from the RE (i.e., TEOAE probe in the RE) with contralateral acoustic stimulation (i.e., noise presented to the LE) from TEOAE response from the RE (i.e., TEOAE probe in the RE) without contralateral acoustic stimulation. The average of TEOAE responses (dB SNR) across frequencies (1000 – 4000Hz) and the amount of MOC-induced TEOAE suppression for each ear were used for statistical analyses.

5.3.5.2 Electrophysiological Measure

speech-ABR provides the opportunity to objectively examine the ability of the brainstem to accurately encode timing information in older adults (Vander Werff & Burns, 2011; Anderson et al., 2012). Speech-ABR for right and left ears was elicited and registered using a two-channel Intelligent Hearing Systems (IHS, Miami, FL, USA) SmartEP module (version 3.95). Electrodes placed at Fz (positive), A1 and A2 (negative), and the forehead (ground) in accordance with the International 10 to 20 system EEG were used for all recordings. Contact impedance was maintained below 5 k Ω , and inter-electrode impedance was maintained below 3 k Ω . Speech-ABR was elicited by a 40-ms synthesized /da/ syllable provided by the IHS SmartEP module. This syllable contains a release burst and voiced formant transition with a fundamental frequency that linearly rises from 103 to 125 Hz with voicing beginning at 5 ms and an onset release burst during the first 10 ms (Skoe & Kraus, 2010). Although the stimulus does not contain a steady-state portion, it is psychophysically perceived as a consonant-vowel speech syllable (Johnson et al., 2005). The 40-ms /da/ stimulus was monaurally presented to right and left ears at 80 dB nHL in alternating polarity

at a rate of 10.9/s. The order of ear presentation was randomized across participants. A time window of 71.81 ms (including a 20-ms prestimulus time) and online filter setting of 50-3000 Hz were used for recording. Brainstem responses were then offline bandpass filtered from 70 to 2000 Hz to filter out cortical activity while maximizing SNR and the detection of transient peaks (such as the onset). Trials with artifact exceeding $\pm 30 \mu\text{V}$ were automatically excluded from the average. A grand average of 5000 (two subaverages of 2500 sweeps) artifact-free responses were obtained for each ear. This number of artifact-free responses was chosen because it falls between the epochs' range (1600 to 6400) required to record speech-ABRs with clearly identifiable peaks to the 40-ms /da/ syllable (BinKhamis et al., 2019). Participants were seated in a comfortable reclining chair in a quiet room with lights dimmed. Both ears were plugged with the insert earphone during the session, regardless of which ear was stimulated. Participants were asked to relax with their eyes closed.

For each participant, latencies and amplitudes for brainstem onset (V and A) and offset (O) peaks were identified and analyzed using previously described latency values (Skoe et al., 2015). These peaks were selected because they represent the brainstem response to temporal features in the transient range of speech sound stimulus (Abrams et al., 2006). Latencies and amplitudes of individual peaks for the speech stimuli were further analyzed using an open-source, MATLAB-based toolbox developed and distributed by Erika Skoe and Trent Nicol from the Auditory Neuroscience Laboratory, Northwestern University (Brainstem Toolbox, 2008). Using this program, visually picked peak latencies and corresponding amplitudes previously obtained were adjusted slightly (within ± 2 sampling points) to obtain the absolute minimum or maximum (Skoe & Kraus, 2010). In addition, the root mean square (RMS) and the signal-to-noise ratio (SNR) for each neural response from the RE and LE were calculated. These magnitude measures provide

information about the robustness of auditory processing (Krizman & Kraus, 2019). The analysis was also conducted using the above-mentioned MATLAB-based toolbox (Brainstem Toolbox, 2013).

5.3.5.3 Data Processing of Auditory Measures

The difference in test results between right and left ear presentation were calculated for each auditory outcome (i.e., pure-tone threshold, TEOAE response, MOC-induced TEOAE suppression, and speech-ABR) with the aim to obtain the magnitude of the ID in sensory processing at lower portions of the auditory system. The ID was obtained by subtracting the LE response from the RE response ($RE - LE$). However, to enable positive and negative values to continuously indicate sensory processing in the right and left ears, respectively, the ID formula was inverted ($LE - RE$) for measures at which lower values represent better results (e.g., hearing thresholds and speech-ABR latencies). Thus, positive values indicate an ID favoring the right ear pathway and negative values indicate an ID favoring the left ear pathway.

5.3.6 Statistical Analyses

Repeated measure analysis of variance was used to determine possible differences between right and left ear results for the *iDichotic* test. Repeated measure analysis was also computed to determine possible ear differences in sensory processing for all auditory measures (i.e., stimulated ear as within-subject factor). The assumptions of normality, equal variance, and sphericity were checked. Then, correlation analyses were conducted to investigate the association between DL results (LI) and cognitive measures and the ID for each auditory measure. To prevent spurious results from correlation analyses, which can be overly biased by outlying data points, all extreme

scores beyond ± 3.29 standard deviations of the mean were removed from the raw speech-ABR values before calculating the ID (Field, 2013). Bivariate regression analyses were then conducted to examine possible associations between the LI (dependent variable) for each DL paradigm (i.e., nonforced and forced attention) and the continuous variables that were significantly correlated with each of the LIs in the correlation analyses. Lastly, multivariate regression models were performed to separately model the association between the LI for each DL paradigm and the variables that were significantly associated with the LIs in the bivariate linear regression models. A backward elimination technique was used in the multivariate models to select those variables remaining significant in the adjusted analysis, using a selection criterion of $\alpha < .05$. All statistical analyses were performed using SPSS software version 24 (SPSS Inc., Chicago, USA).

5.4 Results

5.4.1 iDichotic Test

Repeated measure analysis was performed to explore for possible significant differences for the *iDichotic* results between the right and left ears for each DL paradigm. For the nonforced paradigm, the mean RE score was 51.07 % while the LE score was 21.89 %. The RE score was significantly higher than the LE score [$F(1, 67) = 84.246$; $p < .001$], resulting in a LI or REA for the nonforced paradigm of 36.91 %. For the forced attention paradigm, the attended ear scores for both forced-right and forced-left conditions were considered for analysis. Results revealed that the mean score from the RE was 56.74 % and was 26.64 % from the LE. The RE score was significantly higher than the LE score [$F(1, 67) = 68.587$; $p < .001$] which resulted in a LI or a REA of 34.87 %. Figure 1 shows the ear scores and the LI expressed as percent of correct reports for both DL paradigms.

5.4.2 Cognitive Test

Descriptive statistics for cognitive measures (mean, SD, and range) for the entire group are summarized in Table 1. TMT A and TMT B time to completion score was within normal range values based on the Wechsler (1997) performance description system (Ashendorf et al., 2008). The TMT ratio score was 2.13, which suggests equal performance on both subtests (Golden et al., 1981). It is worth noting that high TMT ratio scores might suggest impairment in cognitive flexibility (Stuss et al., 2001).

5.4.3 Auditory Measures

5.4.3.1 Hearing Thresholds

Table 2 displays the mean audiometric thresholds (250 to 8000 Hz) for both ears along with the mean ID (LE - RE) for each tested frequency and the average of pure-tone thresholds across frequencies (250-3000 Hz). The statistical analysis revealed no significant differences for pure-tone thresholds between ears in the frequency range between 250 and 8000 Hz. Similarly, the average of pure-tone thresholds across frequencies (250-3000 Hz) was not significantly different between both ears. Figure 2 displays the ID for the average of pure-tone thresholds for each single participant.

5.4.3.2 TEOAE and Speech-ABR Measures

Table 3 displays the mean and SD for TEOAE and speech-ABR measures for both ears along with the mean ID. Overall, the occurrence of measurable otoacoustic emissions above noise level (SNR ≥ 3 dB) was 86.76 % in the RE and 85 % in the LE. Figures 3A and 3B display individual participants' ID for the average of TEOAE responses and MOC-induced TEOAE suppression, respectively. There was no significant difference for the average of TEOAE responses (dB SNR)

across frequencies (1000-4000 Hz) between right and left ears. In addition, the amount of MOC-induced TEOAE suppression (dB SNR) did not significantly differ between both ears.

Regarding the speech-ABR, significant differences in latency were found for the onset peak (A) [$F(1, 53) = 5.661$; $p = .021$] and offset peak (O) [$F(1, 61) = 18.893$; $p < .0001$] between right and left ears. RE latencies for both peaks were significantly shorter than LE latencies (see Figure 4). No significant latency differences ($p > 0.05$) were found between ears for peak V. Note that three participants were excluded from the analysis because their raw speech-ABR responses were deemed as outliers (extremes scores beyond ± 3.29 standard deviations). Figure 5 displays the ID for speech-ABR measures (i.e., peaks V, A, and O) for each single participant, excluding the three participants who were removed from the inferential analysis. Finally, there were not any statistically significant differences ($p > 0.05$) for the amplitude and magnitude measures between the RE and the LE.

5.4.4 Correlation Analyses

The inferential statistics on the correlations are presented in Table 4. In the nonforced paradigm, the LI (or REA) was negatively correlated with the TMT-A. Similarly, the LI was positively correlated with the ID for the average of pure-tone thresholds across frequencies (250-3000 Hz), the ID for the average of TEOAE response across frequencies (1000-4000 Hz), and the ID for MOC-induced TEOAE suppression (see Table, Supplemental Digital Content 1, which shows the correlation coefficients between the nonforced paradigm results (RE, LE and LI), cognitive measures, and auditory outcomes for right and left ear separately). Similar results were observed for the forced attention paradigm. The LI was positively correlated with the TMT ratio score.

Additionally, the LI was positively correlated with the ID for the average of pure-tone thresholds across frequencies, the ID for the average of TEOAE response across frequencies, and the ID for MOC-induced TEOAE suppression (see Table, Supplemental Digital Content 2, which shows the correlation coefficients between the forced attention paradigm results (RE, LE and LI), cognitive measures, and auditory outcomes for right and left ear separately). None of the LIs of both DL paradigms were significantly correlated with the ID for speech-ABR latency, amplitude, and magnitude measures. Overall, the positive correlations between the LI for DL and ID values indicate an association between the magnitude of the REA for DL and ID favoring the RE.

5.4.5 Bivariate and Multivariate Regression Analyses

Using bivariate regression analyses, the variables significantly associated with the LI for the nonforced paradigm were the TMT-A, the ID for the average of pure-tone thresholds, the ID for the average of TEOAE responses, and the ID for MOC-induced TEOAE suppression. Variables significantly associated with the LI for the forced attention paradigm included the TMT ratio score, the ID for the average of pure-tone thresholds, the ID for the average of TEOAE responses, and the ID for MOC-induced TEOAE suppression. Figures 6 and 7 show the scatterplots and linear regression lines of the LIs from both nonforced and forced attention paradigms with all the variables that were significantly associated.

Using multivariate regression analyses for the LI for the nonforced and forced attention paradigms independently, the variables remaining significantly associated with the LI for the nonforced paradigm in the final multivariate model were the TMT-A, the ID for the average of pure-tone thresholds, and the ID for MOC-induced TEOAE suppression [$F(3, 62) = 7.887, p < .001$]. These three variables accounted for 27.6 % of the total variance of the LI for the nonforced paradigm.

The LI for the forced attention paradigm was best predicted by the TMT ratio score, the ID for the average for pure-tone thresholds, and the ID for MOC-induced TEOAE suppression [$F(3, 62) = 7.819, p < .001$], explaining 27.4 % of the total variance of the LI for the forced attention paradigm. Table 5 shows the bivariate and multivariate models for the LI of each DL paradigm (nonforced and forced attention) after elimination of those variables that did not significantly contribute to each model.

5.5 Discussion

The present study examined the association between the magnitude of interaural differences (ID) in sensory processing at lower levels of the auditory system and the magnitude of the REA for DL among older adults. Specifically, it was hypothesized that an increased ID in peripheral and brainstem auditory processing accounted at least in part for the increased magnitude of the REA in DL among older adults with age-appropriate hearing. Multivariate regression models revealed that ID in pure-tone thresholds, and ID in MOC-induced TEOAE suppression significantly accounted for the increased magnitude of the REA in DL among older adults. Contrary to the hypothesis, ID in speech-ABR measures were not associated with the magnitude of the REA. Speed of processing and cognitive flexibility also explained the increased magnitude of the REA in older adults.

5.5.1 Audibility effects on the REA in DL

The ID for pure-tone thresholds accounted for almost 17 % and 15 % of the total variance of the magnitude of the REA for the nonforced and forced attention paradigms, respectively. It has been suggested that a substantial ID in audibility is likely to increase the asymmetry between ears for DL tasks (Speaks et al., 1983; Musiek & Chermak, 2015). To eliminate this potential effect, only older adults with bilateral normal hearing for their age (ISO 7029, 2000) were selected. As a result,

the average of pure-tone thresholds was not significantly different between both ears. As it can be observed in Figure 2, some participants exhibited better audibility for the RE and others for the LE, thus as a group, no significant differences between RE and LE for the average of pure-tone thresholds were found. Notwithstanding the absence of significant audibility difference between ears, the results indicated that as the ID became more positive (i.e., better audibility in the RE relative to the LE), the REA's magnitude increased. Two complementing hypotheses may explain these results. First, it is possible that an ID in audibility favoring the RE improved the perceptual saliency of the RE stimuli, increasing the REA. This may occur because higher auditory input results in a stronger neural representation of the speech stimuli from the ear exposed to the louder stimulus (Boudreau & Tsuchitani, 1968). Previous studies in young adults investigating the effect of sensory/acoustic influences on the REA in DL have revealed that a 3dB interaural intensity difference in favor of the RE input is enough to increase the magnitude of the REA (Hugdahl et al., 2008; Westerhausen et al., 2009). In older adults, similar results have been demonstrated whereby a 5dB interaural intensity difference favoring the RE is likely to exert the same effect on the REA's magnitude (Passow et al., 2012, 2014). In this study, the ID in audibility favoring the RE varied from 1 to 6 dB which is consistent with the interaural intensity difference capable of increasing the REA in young and older adults as mentioned above. Thus, this small ID in audibility may have led to a larger REA for DL by strengthening the neural representation of the acoustic features of the RE input (Boudreau & Tsuchitani, 1968). According to Westerhausen (2019), the effect of an interaural intensity difference on perceptual laterality in DL might be linear and thus, a similar effect should be expected on the REA's magnitude due to an ID in audibility. This linear effect could potentially explain the significant association between the magnitude of the REA and the magnitude of ID in audibility observed in the linear regression models.

In addition, since an increased ID in audibility favoring RE implies weaker LE audibility, it is possible that the results rather represent reduced neural representation of acoustic features for LE input. In other words, instead of enhanced RE processing (as mentioned above), the ID may have triggered a poorer LE processing. Note that in the current study, participants presented with worse hearing thresholds in the LE than the RE despite showing no significant difference between ears (Table 2). Consistent with Dorman et al. (1985), poorer auditory thresholds, even in the presence of normal age-appropriate hearing, is associated with older adults' difficulties to process spectrotemporal acoustic cues to identify stop consonant syllables. In addition, CV-syllables minimize the relevance of cognitive-control processes and lexical component (i.e., internal redundancy) in DL tasks as opposed to digits and sentences which provide more lexical information (Findlen & Roup, 2011). Therefore, older adults must strongly rely on external redundancy (i.e., acoustic features of the speech stimuli) (Bocca & Calero, 1963) and bottom-up processing to accurately process CV-syllables. Thus, the ID in audibility in disfavor of the LE observed in this study may have been enough to reduce the access to acoustic features for LE stimuli. Consequently, this reduction elicited a poorer neural representation of the spectrotemporal acoustic features needed to identify the syllable ultimately declining LE performance.

5.5.2 TEOAE effects on the REA in DL

The REA for DL was significantly associated with the ID for TEOAE response. This variable accounted for almost 7.5% and 6.6% of the total variance of the magnitude of the REA for the nonforced and forced attention paradigms, respectively. Results from this study also showed that the average for TEOAE response was not significantly different between right and left ears. This result is not in agreement with previous studies in young and older adults with normal hearing

thresholds demonstrating significantly larger TEOAE response amplitudes in the RE compared with the LE (e.g., Khalfa et al., 1997; Tadros et al., 2005). As shown in Figure 3A, the fact that as a group some participants exhibited higher TEOAE responses for the RE and others higher TEOAE for the LE could explain the absence of significant differences between right and left ears found in this study. Despite of this, averaged TEOAE in the RE were higher relative to the LE. Thus, more robust (higher SNR) TEOAE in the RE than the LE could still reflect a lateralization of active cochlear mechanisms (Brownell, 1990), suggesting that outer hair cells in the RE are more efficient and/or more reactive than in the LE (Khalfa et al., 2001b). This is relevant considering that one of the roles of outer hair cells is to amplify spectrotemporal aspects of sound coding which are essential for speech perception (Moore & Hunter, 2013). Accordingly, the correlation between the REA for DL and the ID for TEOAE in favor of the RE may imply that more robust TEOAE boosted the neural representation of the RE input which facilitated the access to acoustic features improving RE processing and ultimately increasing the REA. However, considering that an increased ID for TEOAE in favor of the RE indicates less robust TEOAE in the LE, it is thus possible that the results rather suggest an increase in the magnitude of the REA for DL among older adults due to worse LE performance. That is, less robust TEOAE in the LE relative to the RE could have diminished the neural representation for LE stimuli limiting the access to spectrotemporal acoustic features which eventually weakened LE processing. As previously mentioned, less robust TEOAE in the LE than the RE may be an effect of the rightward peripheral laterality for cochlear processing. However, since there was no significant right/left TEOAE difference, less robust TEOAE in the LE could also be the result of the slightly poorer hearing sensitivity in the LE relative to the RE observed in this study (Keppler et al., 2010).

It should be mentioned that the ID for TEOAE response did not remain as a significant variable in the final multivariate regression models. Correlation analyses revealed that both the ID for TEOAE response and the ID for MOC-induced TEOAE suppression were significantly correlated (see Table 4). MOC-induced TEOAE suppression represents the difference between TEOAE response with and without contralateral acoustic stimulation. Thus, we believe that the ID for TEOAE response did not remain as an explanatory variable in the final multivariate regression models due to collinearity (Fields, 2013).

5.5.3 MOC-induced TEOAE suppression effects on the REA in DL

The ID for MOC-induced TEOAE suppression was significantly associated with the REA's magnitude in DL for both nonforced and forced attention paradigms, explaining respectively 9.1 % and 5.9 % of their variance. Like the results obtained in TEOAE, the magnitude of MOC-induced TEOAE suppression was not significantly different between ears. This lack of significance may be attributed to the fact that as a group almost the same number of participants showed higher MOC-induced TEOAE suppression in the right as in the LE (see Figure 3B). Albeit the absence of significant MOC-induced TEOAE suppression difference between ears, the results showed that as the ID became more positive (i.e., more MOC-induced TEOAE suppression in the RE [noise left] relative to the LE), the REA increased. This result suggests that MOC efferent reflex (suppression) could be involved in DL performance, although its exact role is unclear. It has been proposed that the inhibitory function of the efferent auditory pathway (MOC bundle) might improve coding of speech signals in the presence of competing noise (Kalaiah et al., 2017). In fact, increased MOC-induced TEOAE suppression has been related to improved performance in perceptual processes such as speech perception in noise (Bidelman & Bhagat, 2015). Thus, if DL is considered as a challenging competing auditory task—whereby the simultaneous auditory stimulus coming from

the opposite ear is thought to be competitive—it could be possible that the MOC system was activated during DL due to the binaural presentation of the speech sounds. Accordingly, a positive ID in MOC-induced TEOAE suppression could indicate that a more effective MOC system in the RE exerted more TEOAE suppression when competing speech stimuli came from the contralateral ear. In turn, this would result in more accurate processing of the RE stimuli, ultimately increasing the REA during DL tasks. However, a more positive ID for MOC-induced TEOAE suppression also implies less TEOAE suppression in the LE. Thus, changes in the REA's magnitude may have also been related to worse LE performance in DL due to reduced TEOAE suppression when competing speech stimuli came from the RE. Reduced MOC-induced TEOAE suppression in the LE has been significantly associated with worse DL performance in the LE (Khalfa et al., 2001a). Moreover, the ID for the suppressed TEOAE has been significantly correlated with the REA in DL in young adults (Markevych et al., 2011). Specifically, as the ID became more negative (i.e., TEOAEs in the LE were less suppressed by noise from the RE), LE performance in DL declined, enhancing the REA. Overall, these results suggest that a decline in LE performance may be related to a less effective MOC system in the LE which is not capable to suppress the competing stimuli coming from the RE during DL stimulation.

It is striking to note that ID in MOC-induced TEOAE suppression was correlated to the REA's magnitude in DL considering that there were no significant differences in MOC efferent reflex (suppression) between both ears. An alternative explanation for this finding could be that such an association may reflect cortical influences on the periphery that are specific to language. It has been suggested that the cortex might be able to regulate peripheral processing via the olivocochlear bundle by exerting top-down influences important for auditory information (Khalfa et al., 2001a). Consistent with this, the LH may be able to sample rapid time-varying phonetic cues (e.g., voice

onset time) important to distinguish stop voicing contrasts (e.g., /pa/ vs /ba/) on a shorter timescale than the RH (Poeppel, 2003). Thus, it may be that cortical efferents from the LH language centers projecting to the brainstem were strongly activated during DL stimulation. Such a cortical modulation could have improved syllable identification on the RE ultimately leading to a larger REA for DL. Thus, our task may have been more dependent on cortical influences coming from the language-dominant LH. This could potentially explain the association between the REA's magnitude in DL and the ID in MOC-induced TEOAE suppression notwithstanding the absence of significant differences in MOC efferent reflex between the right and left ears.

5.5.4 Speech-ABR effects on the REA in DL

Results from the study revealed that there were not statistically significant amplitude and magnitude differences between the neural response from the RE and the LE among older adults. However, significantly delayed neural latencies for speech-ABR onset (i.e., A) and offset (i.e., O) peaks were found in the LE compared to the RE in older adults. Figure 4 shows that most of the participants exhibited faster subcortical neural timing for s-ABR transient components in the RE than the LE. Delayed neural encoding for speech-ABR transient components in LE than RE presentation has been shown in older adults (Vander Werff & Burns, 2011). In addition, delayed neural encoding at the brainstem level is consistent with an increased difficulty to identify spectrotemporal speech cues of stop consonants among older adults (Parbery-Clark et al., 2012). Nevertheless, ID in neural timing for speech-ABR measures were not significantly associated with the REA's magnitude for DL in older adults. These results were rather unexpected considering that interaural latency differences for click-ABR (i.e., peak V and interpeak I-V) have been significantly correlated with the magnitude of the REA in DL to CV-syllables in young adults (Hu & Lau, 2017).

Moreover, decreased DL scores in the RE have been significantly correlated with increased latencies for speech-ABR onset (i.e., V-A) components in young adults (Lotfi et al., 2019). We cannot fully explain why subcortical neural timing differences between both ears were not significantly associated with the REA's magnitude for DL in older adults, despite significant differences between ears for speech-ABR latencies. We propose one hypothesis for these findings. It has been suggested that brainstem processing is shaped by descending corticofugal "top-down" influences (Suga, 2008) leading to the subcortical malleability of neural timing encoding (Tzounopoulos & Kraus, 2009). Consistent with this view, previous studies measuring the frequency following response in a DL paradigm have shown that increased attentional control may modulate the ABR in humans (Galbraith et al., 1998; Lehmann & Schönwiesner, 2014). Thus, considering that DL tasks require controlled attention capacity (Hugdahl, 2003; Hugdahl et al., 2003), we hypothesize that top-down influences (e.g., attentional control) enhanced neural encoding of speech sounds during dichotic stimulation thereby attenuating any potential effects due to ID in neural timing at the brainstem level on DL performance and ultimately on the magnitude of the REA. Further studies should investigate speech-ABR using dichotic stimulation with CV syllables with controlled attention to right or left ear to test the hypothesis.

5.5.5 Cognitive Effects on the REA in DL

Regarding cognitive measures, both speed of processing and cognitive flexibility was significantly associated with the REA in DL among older adults. Speed of processing uniquely contributed to 9.0 % of the variance of the magnitude of the REA in the nonforced paradigm. The nonforced paradigm minimizes the relevance of cognitive-control processes by not requiring stimulus localization and response selection processes (Westerhausen et al., 2015). The instruction used

however, that is, requiring as response only the stimulus perceived clearest after each one-pair presentation trial might create a response conflict (van Veen et al., 2001). This conflict may force participants to develop a response strategy, for example by rapidly deciding to direct attention selectively to the right or left stimuli (Westerhausen et al., 2019). Considering that in the nonforced paradigm the active stimulus-driven mechanism conveys a verbal processing advantage to the RE stimuli due to the direct access to the LH (Hugdahl, 2003; Hugdahl et al., 2009), a reasonable conclusion is therefore that faster speed of processing reflects a top-down decision strategy to selectively attend to the RE to benefit from the stimulus-driven processing advantage of the RE stimuli over the LE stimuli during DL tasks.

Cognitive flexibility significantly accounted for 8.2 % of the variance of the magnitude of the REA in the forced attention paradigm. Cognitive flexibility contributes to the individual's set-shifting capacity to switch attention rapidly between two tasks (Miyake et al., 2000; Stuss et al., 2001). Studies investigating directed attention on DL suggest that older adults exhibit a reduced ability to switch attention (i.e., reduced cognitive flexibility) from the RE to the LE during the forced-left condition, while no difficulties are found in the forced-right condition (Andersson et al., 2008; Takio et al., 2009). Moreover, reduced cognitive flexibility in older adults has been significantly correlated with RE score during the forced-left condition in DL (Hommet et al., 2010). Therefore, an increased REA in DL attributed to cognitive flexibility might reflect older adult's difficulties to switch attention to the LE stimuli while simultaneously suppressing the RE stimuli during the forced-left condition. Results from the present study are in line with this hypothesis as they show that reduced cognitive flexibility was significantly associated with poor LE performance in DL, while RE performance was not associated with this cognitive measure (see Table, Supplemental Digital Content 2). In addition, these findings are in line with previous research suggesting that

older adults show a reduced capacity for top-down attentional control modulation only in the forced-left condition (Andersson et al., 2008; Takio et al., 2009).

DL performance requires cognitive control to parse with the processing conflict involved in perceiving two similar syllables dichotically (Hugdahl et al., 2009). Results from this study corroborate the involvement of cognitive control in DL by demonstrating that both speed of processing and cognitive flexibility are significantly associated with the magnitude of the REA in DL among older adults. The REA, as revealed in the DL procedure, involves activation not only of temporal areas (Jäncke & Shah, 2002) but also of frontal areas (e.g., prefrontal cortex) which have been linked to cognitive abilities essential for processing dichotic stimulus such as speed of processing and cognitive flexibility (Thomsen et al., 2004 a,b). Therefore, it may be suggested that the presence of a REA in DL may index the integrity of general cortical mechanisms linked to cognitive abilities among older adults.

5.5.6 The increased REA for DL among older adults

As stated in the “introduction” section, two main hypotheses have been proposed to explain age-related changes in the magnitude of the REA in DL. Accordingly, the source of the increased REA’s magnitude in DL with advancing age may originate from either an age-related decline in cognitive abilities, such as working memory, attention, processing speed, and inhibitory control (Bellis & Wilber, 2001; Hällgren et al., 2001; Hommet et al., 2010); and/or decreased central auditory processing due to an age-related decline of corpus callosum functioning resulting in reduced interhemispheric interaction (Gootjes et al., 2006). Results from the present study strengthen the age-related cognitive hypothesis by providing data indicating that both speed of

processing and cognitive flexibility contribute to the enlarged REA among older adults. In addition, the current study provides supporting data suggesting that age-related changes in the magnitude of the REA may also originate from interaural processing differences occurring at lower portions of the auditory pathways, by affecting DL performance, particularly on LE processing, at an early, preattentive bottom-up sensory stage of auditory processing.

Initially, it could be argued that our findings might be the result of the “in built” asymmetry of the auditory system (Hewitt, 2018), which enhances auditory processing from the RE compared to the LE even at peripheral and brainstem levels of the auditory pathways (Khalfa et al., 1997; Philibert et al., 1998; Hornickel et al., 2009a). However, most of the auditory outcomes from the present study were not significantly different between right and left ears. Notwithstanding, auditory results were consistently poorer in the LE relative to the RE. It has been proposed that the auditory pathway subserving left ear input might be more affected by aging than the RE auditory pathway (Gates et al., 1990; Gates & Cooper, 1991; Jerger et al., 1994; Weihing & Musiek, 2014). In line with this, it may be hypothesized that older adults have a weaker LE pathway beginning at early peripheral and brainstem portions of the auditory system which declines perceptual auditory processing of the LE stimuli, reducing LE performance in DL and ultimately increasing the REA. In other words, LE stimuli somehow triggers a poorer neural representation of spectrotemporal acoustic features, which is further reduced by the age-related degradation of the interhemispheric transfer (Goldstein & Braun, 1974; Gootjes et al., 2004, 2006). Thus, the auditory image arriving at the auditory cortex from the LE pathway is less redundant (i.e., less robust) than the auditory image that arrives at the auditory cortex from the RE pathway. Therefore, based on the results of the current study we hypothesize that the increased REA for speech stimuli in DL tasks in older adults is due to reduced cognitive control to LE stimuli, reduced inter-hemispheric transfer function

and reduced auditory processing of LE stimuli as compared to RE stimuli. The findings from the present study particularly complement with the structural model of DL proposed by Kimura (1961) by suggesting that age-related declines preferentially targeting the LE pathway contribute to the magnitude of the REA for speech stimuli in older adults.

5.6 Limitations

Two main limitations are identified in the present study. First, the role of subcortical processing on DL performance may have been limited by the 40-ms /da/ syllable chosen to examine neural representation of temporal aspects of speech at the brainstem level. For example, no associations between the magnitude of the REA in DL and speech-ABR neural timing responses for transient peaks were found. Also, it has been shown that subcortical differentiation of contrastive speech sounds such as stop consonants may be represented by latency shifts during the formant transition (e.g., Johnson et al., 2008; Hornickel et al., 2009b). Because the synthesized 40-ms /da/ syllable used contained a very short, voiced formant transition portion, it was not possible to determine whether interaural latency differences in the peaks corresponding to the formant structure of the syllable could have explained the increased magnitude of the REA in DL. The other main limitation relates to the quantification of the amount of MOC-induced TEOAE suppression. The suppression effect was based upon the difference between the average TEOAE responses across frequencies (1-4 kHz) with and without contralateral acoustic stimulation. Suppression effects are frequency specific, with the greatest amount of suppression observed within the 1.0–4.0 kHz range. MOC-induced TEOAE suppression was not measured in a frequency-specific manner and thus, their effect may have been underestimated.

5.7 Conclusions

The current study identified associations between interaural processing differences at lower level of the auditory pathways and the REA in DL among older adults. This is the first report showing that small interaural audibility differences in older adults with age-appropriate hearing could be implicated on the pronounced magnitude of the REA for DL normally observed in this population. In addition, the association between ID in MOC-induced TEOAE suppression and the REA's magnitude suggests that MOC efferent reflex could be involved in DL performance and, more generally, in a complex challenging competing auditory task that does not involve background noise. However, it must be kept in mind that such an effect could also be attributed to top-down cortical influences conveyed to auditory periphery via the efferent pathways. We also found that ID in speech-ABR measures do not explain changes in the REA's magnitude in DL. We hypothesize that top-down corticofugal influences enhanced brainstem representation of selective features of speech sounds during DL and reduced any potential effect attributed to ID in neural timing for speech encoding. Findings from the present study lend further support to the structural model of DL (Kimura, 1961) by providing data suggesting that changes in the magnitude of the REA in DL among older adults may also originate from ID in sensory processing at lower levels of the auditory system. Furthermore, by demonstrating that both speed of processing and cognitive flexibility contributes to the enlarged REA among older adults, results from the present study bolster the relevance of cognitive processing in DL performance.

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5.9 References

- Abrams, D. A., Nicol, T., Zecker, S.G., Kraus, N. (2006). Auditory brainstem timing predicts cerebral asymmetry for speech. *J Neurosci.* 26:11131–7.
- Andersson, M., Reinvang, I., Wehling, E., Hugdahl, K., & Lundervold, A. J. (2008). A dichotic listening study of attention control in older adults. *Scandinavian Journal of Psychology*, 49(4), 299-304.
- Ashendorf, L., Jefferson, A. L., O'Connor, M. K., Chaisson, C., Green, R. C., & Stern, R. A. (2008). Trail Making Test errors in normal aging, mild cognitive impairment, and dementia. *Archives of clinical neuropsychology: the official journal of the National Academy of Neuropsychologists*. 23; (2): 129–137.
- Bellis, T. J., & Wilber, L. A. (2001). Effects of aging and gender on interhemispheric function. *Journal of Speech Language & Hearing Research*. 44;(2): 246-263.
- Bidelman, G., & Bhagat, S. (2015). Right-ear advantage drives the link between olivocochlear efferent ‘antimasking’ and speech-in-noise listening benefits. *NeuroReport*. 26: 483–487
- BinKhamis, G., Léger, A., Bell, S. L., Prendergast, G., O’Driscoll, M., & Kluk, K. (2018). Speech auditory brainstem responses: Effects of background, stimulus duration, consonant–vowel, and number of epochs. *Ear and hearing*, 40(3): 659-670
- Bless, J. J., Westerhausen, R., Arciuli, J., Kompus, K., Gudmundsen, M., & Hugdahl, K. (2013). “Right on all occasions?”—On the feasibility of laterality research using a smartphone dichotic listening application. *Frontiers in Psychology*, 4, 42.
- Bocca E, Calearo C. (1963). Central hearing processes. In: Jerger J, ed. *Modern Developments in Audiology*. New York: Academic Press, 337–370
- Boudreau, J. C., & Tsuchitani, C. (1968). Binaural interaction in cat superior olive S segment. *Journal of Neurophysiology*, 31, 442–454.
- Bryden, M. P. (1988). An overview of the dichotic listening procedure and its relation to cerebral organization. In: Hugdahl, K. (Ed.), *Handbook of Dichotic Listening: Theory, Methods and Research*. Wiley and Sons, New York, pp. 1- 44
- Bryden, M. P., Munhall, K., & Allard, F. (1983). Attentional biases and the right-ear effect in dichotic listening. *Brain and Language*, 18, 236–248.

Davis, T., Stanley, N., & Foran, L. (2015). Age-Related Effects of Dichotic Attentional Mode on Interaural Asymmetry: An AERP Study with Independent Component Analysis. *J Am Acad Audiol* 26:461–477

Dean, I., Harper, N. S., & McAlpine, D. (2005). Neural population coding of sound level adapts to stimulus statistics. *Nature neuroscience*, 8(12), 1684-1689.

Della Penna, S., Brancucci, A., Babiloni, C., Franciotti, R., Pizzella, V., Rossi, D., et al., (2007). Lateralization of dichotic speech stimuli is based on specific auditory pathway interactions: neuromagnetic evidence. *Cerebral Cortex*, 17(10), 2303-2311.

Dolcos, F., Rice, H. J., & Cabeza, R. (2002). Hemispheric asymmetry and aging: Right hemisphere decline or asymmetry reduction. *Neuroscience & Biobehavioral Reviews*, 26(7), 819–825.

Dorman, M. F., Marton, K., & Hannley, M. T. (1985). Phonetic identification by elderly normal and hearing-impaired listeners. *J Acoust Soc Am*, 77, 664–670.

Eliasson, S., & Gisselsson, L. (1955). Electromyographic studies of the middle ear muscles of the cat. *Electroencephalography and clinical neurophysiology*, 7(3), 399-406.

Emmerich, D., Harris, J., William, S., Srping, B., & Springer, S. (1988). The relationship between auditory sensitivity and ear asymmetry on a dichotic listening task. *Neuropsychologia*. 26; (1): 133-143

Feeney, M. P., Keefe, D. H., Marryott, L. P. (2003). Contralateral acoustic reflex thresholds for tonal activators using wideband energy reflectance and admittance. *J Speech Lang Hear Res*, 46, 128–136.

Field, A. (2013). *Discovering statistics using IBM SPSS statistics*. sage.

Findlen, U. M., & Roup, C. M. (2011). Dichotic speech recognition using CVC word and nonsense CVC syllable stimuli. *Journal of the American Academy of Audiology*, 22(1), 13-22.

Fischer, M., Cruickshanks, K., Nondahl, D., Klein, B., Klein, R., Pankow, J., Tweed, T., Dalton, D., & Paulsen, A. (2017). Dichotic Digits Test Performance Across the Ages: Results from Two Large Epidemiologic Cohort Studies. *Ear Hear*. 38(3): 314-320.

Garinis, A. C., Glatcke, T., & Cone, B. K. (2011). The MOC reflex during active listening to speech. *Journal of Speech, Language, and Hearing Research*.

- Gates, G., & Cooper JC Jr. (1991). Incidence of hearing decline in the elderly. *Acta Otolaryngologica*. 111; (2): 240-248
- Gates GA, Cooper JC, Kannel WB, Miller NJ. (1990) Hearing in the Elderly: The Framingham Cohort, 1983-1985. Part I. Basic Audiometric Test Results. *Ear Hear*. 11: 247–256.
- Golden, C. J., Osmon, D. C., Moses, J. A., & Berg, R. A. (1981). Interpretation of the Halstead-Reitan neuropsychological test battery. New York, NY: Grune & Stratton.
- Goldstein, S. G., & Braun, L. S. (1974). Reversal of expected transfer as a function of increased age. *Perceptual and Motor Skills*, 38, 1139-1145.
- Goldstein, G., & Shelly, G. (1981). Does the right hemisphere age more rapidly than the left? *Journal of Clinical Neuropsychology*, 3, 65–78.
- Gootjes, L., Bouma, A., Van Strien, J.W., Schijndel, R.V., Barkhof, F., Scheltens, P. (2006). Corpus callosum size correlates with asymmetric performance on a dichotic listening task in healthy aging but not in Alzheimer's disease. *Neuropsychologia*. 44: 208–217.
- Gootjes, L., VanStrien, J.W., Bouma, A. (2004). Age effects in identifying and localizing dichotig stimuli—a corpus-calosum deficit. *Journal of Clinical and Experimental Neuropsychology*. 26: 826–837.
- Graham, R. L., & Hazell, J. W. P. (1994). Contralateral suppression of transient evoked otoacoustic emissions: intra-individual variability in tinnitus and normal subjects. *British journal of audiology*, 28(4-5), 235-245.
- Guinan, J. J. Jr. (2006). Olivocochlear efferents: Anatomy, physiology, function, and the measurement of efferent effects in humans. *Ear Hear*. 27, 589–607.
- Guinan, J. J. Jr. (2018). Olivocochlear efferents: Their action, effects, measurement and uses, and the impact of the new conception of cochlear mechanical responses. *Hearing Research* 362: 38-47
- Guinan, J. J. Jr., Backus, B. C., Lilaonitkul, W., and Aharonson, V. (2003). Medial olivocochlear efferent reflex in humans: Otoacoustic emission (OAE) measurement issues and the advantages of stimulus frequency OAEs. *J. Assoc. Res. Otolaryngol*. 4: 521–540
- Hällgren, M., Larsby, B., Lyxell, B., & Arlinger, S. (2001). Cognitive effects in dichotic speech testing in elderly persons. *Ear & Hearing*. 22; (2): 120-129.

Hewitt, D. (2018). Life experience and the asymmetry of the human auditory system: clinical and auditory science laboratory implications. *F1000Research*, 7(675), 675.

Hiscock, M., & Kinsbourne, M. (2011). Attention and the right-ear advantage: What is the connection? *Brain and Cognition*, 76(2), 263–275.

Hommet, C., Mondon, K., Berrut, G., Gouyer, Y., Isingrini, M., Constans, T., & Belzung, C. (2010). Central auditory processing in aging: the dichotic listening paradigm. *Journal of Nutrition, Health & Aging*, 14(9), 751-756.

Hood, L. J., Hurley, A., Goforth, L., Bordelon, J., Berlin, C. I. (1997). Aging and efferent suppression of otoacoustic emissions. *ARO abstr* 20: 167.

Hornickel, J., Skoe, E., & Kraus, N. (2009). Subcortical laterality of speech encoding. *Audiology and Neurotology*, 14(3), 198-207.

Hu, X. J., & Lau, C. C. (2017). Central conduction time in auditory brainstem response and ear advantage in dichotic listening across menstrual cycle. *PloS one*, 12(11).

Hugdahl, K. (2003). Dichotic listening in the study of auditory laterality. In K. Hugdahl and R. J. Davidson (Eds.), *The asymmetrical brain* (pp. 441–476). Cambridge, MA: MIT Press.

Hugdahl, K. & Andersson, L. (1986). The “forced-attention paradigm” in dichotic listening to CV-syllables: a comparison between adults and children. *Cortex*, 22(3), 417–432.

Hugdahl, K., & Helland, T. (2013). Central auditory processing as seen from dichotic listening studies. In Musiek, F. & Chermak, G. (Eds.). (2013). *Handbook of central auditory processing disorder, volume I: Auditory Neuroscience and Diagnosis* (Vol. 1). Plural Publishing.

Hugdahl, K., Rund, B. R., Lund, A., Asbjørnsen, A., Egeland, J., Landrø, N. I., Roness, A., Stordal, K. & Sundet, K. (2003). Attentional and executive dysfunctions in schizophrenia and depression: Evidence from dichotic listening performance. *Biological Psychiatry*, 53, 609–616.

Hugdahl, K., Westerhausen, R., Alho, K., Medvedev, S., & Hämäläinen, H. (2008). The effect of stimulus intensity on the right ear advantage in dichotic listening. *Neuroscience Letters*, 431, 90 – 94.

Hugdahl, K., Westerhausen, R., Alho, K., Medvedev, S., Laine, M., Hämäläinen, H., (2009) Attention and cognitive control: unfolding the dichotic listening story. *Scand. J. Psychol.* 50; (1): 11- 22.

International Organization for Standardization. (2000) Acoustics Statistical Distribution of Hearing Thresholds as a Function of Age. ISO 7029. Geneva: ISO.

Jäncke, L., & Shah, N. J. (2002). Does dichotic listening probe temporal lobe functions?. *Neurology*, 58(5), 736-743.

Jerger, J. (1970) Clinical Experience with impedance audiometry. *Arch Otolaryng*, 92, 311-324

Jerger, J., Chmiel, R., Allen, J., & Wilson, A. (1994). Effects of age and gender on dichotic sentence identification. *Ear & Hearing*, 15(4), 274-286.

Jerger, J., & Martin, J. (2006) Dichotic listening tests in the assessment of auditory processing disorders. *Audiological Medicine*. 4: 25-34.

Johnson, K. L., Nicol, T. G., & Kraus, N. (2005). Brain stem response to speech: a biological marker of auditory processing. *Ear and hearing*, 26(5), 424-434.

Kam, A., & Keith, R. (2010). Aging effect on dichotic listening of Cantonese. *International Journal of Audiology*, 49(9), 651-656.

Kalaiah, M. K., Nanchirakal, J. F., Kharmawphlang, L., & Noronah, S. C. (2017). Contralateral suppression of transient evoked otoacoustic emissions for various noise signals. *Hearing, Balance and Communication*, 15(2), 84-90.

Khalifa, S., Bougeard, R., Morand, N., Veuillet, E., Isnard, J., Guenot, M., ... & Collet, L. (2001). Evidence of peripheral auditory activity modulation by the auditory cortex in humans. *Neuroscience*, 104(2), 347-358.

Khalifa, S., & Collet, L. (1996) Functional asymmetry of medial olivo-cochlear system in humans. Towards a peripheral auditory lateralization. *Neuroreport*. 7: 993-996.

Khalifa, S., Micheyl, C., Veuillet, E., & Collet, L. (1998) Peripheral auditory lateralization assessment using TEOAEs. *Hearing Research*. 121, 29–34.

Kemp, D. T. (2002). Otoacoustic emissions, their origin in cochlear function, and use. *British Medical Bulletin*, 63, 223–241.

Keppler, H., Dhooge, I., Corthals, P., Maes, L., D'haenens, W., Bockstaël, A., ... & Vinck, B. (2010). The effects of aging on evoked otoacoustic emissions and efferent suppression of transient evoked otoacoustic emissions. *Clinical Neurophysiology*, 121(3), 359-365.

- Kimura, D. (1961). Some effects of temporal-lobe damage on auditory perception. *Canadian Journal of Psychology*, 15, 156–165.
- Kimura, D. (1967). Functional asymmetry of the brain in dichotic listening. *Cortex* (3), 163-168.
- Kinsbourne, M. (1970). The cerebral basis of lateral asymmetries in attention. *Acta Psychol* (33), 193-201.
- Kinsbourne, M. (1970). The cerebral basis of lateral asymmetries in attention. *Acta Psychol* (33), 193-201.
- Krizman, J., & Kraus, N. (2019). Analyzing the FFR: A tutorial for decoding the richness of auditory function. *Hearing research*, 382, 107779.
- Lehmann, A., & Schönwiesner, M. (2014). Selective attention modulates human auditory brainstem responses: relative contributions of frequency and spatial cues. *PloS one*, 9(1), e85442.
- Lotfi, Y., Moossavi, A., Javanbakht, M., & Zadeh, S. F. (2019). Speech-ABR in contralateral noise: A potential tool to evaluate rostral part of the auditory efferent system. *Medical hypotheses*, 132, 109355.
- Markevych, V., Asbjørnsen, A., Lind, O., Plante, A., & Cone, B. (2011) Dichotic listening and otoacoustic emissions: shared variance between cochlear function and dichotic listening performance in adults with normal hearing. *Brain Cogn.* 76; (2): 332–339.
- Martin, J., & Jerger, J. (2005) Some effects of aging on central auditory processing. *Journal of Rehabilitation Research & Development*, 42(4 Suppl 2), 25-44.
- Mishra, S. K. (2014). Medial efferent mechanisms in children with auditory processing disorders. *Frontiers in human neuroscience*, 8, 860.
- Mishra, S. K., & Lutman, M. E. (2013). Repeatability of click-evoked otoacoustic emission-based medial olivocochlear efferent assay. *Ear and hearing*, 34(6), 789-798.
- Mishra, S. K., & Lutman, M. E. (2014). Top-down influences of the medial olivocochlear efferent system in speech perception in noise. *PLoS One*, 9(1), e85756.
- Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., and Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex “Frontal Lobe” tasks: a latent variable analysis. *Cogn. Psychol.* 41, 49–100.

- Murugasu, E., & Russell, I. J. (1996). The effect of efferent stimulation on basilar membrane displacement in the basal turn of the guinea pig cochlea. *Journal of Neuroscience*, 16(1), 325-332
- Musiek, F., & Weihing, J (2011) Perspectives on dichotic listening and the corpus callosum. *Brain and Cognition*. 76: 225–232
- Musiek, F. E., & Chermak, G. D. (2015). Psychophysical and behavioral peripheral and central auditory tests. In *Handbook of clinical neurology* (Vol. 129, pp. 313-332). Elsevier.
- Nasreddine, Z., Phillips, N., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Chertkow, H. (2005) The Montreal Cognitive Assessment, MoCA- A Brief Screening Tool for Mild Cognitive Impairment. *Journal of American Geriatrics Society*, 53(4), 695-699.
- Oldfield, R. (1971) The assessment and analysis of handedness the edinburgh inventory. *Neuropsychologia*, 9, 97-113.
- Passow, S., Westerhausen, R., Hugdahl, K., Wartenburger, I., Heekeren, H. R., Lindenberger, U., & Li, S. C. (2014). Electrophysiological correlates of adult age differences in attentional control of auditory processing. *Cerebral Cortex*, 24(1), 249-260.
- Passow, S., Westerhausen, R., Wartenburger, I., Hugdahl, K., Heekeren, H. R., Lindenberger, U., & Li, S.-C. (2012). Human aging compromises attentional control of auditory perception. *Psychology and Aging*, 27(1), 99–105.
- Philibert, B., Veuillet, E., & Collet, L. (1998). Functional asymmetries of crossed and uncrossed medial olivocochlear efferent pathways in humans. *Neuroscience letters*, 253(2), 99-102.
- Reitan, R. M., and Wolfson, D. (1993). *The Halstead-Reitan Neuropsychological Test Battery: Theory and Clinical Interpretation*, 2nd Edn. Tuscon, AZ: Neuropsychology Press.
- Roup, C. M., Wiley, T. L., & Wilson, R. H. (2006). Dichotic word recognition in young and older adults. *Journal of the American Academy of Audiology*. 17; (4): 230-240
- Sánchez-Cubillo I, Periáñez JA, Adrover-Roig D, Rodríguez-Sánchez JM, Ríos-Lago M, Tirapu J, et al. (2009). Construct validity of the Trail Making Test: role of task-switching, working memory, inhibition/interference control, and visuomotor abilities. *J Int Neuropsychol Soc*.15:438– 450.
- Siegel, J. H., & Kim, D. O. (1982). Efferent neural control of cochlear mechanics? Olivocochlear bundle stimulation affects cochlear biomechanical nonlinearity. *Hearing research*, 6(2), 171-182.

- Simmons, F. B., & Beatty, D. L. (1962). A theory of middle ear muscle function at moderate sound levels. *Science*, 138(3540), 590-592.
- Skoe E. & Kraus, N. (2010). Auditory brainstem response to complex sounds: A tutorial. *Ear Hear*, 31, 302.
- Skoe, E., Krizman, J., Anderson, S., & Kraus, N. (2015). Stability and plasticity of auditory brainstem function across the lifespan. *Cereb Cortex*, 25, 1415–1426.
- Speaks, C., Bauer, K. & Carlstrom, J. (1983). Peripheral Hearing Loss Implications for Clinical Dichotic Listening Tests. *Journal of Speech and Hearing Disorders*, 48, 135–139.
- Speaks, C., Blecha, M. & Schilling, M. (1980). Contributions of monotic intelligibility to dichotic performance. *Ear and hearing*, 1, 259–266.
- Stuss DT, Bisschop SM, Alexander MP, Levine B, Katz D, Izukawa D. (2001). The Trail Making Test: a study in focal lesion patients. *Psychol Assess*, 13:230–239.
- Tabachnick BG, Fidell LS. (2007) Using multivariate statistics. Boston: Allyn & Bacon.
- Takio, F., Koivisto, M., Jokiranta, L., Rashid, F., Kallio, J., Tuominen, T., Hämäläinen, H. (2009). The effect of age on attentional modulation in Dichotic listening. *Developmental Neuropsychology*, 34(3), 225–239.
- Thomsen, T., Rimol, L. M., Ersland, L., & Hugdahl, K. (2004a). Dichotic listening reveals functional specificity in prefrontal cortex: an fMRI study. *Neuroimage*, 21(1), 211-218.
- Thomsen, T., Specht, K., Hammar, Å., Nytingnes, J., Ersland, L., & Hugdahl, K. (2004b). Brain localization of attentional control in different age groups by combining functional and structural MRI. *Neuroimage*, 22(2), 912-919.
- van Veen, V., Cohen, J. D., Botvinick, M. M., Stenger, V. A., & Carter, C. S. (2001). Anterior cingulate cortex, conflict monitoring, and levels of processing. *Neuroimage*, 14(6), 1302-1308.
- Vander Werff, K. R., & Burns, K. S. (2011). Brain stem responses to speech in younger and older adults. *Ear and hearing*, 32(2), 168-180.
- Wechsler D. (1997) Wechsler Adult Intelligence Scale – III. San Antonio, TX: The Psychological Corporation.

Weihing, J., & Musiek, F. (2014). The influence of aging on interaural asymmetries in middle latency response amplitude. *Journal of the American Academy of Audiology*, 25(4), 324-334.

Wertheimer, I. (2017). Development of 90th Percentile Norms for Ipsilateral Acoustic Reflex Thresholds: A Feasibility Study.

Westerhausen, R. (2019) A primer on dichotic listening as a paradigm for the assessment of hemispheric asymmetry. *Laterality: Asymmetries of Body, Brain and Cognition*, 1-32.

Westerhausen, R., Bless, J., & Kompus, K. (2015). Behavioral Laterality and Aging: The Free-Recall Dichotic-Listening Right-Ear Advantage Increases With Age. *Developmental Neuropsychology*, 40(5), 313-327.

Westerhausen, R., & Hugdahl, K. (2008). The corpus callosum in dichotic listening studies of hemispheric asymmetry: a review of clinical and experimental evidence. *Neuroscience & Biobehavioral Reviews*, 32(5), 1044-1054.

Westerhausen, R., Moosmann, M., Alho, K., Medvedev, S., Hämäläinen, H., & Hugdahl, K. (2009). Top-down and bottom-up interaction: Manipulating the dichotic listening ear advantage. *Brain Research*, 1250, 183–189.

Wilson, R. H., & Leigh, E. D. (1996) Identification performance by right- and left-handed listeners on dichotic CV materials. *J Am Acad Audiol*. 7;(1): 1-6.

5.10 Tables and figures

Table 1. Mean, SD, and range of the cognitive tests

Variables	All (n = 68)		<i>Min</i>	<i>Max</i>
	<i>Mean</i>	<i>SD</i>		
TMT-A (sec)	38.09	11.65	20	71
TMT-B (sec)	76.64	23.84	39	127
TMT ratio score	2.13	0.53	1.13	3.38
TMT = Trail making test				

Table 2. Mean pure-tone hearing thresholds and standard error (SE) for the right ear, left ear and mean interaural difference (ID) for all participants.

<i>Frequency (Hz)</i>	<i>Right ear</i>	<i>Left ear</i>	<i>ID</i>	<i>F</i>	<i>p-value</i>
	<i>Mean (SE)</i>	<i>Mean (SE)</i>	<i>Mean (SE)</i>		
250	11.76 (0.65)	11.76 (0.76)	0.00 (0.50)	0.000	1.000
500	11.91 (0.62)	12.72 (0.62)	0.80 (0.43)	3.385	0.070
1000	12.05 (0.84)	11.54 (0.85)	-0.51 (0.58)	0.075	0.382
2000	15.95 (0.98)	16.76 (1.18)	0.80 (0.71)	1.279	0.262
3000	22.13 (1.29)	23.38 (1.43)	1.39 (0.70)	3.809	0.055
4000	27.86 (1.51)	29.04 (1.55)	1.17 (0.61)	3.697	0.059
6000	38.01 (2.09)	39.19 (2.13)	1.17 (1.02)	2.498	0.119
8000	45.29 (2.57)	46.61 (2.54)	1.25 (1.18)	1.198	0.294
Pure-tone average (250-3000)	14.77 (7.03)	15.27 (7.62)	0.50 (0.36)	1.902	0.172

Table 3. Mean, standard deviation (SD) for the right and left ears and mean interaural difference (ID) for cochlear and speech-ABR measures.

	<i>Right ear</i>	<i>Left ear</i>	<i>ID</i>		
<i>Measures</i>	<i>Mean (SD)</i>	<i>Mean (SD)</i>	<i>Mean (SD)</i>	<i>F</i>	<i>p-value</i>
TEOAE (dB SNR)	7.18 (3.52)	6.68 (3.38)	0.50 (2.95)	1.373	.175
Suppression (dB SNR)	3.43 (2.00)	3.78 (1.99)	-0.34 (2.35)	-1.183	.241
Lat V [⊥] (ms)	7.08 (0.42)	7.16 (0.40)	0.07 (0.39)	1.992	.164
Lat A [⊥] (ms)	8.08 (0.51)	8.27 (0.59)	0.18 (0.56)	5.661	.021*
Lat O [⊥] (ms)	48.95 (1.23)	49.64 (1.13)	0.69 (1.26)	18.893	.000***
Amp V (μV)	0.17 (0.15)	0.23 (0.22)	-0.05 (0.29)	2.070	.156
Amp A (μV)	-0.19 (0.16)	-0.25 (0.26)	0.05 (0.26)	2.597	.113
Amp O (μV)	-0.24 (0.24)	1.76 (1.58)	0.07 (0.39)	2.021	.161
RMS (μV)	0.48 (0.29)	0.55 (0.32)	-0.07 (0.32)	3.008	.088
SNR	1.57 (0.83)	1.62 (1.21)	-0.05 (1.28)	0.124	.726

Abbreviations: TEOAE = Transient evoked otoacoustic emission response; Suppression = MOC-induced TEOAE suppression amount determined by subtracting TEOAE response with contralateral acoustic stimulation from those without. Lat V = Speech-ABR latency for onset V; Lat A = Speech-ABR latency for onset A; Lat O = Speech-ABR latency for offset O; ⊥ = denotes measures were the ID was calculated inverting the formula (LE-RE); Amp V = Speech-ABR amplitude for onset V; Amp A = Speech-ABR amplitude for onset A; Amp O = Speech-ABR amplitude for offset O; RMS = Root mean square; SNR = Signal-to-noise-ratio. * p < 0.05; *** p < 0.001

Table 4. Pearson’s correlation coefficients between the laterality index for the *idichotic (NF and FA paradigms)*, cognitive measures and interaural difference (ID) for each auditory outcome.

	LI NF	LI FA	TMT-A	TMT-B	TMT-RS	ID PTA	ID TEOAE	ID Suppression	ID Lat V	ID Lat A	ID Lat O	ID Amp V	ID Amp A	ID Amp O	ID RMS	ID SNR
LI NF	*															
LI FA	.801**	*														
TMT-A	-.301*	-.173	*													
TMT-B	-.175*	.039	.636**	*												
TMT-RS	.165	.287*	-.419**	.336**	*											
ID PTA	.408**	.386**	-.236	-.078	.249*	*										
ID TEOAE	.273*	.257*	-.016	-.040	.008	.387**	*									
ID Suppression	.303*	.244*	-.028	-.140	-.150	.158	.666**	*								
ID Lat V	-.010	.063	.150	.027	-.118	-.129	.047	-.028	*							
ID Lat A	-.063	.016	.023	-.097	-.012	-.097	.076	-.041	.640**	*						
ID Lat O	.170	.144	-.047	-.193	-.224	-.033	-.057	.078	.022	.137	*					
ID Amp V	.033	.019	.052	.142	.136	.078	.128	.169	.189	-.209	-.014	*				
ID Amp A	-.066	.019	-.339*	.035	.418**	-.058	-.061	.052	-.164	.190	-.021	.269	*			
ID Amp O	-.019	.005	.032	-.025	-.008	-.218	.038	.089	.012	.114	.260*	.188	.245	*		
ID RMS	-.075	-.216	.079	-.229	-.396**	.015	-.057	.077	.049	-.047	-.092	.021	-.381**	-.248	*	
ID SNR	.129	.066	.000	-.245	-.106	-.042	-.079	-.113	.034	-.067	.030	-.281*	-.544**	-.145	.287*	*

LI NF = Laterality index nonforced paradigm; LI FA = Laterality index forced attention paradigm; TMT-A = Trail making test part A; TMT-B = Trail making test part B; TMT-RS = Trail making test ratio score; ID = Interaural difference; PTA = Pure-tone average (250 – 3000 Hz); TEOAE = Transient evoked otoacoustic emission response; Suppression = MOC-induced TEOAE suppression amount determined by subtracting TEOAE response with contralateral acoustic stimulation from those without; Lat V = Speech-ABR latency for onset V; Lat A = Speech-ABR latency for onset A; Lat O =Speech-ABR latency for offset O; Amp V = Speech-ABR amplitude for onset V; Amp A = Speech-ABR amplitude for onset A; Amp O = Speech-ABR amplitude for offset O; RMS = Root mean square; SNR = Signal-to-noise-ratio.*p<0.05; **p<0.01

Table 5. Bivariate and multivariate regression analysis for the laterality index for the iDichotic

Laterality index nonforced paradigm									
Variable	Bivariate Model			Multivariate model			Final Multivariate		
	Beta	p	R ²	Beta	p	R ²	Beta	p	R ²
<i>Cognitive measures</i>									
TMT-A	-.301	.013*	.090	-.220	.057		-.223	.049*	
<i>Auditory Measures</i>									
ID PTA	.408	.000***	.167	.332	.010*		.322	.006**	
ID TEOAE	.273	.026*	.075	-.031	.845				
ID Suppression	.303	.014*	.092	.271	.073		.252	.025*	
						.277***			.276***
Laterality index forced attention paradigm									
Variable	Bivariate Model			Multivariate model			Final Multivariate		
	Beta	p	R ²	Beta	p	R ²	Beta	p	R ²
<i>Cognitive measures</i>									
TMT ratio score	.287	.018*	.082	.303	.010*		.303	.010*	
<i>Auditory Measures</i>									
ID PTA	.386	.001**	.149	.295	.020*		.285	.015*	
ID TEOAE	.257	.037*	.066	-.036	.824				
ID Suppression	.244	.049*	.059	.271	.077		.248	.029*	
						.275**			.274***

Abbreviations: TMT-A = Trail making test part A; TMT ratio score = Trail making test ratio score; ID = Interaural difference; PTA = Pure-tone average (250 – 3000 Hz); TEOAE = Transient evoked otoacoustic emission response; Suppression = MOC-induced TEOAE suppression amount determined by subtracting TEOAE response with contralateral acoustic stimulation from those without. *p < 0.05; **p < 0.01; ***p < 0.001

Supplementary Table S1. Correlation matrix between the nonforced paradigm results (right ear, left ear and LI), cognitive measures, and auditory outcomes for right and left ear separately.

	NF	NF	NF	TMT	TMT	TMT	PTA	PTA	TEOAE	TEOAE	Suppression	Suppression	PeakV	PeakV	PeakA	PeakA	PeakO	PeakO
	RE	LE	LI	A	B	RS	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE
NF RE	*																	
NF LE	-.642**	*																
NF LI	-.233	.141	*															
TMT-A	-.378**	.205	-.299	*														
TMT-B	-.259*	.136	-.175	.636**	*													
TMT RS	.156	-.125	.165	-.419**	.336**	*												
PTA RE	.031	-.173	.119	.026	.202	.216	*											
PTA LE	.256	-.279*	.306*	-.089	.147	.316**	.880**	*										
TEOAE RE	.065	.057	.022	-.082	-.149	-.068	-.441**	-.340**	*									
TEOAE LE	-.208	.215	-.220	-.072	-.120	-.078	-.436**	-.494**	.635**	*								
Suppression RE	.231	-.098	.165	-.163	-.214	-.036	-.343**	-.288*	.708**	.421**	*							
Suppression LE	-.187	.117	-.176	-.118	-.056	.146	-.237	-.282*	.391**	.774**	.306*	*						
PeakV RE	.248	-.059	.113	-.225	-.158	.104	-.138	-.003	.094	-.028	.174	-.066	*					
PeakV LE	.138	-.112	.096	-.082	-.124	-.046	-.196	-.111	-.061	-.115	.134	.032	.363**	*				
PeakA RE	.164	-.031	.060	-.113	.045	.187	-.102	.015	.141	.020	.170	.004	.773**	.498**	*			
PeakA LE	-.053	.007	-.072	-.090	-.084	.133	-.238	-.185	.025	-.048	.077	.106	.272*	.708**	.437**	*		
PeakO RE	.107	-.109	.129	-.023	.068	.198	-.052	.036	.065	-.019	.075	.252*	.174	.258*	.230	.240	*	
PeakO LE	.161	.339**	.317**	-.092	-.153	-.037	-.143	-.058	.062	.036	.065	.190	.137	.197	.045	.210	.438**	*

NF = Nonforced paradigm; RE = right ear; LE = left ear LI= Laterality index; TMT-A = Trail making test part A; TMT-B = Trail making test part B; TMT RS = Trail making test ratio score; PTA = Pure-tone threshold average (250-3000Hz); TEOAE = Transient evoked otoacoustic emission response; SUPP = MOC-induced TEOAE suppression; Peak V = Speech-ABR latency for onset V; Peak A = Speech-ABR latency for onset A; Peak O = Speech-ABR latency for offset O. * p < 0.05; ** p < 0.01

Supplementary Table S2. Correlation matrix between the forced attention paradigm results (right ear, left ear and LI), cognitive measures, and auditory outcomes for right and left ears separately.

	FA	FA	FA	TMT	TMT	TMT	PTA	PTA	TEOAE	TEOAE	Suppression	Suppression	PeakV	PeakV	PeakA	PeakA	PeakO	PeakO
	RE	LE	LI	A	B	RS	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE
FA RE	*																	
FA LE	-.363**	*																
FA LI	-.324**	-.022	*															
TMT-A	-.354**	.007	-.173	*														
TMT-B	-.246*	-.167	.039	.636**	*													
TMT RS	.165	-.290*	.287*	-.419**	.336**	*												
PTA RE	.008	-.162	.105	.026	.202	.216	*											
PTA LE	.168	-.280*	.283*	-.089	.147	.316**	.880**	*										
TEOAE RE	.056	.195	-.071	-.082	-.149	-.068	-.441**	-.340**	*									
TEOAE LE	-.138	.377**	-.292*	-.072	-.120	-.078	-.436**	-.494**	.635**	*								
Suppression RE	.206	.031	.116	-.163	-.214	-.036	-.343**	-.288*	.708**	.421**	*							
Suppression LE	-.106	.155	-.152	-.118	-.056	.146	-.237	-.282*	.391**	.774**	.306*	*						
PeakV RE	.148	.038	.046	-.225	-.158	.104	-.138	-.003	.094	-.028	.174	-.066	*					
PeakV LE	.063	-.081	.104	-.082	-.124	-.046	-.196	-.111	-.061	-.115	.134	.032	.363**	*				
PeakA RE	.085	.080	.000	-.113	.045	.187	-.102	.015	.141	.020	.170	.004	.773**	.498**	*			
PeakA LE	-.026	.008	-.017	-.090	-.084	.133	-.238	-.185	.025	-.048	.077	.106	.272*	.708**	.437**	*		
PeakO RE	.089	-.044	.103	-.023	.068	.198	-.052	.036	.065	-.019	.075	.252*	.174	.258*	.230	.240	*	
PeakO LE	.149	-.227	.266*	-.092	-.153	-.037	-.143	-.058	.062	.036	.065	.190	.137	.197	.045	.210	.438**	*

FA = Forced attention paradigm; RE = right ear; LE = left ear LI= Laterality index; TMT-A = Trail making test part A; TMT-B = Trail making test part B; TMT RS = Trail making test ratio score; PTA = Pure-tone threshold average (250-3000Hz); TEOAE = Transient evoked otoacoustic emission response; SUPP = MOC-induced TEOAE suppression; Peak V = Speech-ABR latency for onset V; Peak A = Speech-ABR latency for onset A; Peak O = Speech-ABR latency for offset O. * p < 0.05; ** p < 0.01

Figure 1. Right and left ear scores and the laterality index (LI) expressed as percent of correct answers (mean and SD) in the *iDichotic* test in both (A) Nonforced (NF) and (B) forced attention (FA) paradigms for the entire group of older adults (n = 68). *** p < 0.001

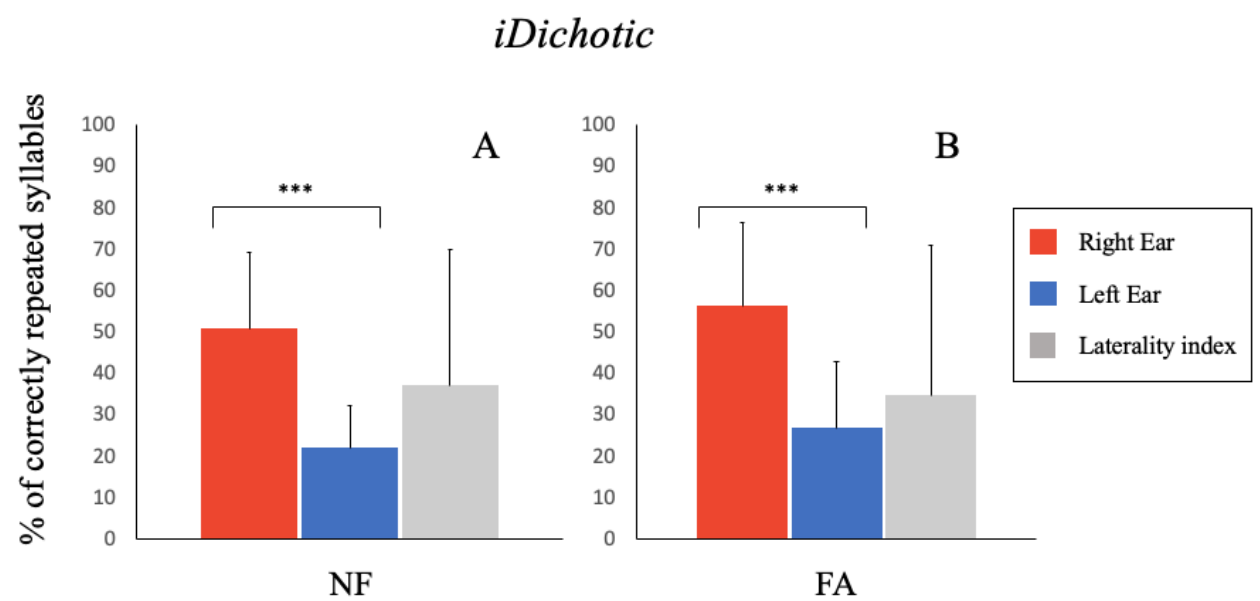


Figure 2. Interaural difference (ID) for the average of pure-tone thresholds across frequencies (250-3000 Hz) for each single participant. Positive values indicate an ID in audibility favoring the right ear and negative values indicate an ID in audibility favoring the left ear.

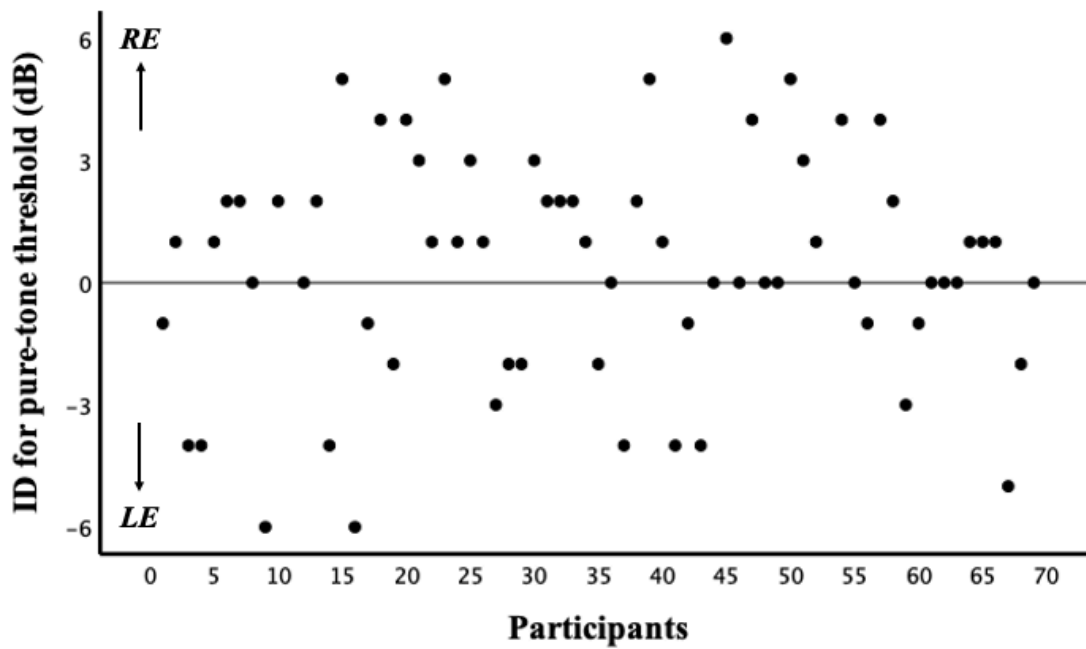


Figure 3. Interaural difference (ID) for (A) the average of TEOAE response across frequencies (1000-4000 Hz) and (B) the amount of MOC-induced TEOAE suppression for each single participant. Positive values indicate an ID in TEOAE response and TEOAE suppression favoring the right ear and negative values indicate an ID favoring the left ear.

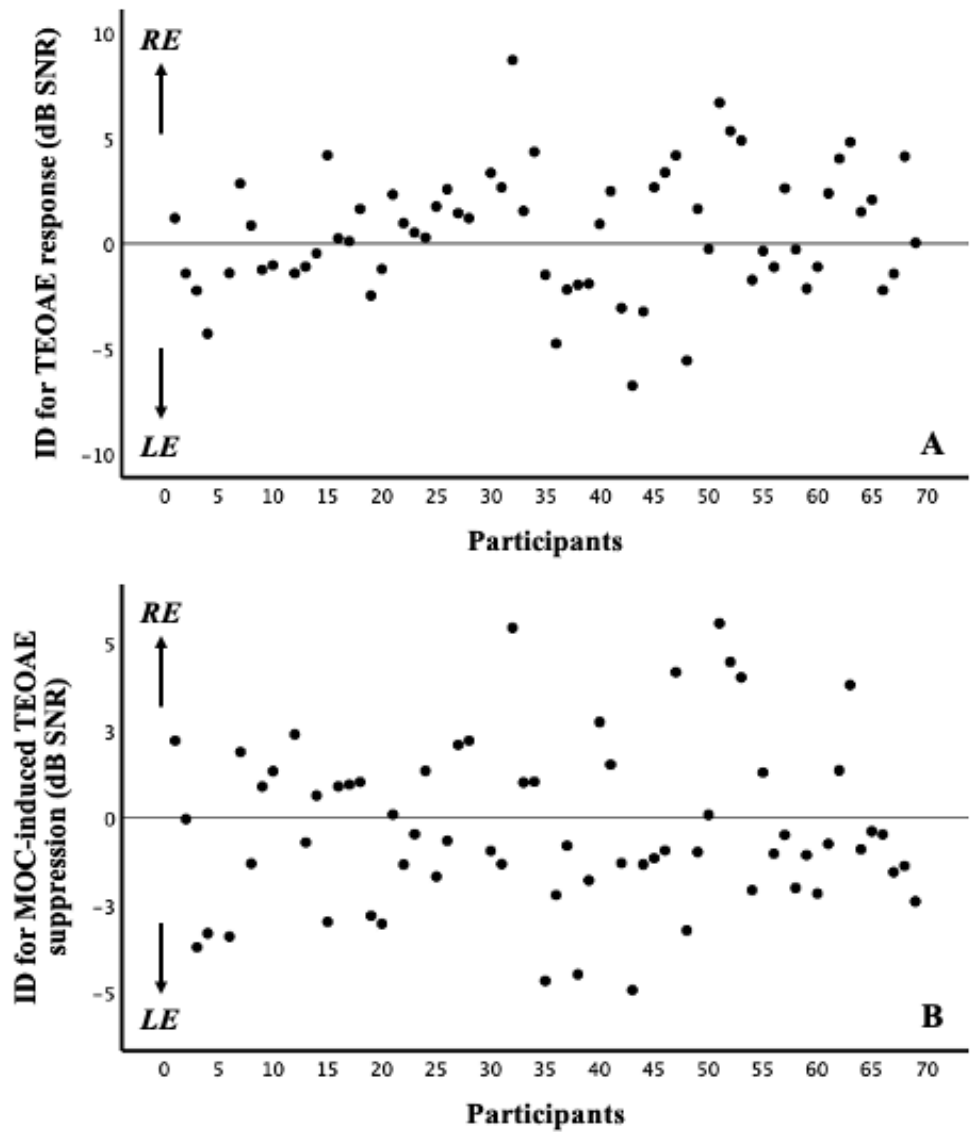


Figure 4. Interaural difference (ID) for (A) the speech-ABR peak V, (B) the speech-ABR peak A, and (C) the speech-ABR peak O for each single participant. Positive values indicate an ID in subcortical neural timing favoring the right ear and negative values indicate an ID favoring the left ear.

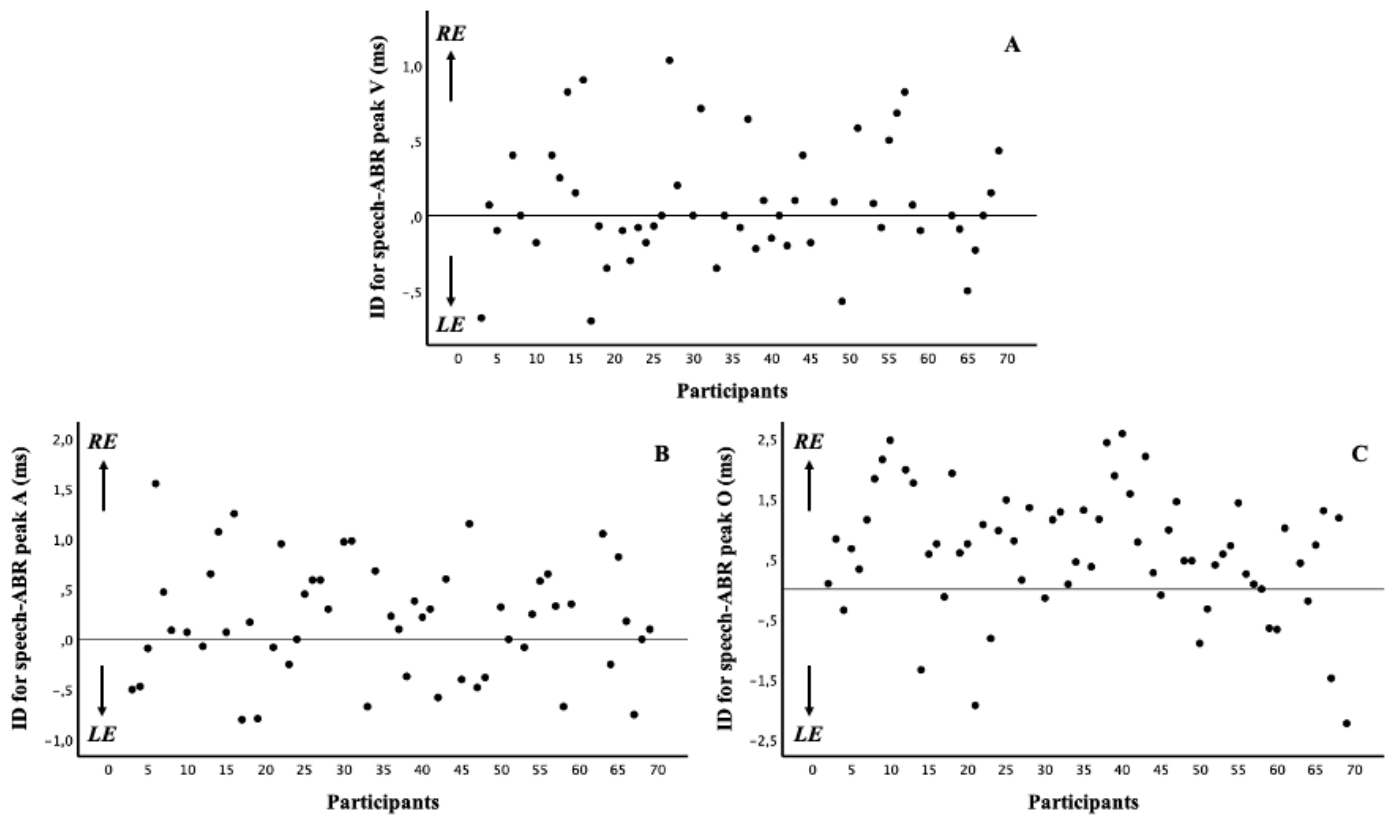


Figure 5. Grand average waveform for the speech-ABR obtained from 4 participants to right (black line) and left (dashed grey line) ear presentation of 40-ms syllable /da/. Lower insets show neural response latency difference for peaks V, A and O between right and left ears.

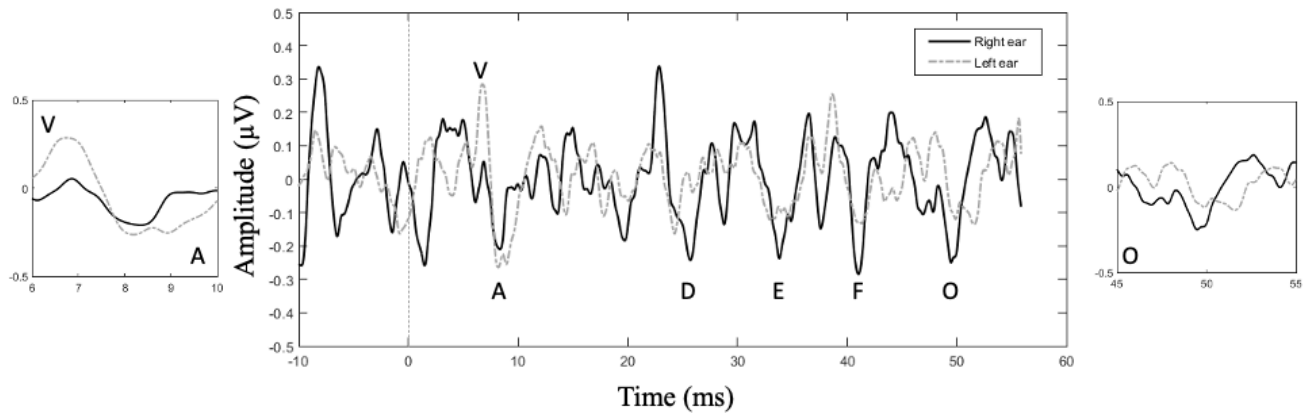


Figure 6. Bivariate scatterplots and linear regression lines (R^2 values) of the LI for the NF paradigm with (A) Trail making test A, and the interaural difference (ID) for (B) the average of pure-tone thresholds across frequencies (PTA; 250-3000 Hz), (C) the average of TEOAE responses across frequencies (1000-4000 Hz) and (D) the amount of MOC-induced TEOAE suppression. Auditory and cognitive measures showed significantly predictive relationships with the LI.

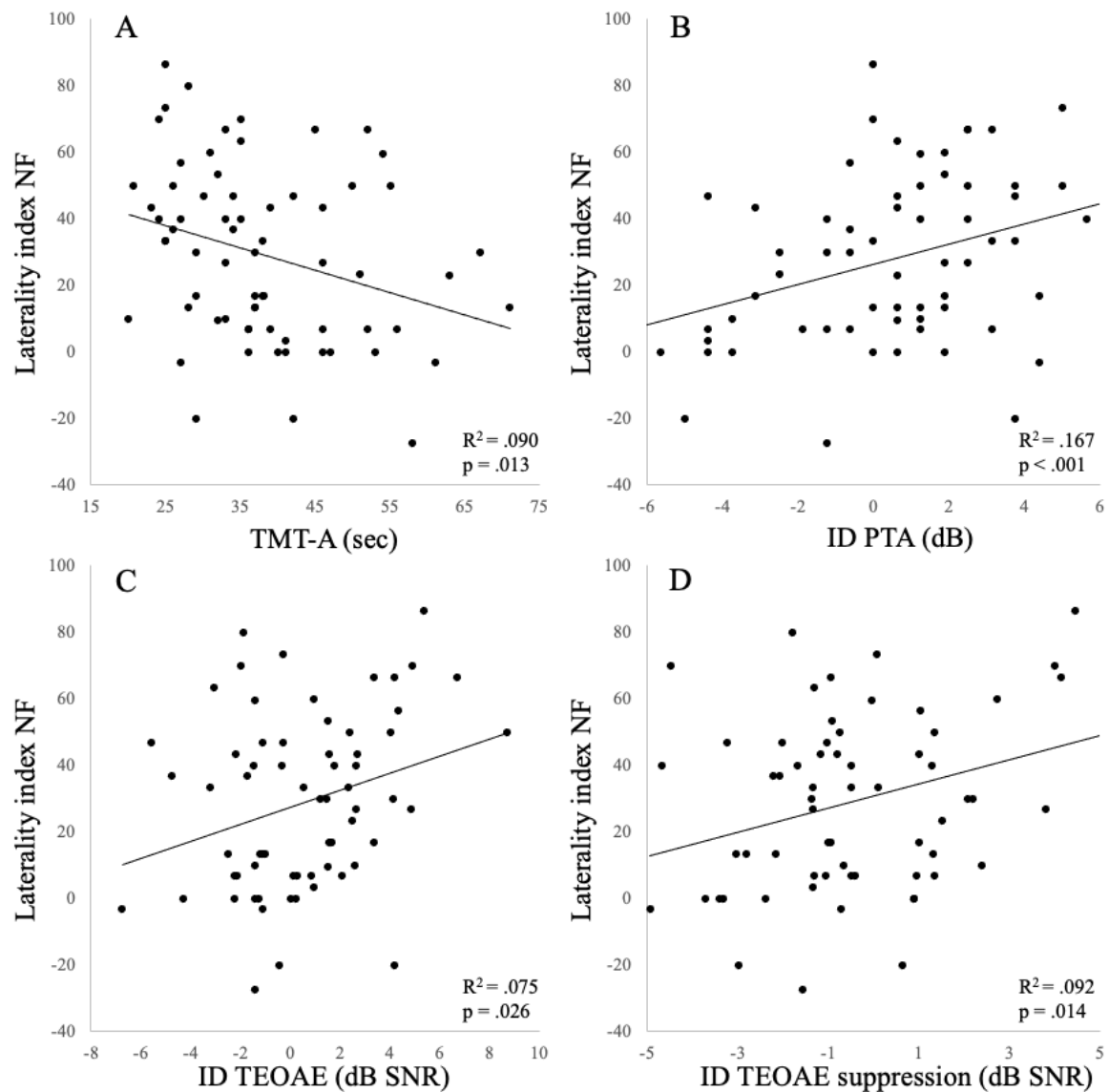
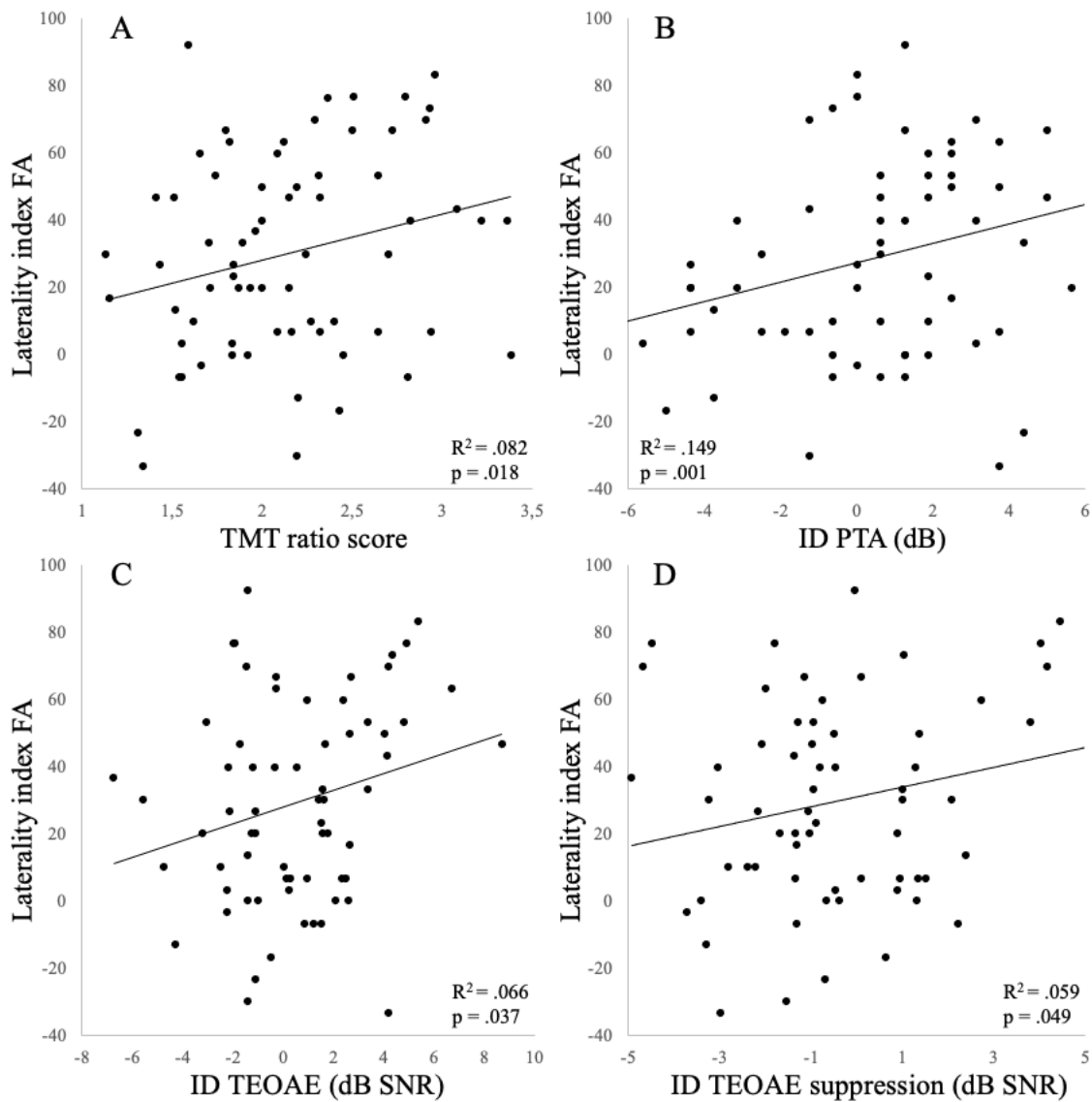


Figure 7. Bivariate scatterplots and linear regression lines (R^2 values) of the LI for the FA paradigm with (A) Trail making test ratio score, and the interaural difference (ID) for (B) the average of pure-tone thresholds across frequencies (PTA; 250-3000 Hz), (C) the average of TEOAE responses across frequencies (1000-4000 Hz) and (D) the amount of MOC-induced TEOAE suppression. Auditory and cognitive measures showed significantly predictive relationships with the LI.



Chapter 6- Article 3

Do interaural peripheral and subcortical processing differences across the auditory pathways contribute to speech in noise perception among older adults?

(in preparation)

Alejandro Ianiszewski-Gómez, Adrian Fuente, Jean-Pierre Gagné

École d'orthophonie et d'audiologie, Faculté de médecine, Université de Montréal, Montréal,
Québec, Canada.

Centre de recherche de l'Institut universitaire de gériatrie de Montréal, Montréal, Québec,
Canada.

6.1 Abstract

The aim of this exploratory study was to investigate whether the magnitude of interaural difference (ID) in sensory processing at lower levels of the auditory system, were associated with speech perception in noise (SIN) performance among older adults with age-appropriate hearing. A cross-sectional study was designed to study this association. Seventy older adults aged between 61 and 90 years (35 females and 35 males), who presented normal hearing according to their age participated in the study. None of the participants reported a history of neurologic, chronic, or middle ear disease. SIN performance in older adults was evaluated with the hearing-in-noise test (HINT) using three simulated noise conditions. Hearing sensitivity, transient evoked otoacoustic emission (TEOAE), and auditory brainstem response to speech stimuli (speech-ABR) were tested in both ears separately. ID were derived by calculating the difference between the right and left ears for each auditory measure. Bivariate and multivariate regression models were constructed to independently investigate possible associations between ID in sensory processing at lower levels of the auditory system and HINT scores. Working memory, as measured with the reading span test (RST), was accounted for in the statistical regression models. Regression models showed that ID in peripheral and subcortical processing were significantly associated with SIN performance among older adults. However, these results were only evident for HINT scores in the left ear. Working memory also explained part of the variance of SIN performance among older adults. ID in sensory processing at lower levels of the auditory system influence SIN performance among older adult listeners with age-appropriate hearing. However, this is only evident on spatially separated listening conditions whereby the weaker auditory pathway is forced to process the speech signal.

Key words: Auditory processing, interaural differences, older adults, noise, speech perception

6.2 Introduction

Understanding speech in a noisy environment is difficult for everyone, particularly for older adults who are more vulnerable to the effects of background noise compared (Ben-David et al., 2012; Gates & Mills, 2005; Gordon-Salant, 2005). Changes in both the peripheral and central auditory system are main determinants of impaired communication in the elderly (Murphy et al., 2006). Moreover, older adults usually require more time to process what they have heard due to slower cognitive functioning (Salthouse, 1996; Ross et al., 2007). Correlational studies indicate that age-related decline in peripheral hearing may be considered as the primary underlying factor contributing to speech perception in noise (SIN) difficulties experienced by older adults (Humes, 1996; Humes et al., 1994; Humes and Roberts, 1990). However, these difficulties may still be present in older listeners even in the absence of hearing impairment (Dubno et al., 2002; Gordon-Salant & Fitzgibbons, 1993; Humes, 1996), suggesting that age-related declines that go beyond sound detection abilities might also contribute to impaired SIN among older listeners (Anderson et al., 2011).

Age-related changes in outer hair cell function, which can be examined using transient evoked otoacoustic emissions (TEOAE), might also increase SIN difficulties among older adults. Declines in outer hair cell function may affect the function of the cochlear amplifier thereby reducing frequency selectivity and sensitivity among older adults (Keppler et al., 2010). This can diminish the cochlear representation of the acoustic spectrum, making it difficult for older adults to separately perceive the spectral cues of speech from those associated to the background noise (Moore, 2007; Johannesen et al., 2016). Furthermore, SIN performance may be affected by age-related changes in central auditory processing. Aging seems to impair the precise subcortical neural representation of temporal information (as assessed by peak timing) in older adults, which is

important for capturing fast changing acoustic transitions that characterize consonants (Anderson et al., 2011; Parbery Clark et al., 2012). Therefore, age-related declines in outer hair cell function and subcortical temporal processing may lead to reduced SIN performance among older adults.

One aspect not usually accounted for by previous research is whether these age-related declines in peripheral and subcortical auditory processing differ between the right and the left auditory pathways, and if so, how they might affect speech understanding in the presence of background noise among older adults. Previous studies have suggested that the auditory structures/pathways subserving left ear (LE) input are somehow more affected by aging than the structures/pathways subserving right ear (RE) input (e.g., Gates et al., 1990; Gates & Cooper, 1991; Jerger et al., 1994; Weihing & Musiek, 2014; Westerhausen et al., 2015). Thus, it may be suspected that aging further decreases peripheral and subcortical processing in the LE than the RE, which may in turn decline overall SIN performance among older adults. Indeed, interaural differences (ID) in sensory processing at lower level of the auditory system have been reported in older adults. Reduced TEOAE responses and delayed neural timing encoding in speech auditory brainstem response (speech-ABR) in the left relative to the right ear have been significantly demonstrated in older adults (Tadros et al., 2005; Vander Werff & Burns, 2011).

However, the association between the magnitude of ID in peripheral and subcortical processing and SIN performance among older adults has not yet been investigated. The ability to understand speech in degraded environment requires an intact auditory system, which enables the segregation of targeted speech signals from background noise (Wahab et al., 2017). Thus, an increased ID in peripheral and subcortical processing could adversely affect older adult's ability to fully exploit spectrotemporal speech cues which may be critical for accurate speech intelligibility particularly

in the presence of background noise (Anderson et al., 2011; 2013). In addition, enlarged sensory (i.e., peripheral, and subcortical) processing differences between right and left auditory pathways could increase SIN difficulties, particularly under listening situations whereby the weaker auditory pathway is forced to extract the speech signal from background noise.

The aim of this exploratory study was to investigate whether the magnitude of ID in peripheral and subcortical processing were associated with SIN performance in older adults. Specifically, we hypothesized that the magnitude of ID in peripheral and subcortical processing would explain SIN performance in older adults when speech and noise came directly from the same direction. We also hypothesized that the magnitude of ID in peripheral and subcortical processing would explain SIN performance in older adults when the weaker auditory pathway was forced to extract the speech signal from spatially separated background noise. We used the hearing-in-noise test (HINT, Nilsson et al., 1994) to test these hypotheses because the HINT evaluates speech intelligibility in different listening conditions that differ only in the location of the noise source: sentences and noise presented simultaneously to both ears (HINT NF); noise presented to the RE with sentences presented in the front (HINT LE); and noise presented to the LE with sentences presented in the front (HINT RE). A sample of older adults with normal hearing thresholds according to their age (ISO 7029, 2000) was selected. In addition, since cognition plays an important role in SIN performance among older listeners (Moore et al., 2014; Füllgrabe et al., 2015), cognitive measures were accounted for in the statistical analysis.

6.3 Materials and methods

The Ethics committee of the Centre de recherche de l'Institut universitaire de gériatrie de Montréal approved the study protocol. All participants signed a consent form prior to being included in the study and monetary compensation was given for their participation.

6.3.1 Participants

The study sample comprised 70 older adults (35 females and 35 males) between the ages of 61 and 90 years (mean \pm Standard Deviation (SD) = 71.70 ± 6.21). All participants presented with no history of middle-ear infections, neurologic conditions, or major chronic health conditions and were all native French speakers. In addition, participants presented with an absence of visible abnormalities of the ear canal during otoscopy examination in both ears. Bilateral type A (normal) tympanograms (tympanic peak pressure between -100 and +50 da Pa and static compliance ≥ 0.3 mL, Jerger 1970) were obtained in all participants with a Zodiac 901 tympanometer (Madsen, GN Otometrics, Denmark). Also, pure-tone audiometry was conducted in both ears with an Interacoustics AC40 clinical audiometer (Interacoustics A/S, Middelfart, Denmark) using ER-3A insert earphones (Etymotic Research, Elk Grove Village, IL, USA), calibrated according to the ANSI S3.6-1996 series. All participants presented with pure-tone thresholds in the frequency range of 250 to 8000 Hz (including 3000 and 6000 Hz) equal to or better than the 25th percentile (i.e. quartile 1) of an otologically screened population of the same age range and sex (ISO 7029, 2000). Moreover, all participants had symmetric hearing thresholds between both ears. The latter was defined as an interaural pure-tone thresholds difference of maximally 10 dB HL at two or less audiometric frequencies between 250 and 8000 Hz (Van Yper et al., 2016). Finally, participants scored at least 26/30 in the Montreal Cognitive Assessment (MoCA, Nasreddine et al., 2005)

suggesting no cognitive impairment. Participants were evaluated in two 2-h sessions. Details about the techniques used are described below.

6.3.2 Speech perception in noise measure

The Hearing-in-Noise Test (HINT, Nilsson et al., 1994) with the Canadian French sentence module (Vaillancourt et al. 2005) was used to evaluate speech perception in noise. All stimuli were delivered through ER-3A earphones. Signal-to-noise ratios (SNRs) for 50 % speech discrimination were calculated. A lower SNR indicates better performance. For each noise condition, a set of 20 sentences spoken by a male native Quebec French speaker was presented in the presence of noise, spectrally matched to the average long-term spectrum of the sentences. The HINT was carried out in a soundproof booth, and all stimuli were delivered using the above-mentioned earphones. The HINT was conducted in three different listening conditions: 1) sentences and noise perceived in the front (HINT NF); 2) noise delivered to the RE with sentences perceived in the front (HINT LE); and 3) noise was delivered to the LE with sentences perceived in the front (HINT RE). During testing, sentences were only played once, and participants were encouraged to repeat the complete sentence and to guess if they were unsure of the sentence heard. The order of presentation of the HINT noise conditions was randomized across participants, and scores were obtained through an adaptive procedure in which the sentence sound pressure levels were varied according to the accuracy of the listener responses.

6.3.3 Working memory measurement

The short French version (60 sentences) of the reading span test (Desmette et al., 1995) was used to assess the participant's working memory capacity. The test was presented using SuperLab™

5.0 stimulus presentation software (Cedrus Corp, San Pedro, CA). The test material consisted of 60 test sentences, divided in three twenty-sentence set. Participants had to read aloud all the sentences presented on a computer monitor and to remember the final word of each sentence. After reading all the sentences, a blank screen appeared and participants had to recall the last word of each sentence, without starting the recall process with the last word of the last sentence read. If the participant failed to recall any of the words within a set the task finalized, and the participant was then required to repeat the same procedure with the two remaining twenty-sentence set. The word span score for each participant was defined as the total number of correctly recalled words in the test divided by the total number of words (maximum of 60 words).

6.3.4 Transient evoked otoacoustic emissions (TEOAEs) measurement

TEOAEs were obtained measured and analyzed for both ears using the SmartTrOAE module (version 5.10, Intelligent Hearing Systems, Miami, FL, USA) connected to an HP Compaq 6200 Pro desktop computer. Participants were instructed to stay as still as possible and to keep their head straight during the TEOAE measurement. TEOAEs were elicited with 75- μ s clicks presented at 80 dB pSPL at the rate of 19.3/s. Responses to a total of 1024 sweeps were averaged. TEOAEs were considered present if the response amplitude exceeded the noise amplitude in at least 3 dB (signal-to-noise ratio [SNR] ≥ 3 dB) at each frequency band from 1 to 4 kHz. TEOAE responses were accepted only if the stimulus stability was ≥ 80 % and wave reproducibility was ≥ 70 % (Hood et al, 1997). The average in dB SNR of TEOAE responses across frequencies (1-4 kHz) was calculated for each ear separately. TEOAEs for each ear were used for statistical analyses.

6.3.5 Speech-ABR measurement

Speech-ABR stimuli was recorded using an Intelligent Hearing System (IHS, Smart EP model) also connected to the above-mentioned desktop computer. Electrodes were placed at Fz (positive), A1 and A2 (negative), and the forehead (ground) in accordance with the International 10 to 20 system EEG were used for all recordings. A 6-formant synthesized 170-ms /da/ syllable was used. The 170-ms /da/ syllable was synthesized at a 40 kHz sampling rate, with an initial 5 ms stop burst and a steady fundamental frequency ($F_0 = 100$ Hz). During the first 50 ms (transition between the stop burst /d/ and the vowel /a/), the first, second, and third formants changed (F_1 , 400-720 Hz; F_2 , 1700-1240 Hz; F_3 , 2580-2500 Hz) but stabilized for the subsequent 120 ms steady-state vowel (see Figure 3A). The speech stimulus was presented separately to the right and left ear at 80 dB SPL in alternating polarity to minimize stimulus artifact. The 170-ms /da/ was presented at a rate of 4.35/s and responses were band-pass filtered online from 0.050 to 3 kHz and then offline band-pass filtered from 0.070 to 2 kHz. This offline frequency range filters out cortical activity while maximizing signal-to-noise ratio (SNR) and the detection of transient peaks, such as the onset (Anderson et al., 2012). Recordings were averaged using a time window of 229.89 ms (including a 40ms prestimulus time and a 19.89 poststimulus time). Trials with amplitudes greater than ± 30 μ V were considered artifact and rejected. Two blocks of 3000 responses were collected and averaged resulting in 6000 response trials for each ear.

Latency peaks of participant's neural responses to speech for each ear were manually obtained. Peaks were labeled according to stimulus onset at time 0 ms such that a peak occurring at ~33-34 ms after stimulus onset would be called Peak 33. The first major peak, in response to the onset of the sound, was identified as Peak 9. Peaks corresponding to the transition were peak 33, 43, 53 and

63. These latencies were chosen based on latencies obtained in earlier studies (Anderson et al. 2012; Parbery-Clark et al. 2012a; Presacco et al., 2015). Latencies of individual peaks were further analyzed using an open-source, MATLAB-based toolbox developed and distributed by Drs Erika Skoe and Trent Nicol from the Auditory Neuroscience Laboratory, Northwestern University (Brainstem Toolbox, 2008). Using this program, manually picked peak latencies were adjusted slightly (within ± 2 sampling points) to obtain the absolute minimum or maximum (Skoe & Kraus, 2010). Based on previous studies (e.g., Parbery-Clark et al., 2012; White-Schwoch et al., 2013), peak latencies were then normalized by subtracting the expected response timing (9 ms for the onset, 33, 43, 53, 63, etc. until 163 ms for the transition and steady state) from the actual response latency. This resulted in a normalized value (ms) with 0 indicating that the peak occurred at its expected latency (see Figure 3C). The onset peak and the transition region from each ear were selected for analysis. A composite peak timing score was created for the transition region. This composite score was calculated by taking the average latency of peaks 33-63 for the transition region, which when reported was denoted $\text{transition}_{\text{mean}}$. The rationale to select these two parts of the response was two-fold: first, the onset and transition regions are more vulnerable to background noise unlike the steady state sustained vowel (Anderson et al., 2010; 2012) and second, both response regions have been significantly correlated with speech perception in noise (Parbery-Clark et al., 2009; 2012).

6.3.6 Data processing of auditory measures

The difference in test results between RE and LE was calculated for each auditory outcome (i.e., pure-tone threshold, TEOAE response, and speech-ABR) with the aim to obtain the magnitude of the ID in sensory processing at lower portions of the auditory system. The ID was obtained by

subtracting the LE response from the RE response (RE - LE). However, to enable positive and negative values to continuously indicate sensory processing in the right and left ears, respectively, the ID formula was inverted (LE - RE) for measures at which lower values represent better results (e.g., hearing thresholds and speech-ABR latencies). Thus, positive values indicate an ID favoring the RE pathway and negative values indicate an ID favoring the LE pathway.

6.3.7 Statistical analysis

Initially, paired samples T-test were computed to compare right and left ear results for TEOAE responses, speech-ABR onset and peak transition_{mean}, and HINT scores for right and left ears. Then, a Pearson correlation matrix between the HINT test results (NF, RE and LE) and the RST along with the ID of each auditory measure was computed. Next, bivariate and multiple regression models were constructed to independently investigate the possible association between the dependent variable (i.e., HINT NF, HINT RE, HINT LE) and the independent variables of RST along with and the ID of each auditory outcome. A backward elimination technique was used in the multiple models to select those variables remaining significant in the adjusted analysis, using a selection criterion of $\alpha < .05$. All statistical analyses were performed using SPSS software version 24 (SPSS Inc., Chicago,)

6.4 Results

6.4.1 Descriptive results

Descriptive statistics (mean and standard deviations) for HINT scores and RST for the entire group are summarized in Table 1.

6.4.2 Comparison of auditory outcomes between right and left ears

No significant difference ($p > 0.05$) was observed for the average of TEOAE responses across frequencies (1- 4 kHz) between the right and the left ears. However, the mean TEOAE response for 2000 Hz in the RE was significantly higher compared to the LE ($t_{69} = 3.382$, $p = 0.001$). TEOAE (1.0 – 4.0 kHz) values and the average TEOAE response for right and left ears are shown in Figure 1.

Comparison for speech-ABR measures between right and left ears were then carried out. There were significant differences between the right and left ears for the speech-ABR onset peak ($t_{65} = -2.608$, $p = 0.011$) and transition_{mean} region ($t_{57} = -2.872$, $p = 0.006$). Latencies for both neural regions were significantly shorter in the RE compared to the LE (Figure 2B and 2C).

Finally, within-group comparisons were performed to find significant differences for HINT scores between right and left ears. Results from this analysis revealed that older adults obtained significantly better results for HINT RE compared to HINT LE ($t_{69} = 2.706$, $p = 0.009$). Figure 3 shows the mean scores for HINT RE, HINT LE and HINT NF.

6.4.3 Correlation analysis

A Pearson correlation matrix between the HINT results, RST, and the ID of each auditory outcome (i.e., TEOAEs, speech-ABR onset peak and transition_{mean} region), was obtained for the entire group of participants ($n = 70$). As Table 2 shows, a significant negative correlation between HINT NF and the RST was found. Similarly, HINT LE was also negatively correlated with the RST. Moreover, HINT LE was positively correlated with the ID for TEOAEs, and the ID for the speech-

ABR transition_{mean}. These results suggest that as the ID in sensory processing increased in favor of the RE, SIN performance in the LE declined (higher SNR). HINT RE did not correlate with any of the variables.

6.4.5 Bivariate and multiple regression analyses

Using bivariate regression analyses, the only variable significantly associated with HINT NF was the RST. Figure 3 shows the scatterplot and linear regression line for HINT NF and the RST. Variables significantly associated with HINT LE included the RST, the ID for TEOAE and the ID for transition_{mean}. Figure 4 shows the scatterplots and linear regression lines for HINT LE with all the variables that were significantly associated. HINT RE was not significantly associated with any of the independent variables.

Using multivariate regression analyses for HINT NF, HINT RE, and HINT LE independently, the variable remaining significantly associated with HINT NF in the final multivariate model was the RST [$F(1, 67) = 10.750, p = .002$]. The results showed that 13.8% of the variability for the HINT NF was explained by the RST. HINT RE was not significantly predicted by any independent variable. HINT LE was best predicted by the RST, the ID for TEOAE, and the ID for transition_{mean} [$F(3, 53) = 8.394, p < .001$], explaining 32.2% of the total variance of HINT LE. Table 4 shows the bivariate and multivariate models for NINT NF, HINT RE, HINT LE, respectively after elimination of those variables that did not significantly contribute to each model.

6.5 Discussion

The aim of this study was to investigate whether the magnitude of ID in sensory processing at lower levels of the auditory system explained SIN performance among older adults with age-

appropriate hearing. We found that ID in peripheral (i.e., TEOAE) and subcortical (i.e., speech-ABR neural timing) processing were significantly associated with SIN scores. This was true only for the HINT LE (i.e., noise delivered to the RE). ID in sensory processing at lower levels of the auditory system did not explain SIN performance for either HINT RE or HINT NF conditions in older adults. We also observed that working memory, as measured with the RST, was significantly associated with SIN performance for HINT NF and HINT LE condition.

The magnitude of ID for TEOAE and for speech-ABR transition_{mean} response was significantly associated with HINT scores in the LE. Specifically, results indicated that as the ID for each auditory outcome became more positive, SIN performance in the LE declined among older listeners (Figure 5). Note that a more positive ID for both auditory outcomes imply lower TEOAE and delayed speech-ABR neural timing encoding in the LE relative to the RE. An ID in sensory processing in disfavor of the LE is in accordance with previous studies in young and older adults suggesting that the LE pathway could be weaker than the RE pathway for auditory processing (e.g., Khalfa & Collet, 1996; Khalfa et al., 1998; Tadros et al., 2005; Hornickel et al., 2009; Vander Werff & Burns, 2011; Ahadi et al., 2014). Some of the results of this study support this claim of a weaker LE pathway for auditory processing. For example, we found evidence of significantly delayed speech-ABR neural timing encoding in the LE compared to the RE. These results are in accordance with those obtained by Vander Werff and Burns (2011) who found delayed neural encoding for speech-ABR components in LE than RE in older adults (Vander Werff & Burns, 2011). Regarding TEOAE response, we did not observe significant right/left differences for the average of TEOAE responses across frequencies (1-4 kHz). However, individual TEOAE responses across the frequency range (1-4 kHz) were in general less robust (lower SNR) in the LE relative to the RE (see Figure 1). Moreover, the mean TEOAE response for 2000 Hz was

significantly lower in the LE compared to the RE. Overall, these results are consistent with the notion that the LE pathway might be weaker than the RE pathway for auditory processing.

An increased ID in peripheral and subcortical auditory processing (i.e., weaker LE than RE pathway for auditory processing) may have declined SIN performance in the LE by reducing the neural representation of spectro-temporal acoustic features of speech. Spectrotemporal cues are essential components of auditory object formation, which represent a necessary element of auditory stream segregation (Shinn-Cunningham and Best, 2008). In light with this, a decrease in outer hair cell function (i.e., lower SNR in the LE relative to the RE) may reduce cochlear frequency selectivity and sensitivity (Robles & Ruggero, 2001). This in turn, could have diminished spectrotemporal sound coding analysis (Oxenham, 2003; Moore & Hunter, 2013), which is essential to segregate speech from background noise (Moore, 2003). In addition, at the brainstem level, precise subcortical representation of neural timing is important for capturing fast-changing acoustic transitions, such as those that characterize speech (Parbery-Clark et al., 2012a, b). This is especially relevant for the transition structure of the syllable which is the most perceptually vulnerable region of the syllable to the effects of noise (Tallal & Stark, 1981). It is thus possible that an increased ID in sensory processing—characterized by lower TEOAE response and delayed speech-ABR neural timing encoding in the LE relative to the RE—diminished older adults' capacity to exploit spectrotemporal acoustic features to extract the speech signal from background noise. Consequently, this reduced capacity to use the acoustic features of speech may have led to poor SIN performance during the HINT LE condition among older adults. This effect was not observed for the HINT RE condition. ID in sensory processing at lower levels of the auditory system were not significantly correlated with SIN scores for HINT RE. This might be because ID in peripheral and subcortical processing were consistently better in the RE, suggesting that the RE

pathway was more efficient than the LE pathway to segregate the speech signal from background noise. In fact, SIN scores for HINT RE were significantly higher than SIN scores for HINT LE (figure 3). Thus, it may be concluded that ID in peripheral and subcortical processing contribute to SIN difficulties in older adults only when the weaker auditory pathway is forced to segregate the speech signal from background noise.

However, ID in sensory processing at lower levels of the auditory system were not significantly associated with SIN scores for HINT NF. We hypothesize that a more efficient RE pathway for speech processing accounted for this result. As mentioned before, ID in sensory processing were consistently better for the RE suggesting that the RE pathway was more efficient than the LE pathway for auditory processing. In addition, it has been suggested that RE processing for speech stimuli is faster and more accurate than LE processing due to the stronger contralateral neural projections from the RE to the language-dominant left hemisphere (Kimura, 2011; Lazard et al., 2012). Consequently, this would lead to better SIN performance when speech stimuli are processed by the RE pathway as opposed to the LE pathway (Bidelman & Bhagat, 2015; Tadros et al., 2005; Tai & Husain, 2018). Therefore, a stronger RE pathway (i.e., peripheral and subcortical) for segregating (i.e., processing) the speech signal from background noise could have compensated for SIN difficulties attributed to a weaker LE pathway during the HINT NF condition. These results agree with previous reports showing that even individuals with asymmetric hearing loss (without a hearing impairment in the best ear) exhibit high SIN performance because the speech signal coming from the better hearing ear may be still successfully processed (Ostler & Crandell, 2001; Barona et al., 2019). Thus, we reject the hypothesis that increased ID in peripheral and subcortical processing accounts for SIN performance in older adults when both ears must process speech and noise coming from the same direction.

Results from the present study also showed that working memory was significantly associated with HINT results (Table 2). These findings agree with previous studies showing that older adults put higher demands on top-down mechanisms such as working memory to interpret complex speech signals (i.e., sentences) in the presence of background noise (Moore et al., 2014; Füllgrabe & Rosen, 2016; Gordon-Salant & Cole, 2016). In fact, working memory capacity was significantly associated with SIN scores for HINT NF and HINT LE. These results may indicate that top-down mechanisms (i.e., working memory) were particularly allocated during those challenging listening conditions where the speech signal was further degraded as result of a weaker LE pathway (Rönnberg et al., 2010). Thus, we hypothesize that top-down mechanisms (i.e., working memory) compensated for reduced speech processing related to a weaker LE pathway. The role of working memory found in this study might be consistent with the Decline Compensation Hypothesis, which posits that decreases in sensory processing (i.e., weaker LE pathway) could be somewhat compensated by drawing on more general cognitive functions (Cabeza and Dennis, 2007).

6.6 Conclusion

Based on the results found in this study, we conclude that ID in sensory processing at lower levels of the auditory system influence SIN performance among older adult listeners. However, this is only true under competing binaural listening conditions whereby the weaker auditory pathway (i.e., LE) is forced to extract the speech signal from background noise. Small ID in peripheral and subcortical auditory processing do not seem to affect overall SIN performance among older adults. It appears that a more efficient auditory pathway (i.e., RE) for speech processing along with top-down mechanisms such as working memory may compensate for some of the SIN difficulties that

could arise in more complex listening situations (i.e., HINT NF) because of reduced sensory processing due to a weaker (i.e., LE) auditory pathway.

6.7 References

- Ahadi, M., Pourbakht, A., Jafari, A. H., & Jalaie, S. (2014). Effects of stimulus presentation mode and subcortical laterality in speech-evoked auditory brainstem responses. *International journal of audiology*, 53(4), 243-249.
- Anderson, S., Parbery-Clark, A., White-Schwoch, T., & Kraus, N. (2012). Aging affects neural precision of speech encoding. *Journal of Neuroscience*, 32(41), 14156-14164.
- Anderson, S., Parbery-Clark, A., Yi, H. G., & Kraus, N. (2011). A neural basis of speech-in-noise perception in older adults. *Ear and hearing*, 32(6), 750.
- Anderson, S., Skoe, E., Chandrasekaran, B., & Kraus, N. (2010). Neural timing is linked to speech perception in noise. *Journal of Neuroscience*, 30(14), 4922-4926.
- Barona, R., Vizcaíno, J. A., Krstulovic, C., Barona, L., Comeche, C., Montalt, J., ... & Polo, C. (2019). Does Asymmetric Hearing Loss Affect the Ability to Understand in Noisy Environments? *The Journal of International Advanced Otology*, 15(2), 267.
- Ben-David BM, Tse VY, Schneider BA. (2012). Does it take older adults longer than younger adults to perceptually segregate a speech target from a background masker? *Hear Res.* 290 (1–2):55–63.
- Bidelman, G. M., & Bhagat, S. P. (2015). Right-ear advantage drives the link between olivocochlear efferent ‘antimasking’ and speech-in-noise listening benefits. *Neuroreport*, 26(8), 483-487.
- Cabeza, R., and Dennis, N. (2007). Neuroimaging of healthy cognitive aging. In F. M. I. Craik and T. A. Salthouse (Eds.), *The Handbook of Aging and Cognition*, Third Edition. London: Psychology Press.
- Desmette, D., Hupet, M., Schelstraete, M. A., & Van der Linden, M. (1995). Adaptation en langue française du « Reading Span Test » de Daneman et Carpenter (1980). *L'année Psychologique*, 95(3), 459-482.
- Füllgrabe, C., Moore, B. C., & Stone, M. A. (2015). Age-group differences in speech identification despite matched audiometrically normal hearing: contributions from auditory temporal processing and cognition. *Frontiers in aging neuroscience*, 6, 347.
- Gates, G., & Cooper JC Jr. (1991). Incidence of hearing decline in the elderly. *Acta Oto-Laryngologica*. 111; (2): 240-248

Gates GA, Cooper JC, Kannel WB, Miller NJ. (1990) Hearing in the Elderly: The Framingham Cohort, 1983-1985. Part I. Basic Audiometric Test Results. *Ear Hear.* 11: 247–256.

Gates, G. A., & Mills, J.H. (2005). Presbycusis. *The Lancet*, 366(9491), 1111-1120.

Gordon-Salant, S. (2005). Hearing loss and aging: New research findings and clinical implications. *Journal of Rehabilitation Research and Development*, 42(4 suppl 2), 9-24.

Gordon-Salant, S., & Cole, S. S. (2016). Effects of age and working memory capacity on speech recognition performance in noise among listeners with normal hearing. *Ear and Hearing*, 37(5), 593-602.

Hood, L. J., Hurley, A., Goforth, L., Bordelon, J., Berlin, C. I. (1997). Aging and efferent suppression of otoacoustic emissions. *ARO abstr* 20: 167.

Hornickel, J., Skoe, E., & Kraus, N. (2009). Subcortical laterality of speech encoding. *Audiology and Neurotology*, 14(3), 198-207.

International Organization for Standardization. (2000) Acoustics Statistical Distribution of Hearing Thresholds as a Function of Age. ISO 7029. Geneva: ISO.

Jerger, J. (1970) Clinical Experience with impedance audiometry. *Arch Otolaryng*, 92, 311-324

Jerger, J., Chmiel, R., Allen, J., & Wilson, A. (1994). Effects of age and gender on dichotic sentence identification. *Ear and hearing*, 15(4), 274-286.

Jerger, J., & Martin, J. (2006). Dichotic listening tests in the assessment of auditory processing disorders. *Audiological Medicine*, 4(1), 25-34.

Johannesen, P. T., Pérez-González, P., Kalluri, S., Blanco, J. L., & Lopez-Poveda, E. A. (2016). The influence of cochlear mechanical dysfunction, temporal processing deficits, and age on the intelligibility of audible speech in noise for hearing-impaired listeners. *Trends in hearing*, 20,

Keppler, H., Dhooge, I., Corthals, P., Maes, L., D'haenens, W., Bockstael, A., ... & Vinck, B. (2010). The effects of aging on evoked otoacoustic emissions and efferent suppression of transient evoked otoacoustic emissions. *Clinical Neurophysiology*, 121(3), 359-365.

Khalifa, S., & Collet, L. (1996) Functional asymmetry of medial olivo-cochlear system in humans. Towards a peripheral auditory lateralization. *Neuroreport*. 7: 993-996.

Khalifa, S., Micheyl, C., Veuillet, E., & Collet, L. (1998) Peripheral auditory lateralization assessment using TEOAEs. *Hearing Research*. 121, 29–34.

- Kimura, D. (2011). From ear to brain. *Brain and Cognition*, 76(2), 214-217.
- Lazard, D. S., Collette, J. L., & Perrot, X. (2012). Speech processing: from peripheral to hemispheric asymmetry of the auditory system. *The Laryngoscope*, 122(1), 167-173.
- Moore, B. C. (2003). Coding of sounds in the auditory system and its relevance to signal processing and coding in cochlear implants. *Otology & neurotology*, 24(2), 243-254.
- Moore, B. C. (2007). *Cochlear hearing loss: physiological, psychological and technical issues*. John Wiley & Sons.
- Moore, D. R., Edmondson-Jones, M., Dawes, P., Fortnum, H., McCormack, A., Pierzycki, R. H., & Munro, K. J. (2014). Relation between speech-in-noise threshold, hearing loss and cognition from 40–69 years of age. *PloS one*, 9(9), e107720.
- Moore, D. R., & Hunter, L. L. (2013). Auditory processing disorder (APD) in children: a marker of neurodevelopmental syndrome. *Hearing, Balance and Communication*, 11(3), 160-167.
- Murphy, D. R., Daneman, M., & Schneider, B. A. (2006). Why do older adults have difficulty following conversations? *Psychology and aging*, 21(1), 49.
- Nasreddine, Z., Phillips, N., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Chertkow, H. (2005) The Montreal Cognitive Assessment, MoCA- A Brief Screening Tool for Mild Cognitive Impairment. *Journal of American Geriatrics Society*, 53(4), 695-699.
- Nilsson, M., Soli, S. D., & Sullivan, J. A. (1994). Development of the Hearing in Noise Test for the measurement of speech reception thresholds in quiet and in noise. *The Journal of the Acoustical Society of America*, 95(2), 1085-1099.
- Ostler, D. A., & Crandell, C. C. (2001). The effects of symmetrical and asymmetrical sensorineural hearing loss on speech perception in noise. *The Journal of the Acoustical Society of America*, 109(5), 2503-2503.
- Oxenham A. J., & Bacon, S. P. (2003). Cochlear compression: perceptual measures and implications for normal and impaired hearing. *Ear and hearing*, 24(5), 352-366.
- Parbery-Clark, A., Anderson, S., Hittner, E., & Kraus, N. (2012a). Musical experience offsets age-related delays in neural timing. *Neurobiology of aging*, 33(7), 1483-e1.

Parbery-Clark, A., Anderson, S., Hittner, E., & Kraus, N. (2012b). Musical experience strengthens the neural representation of sounds important for communication in middle-aged adults. *Frontiers in aging neuroscience*, 4, 30.

Parbery-Clark, A., Skoe, E., & Kraus, N. (2009). Musical experience limits the degradative effects of background noise on the neural processing of sound. *Journal of Neuroscience*, 29(45), 14100-14107.

Presacco, A., Jenkins, K., Lieberman, R., & Anderson, S. (2015). Effects of aging on the encoding of dynamic and static components of speech. *Ear and hearing*, 36(6), e352.

Robles, L., & Ruggero, M. A. (2001). Mechanics of the mammalian cochlea. *Physiological reviews*, 81(3), 1305-1352.

Rönnberg, J., Rudner, M., Lunner, T., & Zekveld, A. A. (2010). When cognition kicks in: Working memory and speech understanding in noise. *Noise and Health*, 12(49), 263.

Ross, B., Fujioka, T., Tremblay, K. L., & Picton, T. W. (2007). Aging in binaural hearing begins in mid-life: evidence from cortical auditory-evoked responses to changes in interaural phase. *Journal of Neuroscience*, 27(42), 11172-11178.

Salthouse, T. A. (1996). The processing-speed theory of adult age differences in cognition. *Psychological review*, 103(3), 403.

Shinn-Cunningham, B. G., & Best, V. (2008). Selective attention in normal and impaired hearing. *Trends in amplification*, 12(4), 283-299.

Skoe E. & Kraus, N. (2010). Auditory brainstem response to complex sounds: A tutorial. *Ear Hear*, 31, 302.

Tadros, S. F., Frisina, S. T., Mapes, F., Kim, S., Frisina, D. R., & Frisina, R. D. (2005). Loss of peripheral right-ear advantage in age-related hearing loss. *Audiology and Neurotology*, 10(1), 44-52.

Tai, Y., & Husain, F. T. (2018). Right-ear advantage for speech-in-noise recognition in patients with nonlateralized tinnitus and normal hearing sensitivity. *Journal of the Association for Research in Otolaryngology*, 19(2), 211-221.

Tallal, P., & Stark, R. E. (1981). Speech acoustic-cue discrimination abilities of normally developing and language-impaired children. *The Journal of the Acoustical Society of America*, 69(2), 568-574.

Vaillancourt, V., Laroche, C., Mayer, C., Basque, C., Nali, M., Eriks-Brophy, A., ... & Giguère, C. (2005). Adaptation of the hint (hearing in noise test) for adult canadian francophone populations. *International Journal of Audiology*, 44(6), 358-361.

Vander Werff, K. R., & Burns, K. S. (2011). Brain stem responses to speech in younger and older adults. *Ear and hearing*, 32(2), 168-180.

Van Yper, L. N., Vermeire, K., De Vel, E. F., Beynon, A. J., & Dhooge, I. J. (2016). Age-related changes in binaural interaction at brainstem level. *Ear and hearing*, 37(4), 434-442.

Vincent, G. K., & Velkoff, V. A. (2010). The next four decades: The older population in the United States: 2010 to 2050 (No. 1138). US Department of Commerce, Economics and Statistics Administration, US Census Bureau.

Wahab, N. A. A., Zakaria, M. N., Rahman, A. H. A., Sidek, D., & Wahab, S. (2017). Listening to Sentences in Noise: Revealing Binaural Hearing Challenges in Patients with Schizophrenia. *Psychiatry Investigation*, 14(6), 786.

Weihing, J., & Musiek, F. (2014). The influence of aging on interaural asymmetries in middle latency response amplitude. *Journal of the American Academy of Audiology*, 25(4), 324-334.

Westerhausen, R., Bless, J., & Kompus, K. (2015). Behavioral Laterality and Aging: The Free-Recall Dichotic-Listening Right-Ear Advantage Increases with Age. *Developmental Neuropsychology*, 40(5), 313-327.

White-Schwoch, T., Carr, K. W., Anderson, S., Strait, D. L., & Kraus, N. (2013). Older adults benefit from music training early in life: biological evidence for long-term training-driven plasticity. *Journal of Neuroscience*, 33(45), 17667-17674.

6.8 Tables and Figures

Table 1. Mean, standard deviation (SD), and range for HINT and RST results

Variables	All (n = 70)			
	Mean	SD	Min	Max
HINT NF (SNR)	-1.90	1.16	-4.70	1.60
HINT RE (SNR)	-9.33	1.87	-13.40	-1.00
HINT LE (SNR)	-8.69	1.73	-12.30	-4.90
RST (%)	30.76	9.87	15.00	58.00

HINT NF = Hearing-in-noise test noise front (i.e., sentences and noise perceived in the front); HINT RE = Hearing-in-noise test right ear (i.e., noise delivered to the left ear); HINT LE = Hearing-in-noise test left ear (i.e., noise delivered to the right ear); RST = Reading span test.

Table 2. Pearson's correlation coefficients between HINT results, working memory, and the interaural difference in sensory processing for each auditory measure.

	HINT NF	HINT RE	HINT LE	RST	ID TEOAE	ID Onset	ID Transition _{mean}
HINT NF	*						
HINT RE	.299*	*					
HINT LE	.438**	.340**	*				
RST	-.372**	-.185	-.325**	*			
ID TEOAE	.089	.124	.245*	.026	*		
ID Onset	.134	.244	.104	-.082	-.100	*	
ID Transition _{mean}	.137	.040	.314*	.065	-.087	.310*	*

HINT NF = Hearing-in-noise test noise front (i.e., sentences and noise perceived in the front); HINT RE = Hearing-in-noise test right ear (i.e., noise delivered to the left ear); HINT LE = Hearing-in-noise test left ear (i.e., noise delivered to the right ear); ID = Interaural difference; TEOAE = Transient evoked otoacoustic emission response; Onset = Speech-ABR latency for onset peak 9; Transition_{mean} = Composite score for the transition region obtained by calculating the normalized average latency of peaks 33-63. * $p < 0.05$.; ** $p < 0.01$

Table 3. Bivariate and multivariate regression analysis for HINT results

HINT NF									
Variable	Bivariate Model			Multivariate model			Final Multivariate model		
	Beta	p	R ²	Beta	p	R ²	Beta	p	R ²
<i>Cognitive measures</i>									
RST	-.372	.002	.138**	-.432	.001		-.372	.002	
<i>Auditory Measures</i>									
ID TEOAE	.089	.465	.008	.089	.472				
ID Onset	.134	.218	.018	.158	.226				
ID Transition _{mean}	.137	.303	.019	.113	.386				
						.236*			.138**
HINT RE									
Variable	Bivariate Model			Multivariate model			Final Multivariate model		
	Beta	p	R ²	Beta	p	R ²	Beta	p	R ²
<i>Cognitive measures</i>									
RST	-.198	.103	.039	-.315	.018				
<i>Auditory Measures</i>									
ID TEOAE	.128	.291	.016	.074	.569				
ID Onset	.243	.059	.059	.253	.066				
ID Transition _{mean}	.040	.767	.002	-.010	.939				
						.168*			
HINT LE									
Variable	Bivariate Model			Multivariate model			Final Multivariate model		
	Beta	p	R ²	Beta	p	R ²	Beta	p	R ²
<i>Cognitive measures</i>									
RST	-.325	.007	.105**	-.338	.005		-.335	.005	
<i>Auditory Measures</i>									
ID TEOAE	.245	.041	.060*	.326	.007		.314	.008	
ID Onset	.104	.406	.011	.027	.825				
ID Transition _{mean}	.314	.016	.099*	.374	.003		.372	.002	
						.329***			.322***

HINT NF = Hearing-in-noise test noise front (i.e., sentences and noise perceived in the front); HINT RE = Hearing-in-noise test right ear (i.e., noise delivered to the left ear); HINT LE = Hearing-in-noise test left ear (i.e., noise delivered to the right ear); RST = Reading span test; REA = Right ear advantage for the dichotic digit test determined by subtracting the left ear score from the right ear score; Δ = Asymmetry index; TEOAE = Transient evoked otoacoustic emission response; Onset = Speech-ABR latency for onset peak 9; Transition_{mean} = Composite score for the transition region obtained by calculating the average latency of peaks 33-63. * $p < 0.05$.; ** $p < 0.01$.; *** $p < 0.001$.

Figure 1. Means and standard error bars for (A) TEOAE dB SNR at 1.0 – 4.0 kHz, and (B) overall response for right and left ears for the entire group of older adults (n = 70).

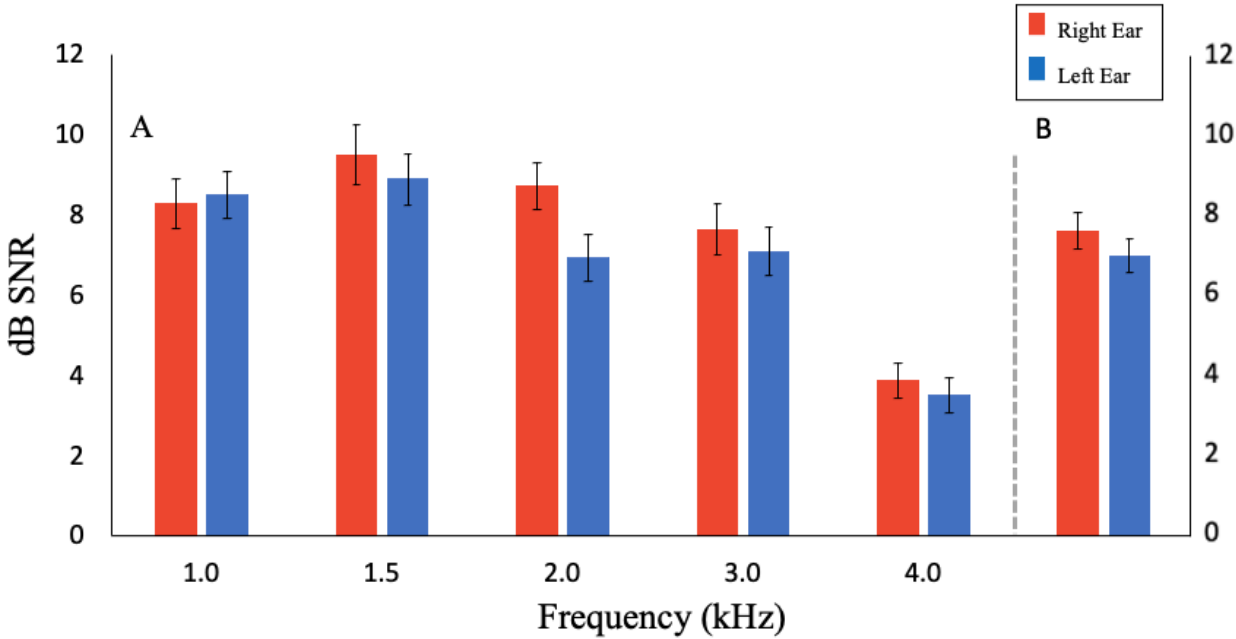


Figure 2. Stimulus waveform (A), grand mean ($n = 70$) brainstem response (B) for the speech syllable /da/ in the right (red) and left (blue) ears divided into 3 regions based on stimulus characteristics: onset, formant transition, and steady-state sustained vowel, and normalized peak latencies (C) for both ears. * $p < 0.05$; ** $p < 0.01$

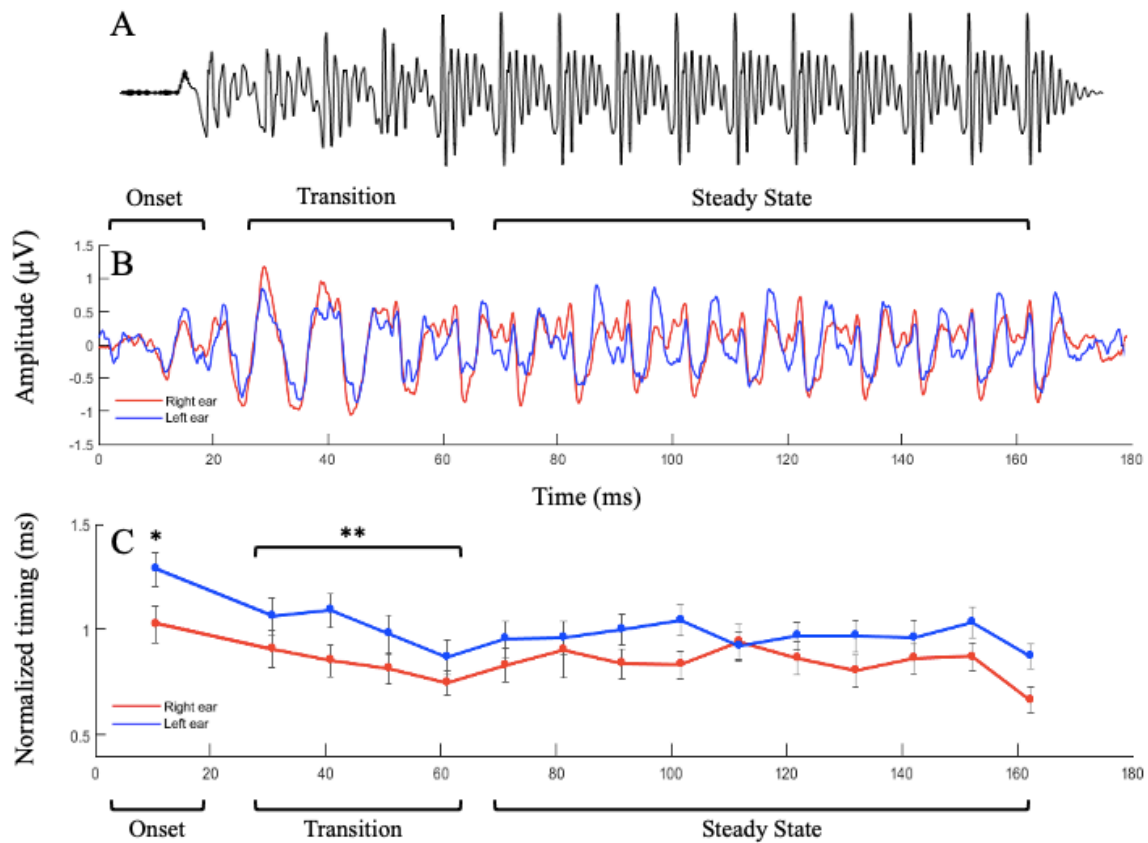


Figure 3. Mean scores and standard deviation for HINT NF, HINT LE and HINT RE for the entire group of older adults (n = 70).

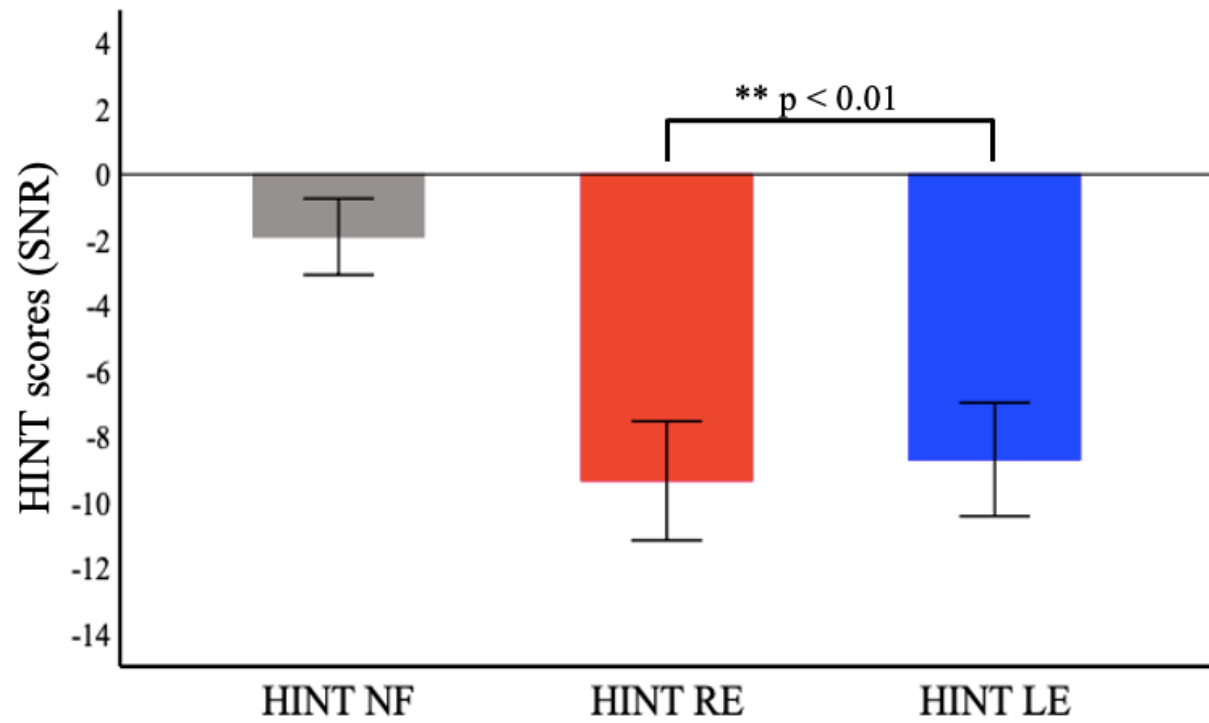


Figure 4. Bivariate scatterplot and linear regression line (R2 value) for HINT NF with the Reading span test (RST).

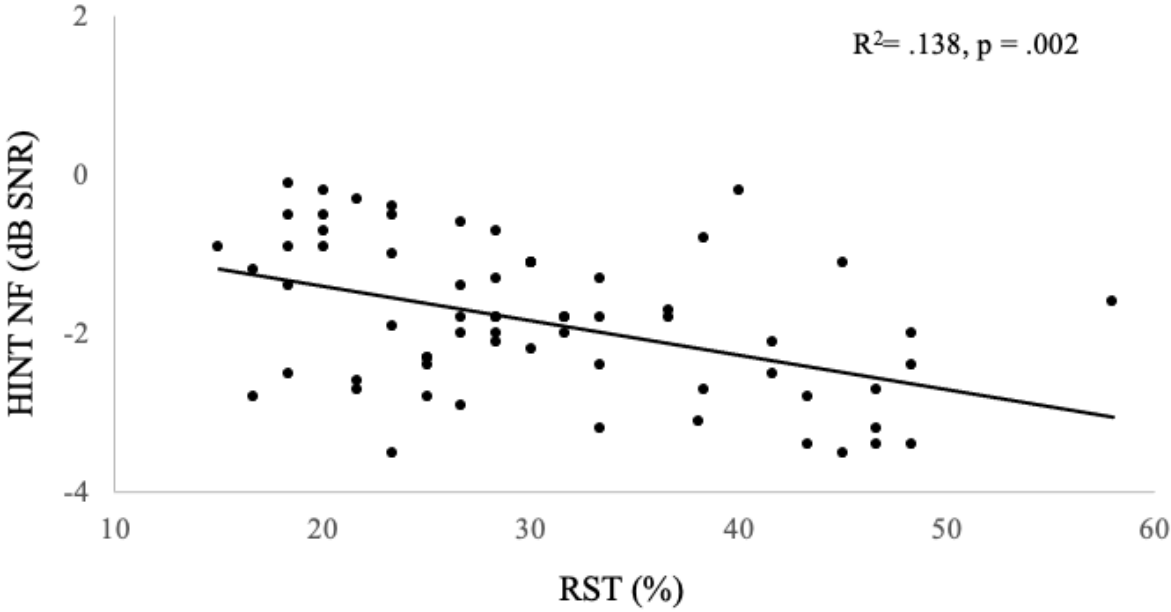
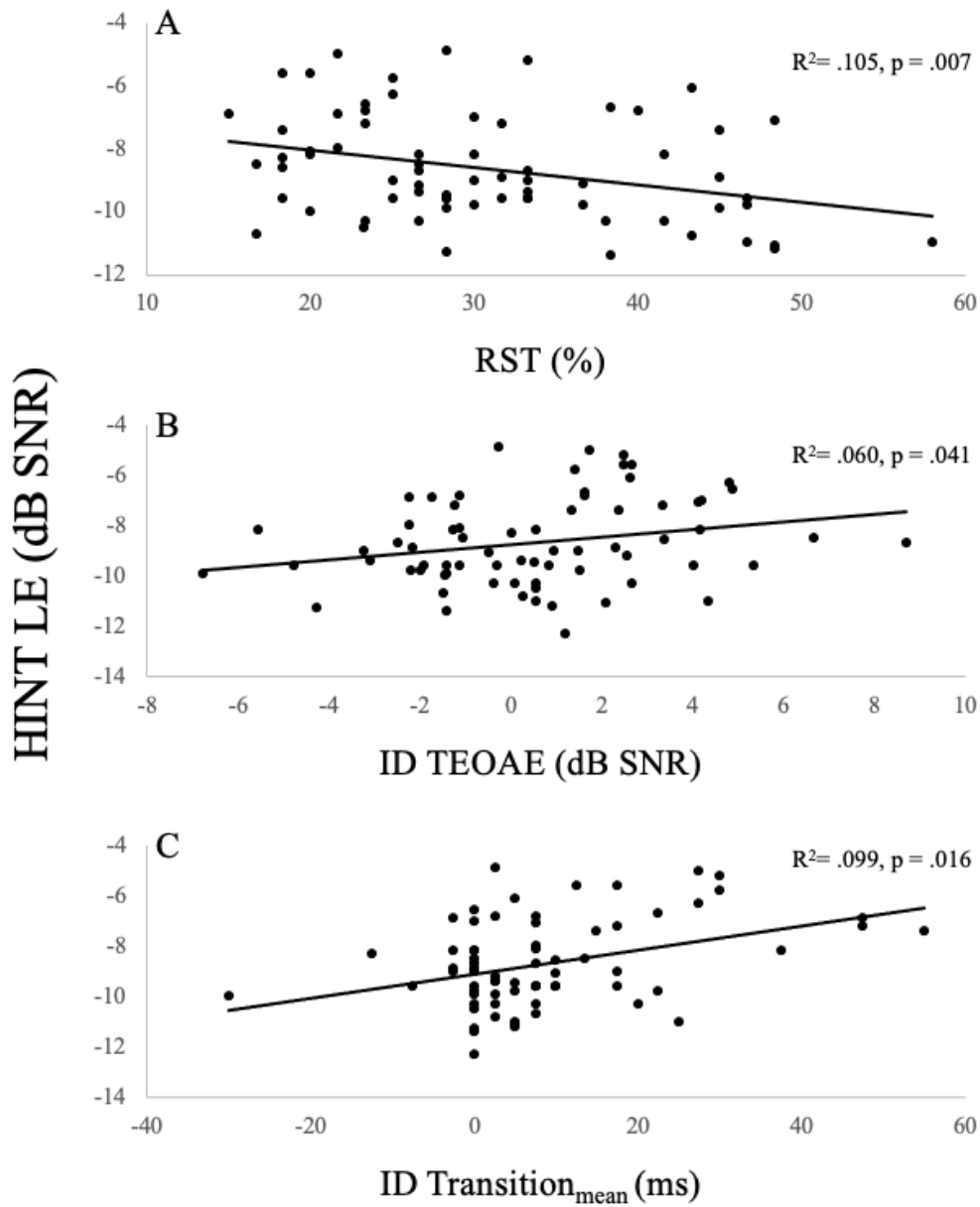


Figure 5. Bivariate scatterplots and linear regression lines (R^2 values) of HINT LE with the RST with (A) the Reading span test (RST); and the interaural difference (ID) for (B) Transient evoked otoacoustic emissions (TEOAE) and (C) Transition mean neural region. Cognitive and auditory measures showed significantly predictive associations with HINT LE.



Chapter 7- General discussion

The purpose of the present doctoral thesis was to investigate whether the magnitude of interaural differences (ID) in sensory processing at lower levels of the auditory system were associated with the magnitude of the REA for DL and with SIN performance among older adults. To this end, three specific objectives were addressed. The first objective was to investigate ID in sensory processing at lower levels of the auditory system in older adults. Specifically, the study aimed to determine whether older adults exhibit peripheral and subcortical processing differences between the right and left auditory pathways. For this, pure-tone thresholds, TEOAE response, MOC-induced TEOAE suppression, and click and speech ABR were measured in both ears separately in a sample of 70 older adults with age-appropriate symmetric hearing. According to the results, both the average of pure-tone thresholds across the frequency range (250-8000 Hz) and the average of TEOAE response across the frequency range (1000-4000 Hz) were not significantly different between both ears (second article). Similarly, the amount of MOC-induced TEOAE suppression did not significantly differ between the right and the left ears (second article). Therefore, at a peripheral level, older adults (as a group) do not exhibit significant differences in sensory processing between the RE and the LE (see discussion below). At a subcortical level, results from the ABR analysis showed no significant differences in auditory brainstem processing (i.e., amplitude and latency) between right and left ear presentation for click stimuli among older adults (first article). However, using speech-like stimuli (e.g., a synthesized 40-and-170ms /da/ syllables) older adults showed significant interaural latency and amplitude differences, with shorter latencies for transient and sustained components for RE presentation (first and third articles), and larger spectral amplitude of the F0 for LE presentation (first article). To the best of knowledge, these are

the first results to demonstrate a clear pattern of brainstem laterality for the encoding of frequency and temporal acoustic components of speech in older adults.

The second objective was to investigate whether the magnitude of ID in sensory processing at lower levels of the auditory system were associated with the increased magnitude of the REA for DL among older adults. To this end, the difference in test results between RE and LE presentation was calculated for each auditory outcome (i.e., pure-tone threshold, TEOAE response, MOC-induced TEOAE suppression, and speech-ABR) with the aim to obtain the magnitude of the ID in sensory processing at lower portions of the auditory system. Moreover, participants had to perform a DL test from which the REA was derived by calculating the LI (for the laterality index formula, see material and methods section, second article). Possible confounding factors such as cognitive abilities, which also account for the larger REA's magnitude for DL in older adults (Hällgren et al., 2001; Andersson et al., 2008; Hommet et al., 2010), were controlled for as covariates in the statistical analyses. According to the results from the multiple regression models, the magnitude of ID in audibility (i.e., pure-tone thresholds) and the magnitude of ID in the amount of MOC-induced TEOAE suppression were significantly associated with the magnitude of the REA for DL (see results article 2). These effects were evident for the laterality index of the nonforced and forced attention paradigms. Conversely, results showed that the magnitude of ID for speech-ABR measures (i.e., neural timing response) were not significantly associated with the REA's magnitude for DL among older adults. Moreover, cognitive measures of speed of processing and mental flexibility significantly contributed to the enlarged REA's magnitude for DL among older adults. These are the first findings to demonstrate that a substantial increase in the magnitude of the REA may also originate from ID in sensory processing occurring at lower portions of the auditory

pathways, by affecting DL performance at an early, preattentive bottom-up sensory stage of auditory processing.

The third objective was to investigate whether the magnitude of ID in sensory processing at lower levels of the auditory system were also associated with SIN ability in older adults. ID in sensory processing were quantified again for each auditory measure and working memory was accounted for in the statistical analyses. SIN performance was evaluated with the HINT using three simulated noise conditions. Results demonstrated that ID in peripheral and subcortical processing were significantly associated with SIN performance among older adults. However, these effects were only evident under competing listening conditions (i.e., HINT LE) whereby the weaker auditory pathway was forced to extract (i.e., process) the speech signal from background noise. Finally, the results from the present thesis also showed that working memory was significantly associated with SIN scores. These findings suggest that top-down mechanisms may have compensated for reduced bottom-up sensory processing attributed to a weaker auditory pathway.

7.1 ID in peripheral and subcortical auditory processing among older adults

It was hypothesized that older adults would exhibit increased ID in sensory processing at lower (i.e., peripheral, and subcortical) levels of the auditory system. This hypothesis was proposed based on the evidence demonstrating significant ID in peripheral and subcortical auditory processing in young adults (Kannan & Lipscomb, 1974; McFadden, 1993; McFadden & Mishra, 1993; Khalfa & Collet, 1996; McFadden et al., 1996; Khalfa et al., 1997; Khalfa et al., 1998; Philibert et al., 1998; Hornickel et al., 2009; Sinha & Basavaraj, 2010; Krishnan et al., 2011; Ahadi et al., 2014; Bidelman & Bhagat, 2015), along with the evidence that suggest that the LE auditory pathway would be slightly more fragile than the RE auditory pathway in resisting the effects of age (e.g.,

Gates et al., 1990; Gates & Cooper, 1991; Jerger et al., 1994; Weihing & Musiek, 2014; Westerhausen et al., 2015). Results from the present thesis support this hypothesis, at least in part. About peripheral auditory function, the main analysis suggests that older adults, as a group, do not exhibit statistically significant differences in peripheral auditory processing between the RE and the LE. However, individual results indicate that most of the participants showed ID in sensory processing among peripheral auditory measures (see Figures 2, 3A and 3B, second article). Thus, the results from the present study were not able to identify a clear (statistically significant) pattern of peripheral auditory lateralization among older adults (as a group) like the one observed in young adults (rightward laterality). Taken at face value, this failure to find a rightward laterality pattern for peripheral auditory processing in older adults (as a group) could suggest that, in general, differences in sensory processing between both ears tend to disappear with increasing age. However, it should be noted that the present findings are also not in accordance with previous studies in older adults with similar hearing characteristics (i.e., symmetric hearing), showing significantly better (lower) hearing thresholds (e.g., Cruickshanks et al., 1998; Gates et al., 1990; Gates et al., 1991; Glorig, 1958) and larger TEOAE response (higher SNR) (e.g., Tadros et al., 2005) in the RE compared to the LE. Moreover, although there were no significant right/left differences for the average of pure-tone thresholds and the average of TEOAE responses across frequencies, overall, older adults did exhibit better (lower) hearing thresholds and larger (higher SNR) TEOAE responses across the frequency range in the RE compared to the LE. It should also be noted that the mean TEOAE response for 2000 Hz was significantly lower in the LE compared to the RE. Taken together, these results could still suggest overall enhanced peripheral auditory processing in the RE than the LE among older adults.

There are several explanations that could account for the absence of a strong pattern of peripheral auditory lateralization even though there was a clear ID in peripheral processing among older adults. One possible explanation for these results could be related to the sample size of the study. Regarding hearing sensitivity, previous studies (e.g., Cruickshanks et al., 1998; Gates et al., 1990; Gates et al., 1991; Glorig, 1958) showing better (lower) hearing thresholds for the RE than the LE among older adults with symmetric hearing have obtained these results with samples sizes ranging from 1500 to 3700, as opposed to the 70 older participants that were involved in the study. Therefore, the present study may have been underpowered to find a statistically significant laterality effect for audibility between both ears. It could be argued, however, whether the small sample used in this study was responsible for the absence of significant right/left TEOAE response differences among older adults. For example, Tadros et al. (2005) reported significant TEOAE differences between both ears in a group sample three times smaller than the current sample ($n = 21$). In addition, previous studies in young adults have also reported significant TEOAE differences between the right and the left ears with similar sample sizes as the present study (e.g., Khalfa et al., 1996, 1997). Thus, the lack of significant right/left TEOAE differences found in this study is unlikely to be explained by the small sample size.

Alternatively, although gender effects were beyond the scope of this thesis, sex differences in auditory function could account for the lack of significant right/left differences for the average of both pure-tone thresholds and TEOAE responses observed in this study. This is because audibility and TEOAE response differences between the right and the left ears are generally confined to males considering that the above-mentioned auditory outcomes are known to be better and more symmetric among females (Chung et al., 1983; Kannan & Lipscomb, 1974; McFadden, 1993). Sex-stratified analysis (not shown) revealed that there was a statistically significant difference between

females and males for the average of pure-tone thresholds across frequencies (250-8000 Hz) for the RE ($t_{68} = -2.076$, $p = 0.042$) and for the LE ($t_{68} = -2.584$, $p = 0.012$). In average, female older adults exhibited better hearing thresholds in the RE and the LE compared to male older adults. Notwithstanding, the average of pure-tone thresholds across frequencies was not significantly different between RE and LE for male ($p = 0.090$) and female ($p = 0.547$) older adults. It should be noted however, that male older adults exhibited significantly worse hearing thresholds across frequencies (except for 500 Hz, 1000 Hz and 8000 Hz) in the LE compared to the RE. With regards to TEOAE responses, a similar trend was observed. There was a statistically significant difference between males and females for the average of TEOAE response across frequencies (1000-4000 Hz) in the LE. Averaged TEOAE responses in the LE were significantly higher in female older adults compared to male older adults ($t_{68} = 3.528$, $p = 0.001$), and this effect was not evident in the RE. In addition, the average of TEOAE response across frequencies was significantly higher in the RE than the LE in male older adults ($t_{33} = 2.354$, $p = 0.025$) but not in female older adults ($p = 0.990$). Thus, considering that sex was equally distributed in this study (35 women and 35 men) and that female older adults showed similar hearing thresholds and TEOAE response between ears, it is possible that ID in audibility and ID in TEOAE were attenuated when the data was collapsed across sex. This could possibly account for the absence of significant right/left audibility and TEOAE differences among older adults (as a group) observed in the present study despite exhibiting clear ID for both auditory measures. Sex differences should be carefully considered in futures studies investigating ID in peripheral auditory processing among older adults.

However, it seems that sex differences are unlikely to explain the lack of significant right/left differences in MOC-induced TEOAE suppression observed in older adults as the MOC system appears to be equally functional in the RE as in the LE for both females and males (Khalifa &

Collet, 1996; Stuart & Cobb, 2015; Stuart & Kerls, 2018). In fact, there was not any statistically significant difference between female and male older adults for the magnitude of MOC-induced TEOAE suppression for the right and left ears. Moreover, there was not any significant difference for the magnitude of MOC-induced TEOAE suppression between the RE and LE for male and female older adults. The absence of significant right/left MOC-induced TEOAE suppression differences is consistent with the results reported by Tadros et al. (2005) who found that older adults with significantly higher TEOAE response in the RE than the LE showed no significant right/left differences in MOC-induced TEOAE suppression. Tadros et al. attributed these results to a loss of the right dominance in MOC function due to aging effects. Indeed, previous studies have reported a decrease in the strength of the MOC system with increasing age (decrease of the OAE suppression effects) among older adults (Parthasarathy et al., 2001; Keppler et al., 2010; Lisowska et al., 2014). However, to accept the idea of a rightward reduction of MOC function due to increasing age, age-related effects should have also occurred asymmetrically thereby diminishing MOC function in the RE but not in the LE, and so far, there is no evidence to support this claim. Therefore, it may be speculated that aging itself could not account for this particular result.

Instead, methodological issues could have likely contributed to the absence of significant right/left MOC-induced TEOAE differences observed among older. For example, the stapedius muscle reflex may potentially contribute to the MOC reflex magnitude by influencing the stimulus and/or emissions as they transmit through the middle ear (Guinan, 2006; Mishra, 2014). Depending on the level, middle ear muscle reflect can be evoked by contralateral broad band noise and/or by OAE-evoking (e.g., click) stimulus. In the present study, the contralateral acoustic noise used to stimulate efferent effects was presented at 60 dB SPL, whereas previous studies that have found significant ID in MOC-induced TEOAE suppression in young adults have used lower (e.g., 30 dB SL) noise

levels (e.g., Khalfa & Collet, 1996; Khalfa et al., 1998). Although 60 dB SPL has been considered as an optimal contralateral acoustic stimulation level (Guinan, 2006), it could also elicit middle ear muscle reflect (Guinan et al., 2003), which may possible alter TEOAE inhibition (Mishra & Lutman, 2013, 2014). Thus, potential middle ear muscle reflex influences could have likely compromised the MOC-induced TEOAE suppression estimation for both the RE and the LE. On average, auditory reflexes in these older adult participants were elicited at 85 dB SPL (for RE and LE) above their threshold of audibility, which exceeded the level of contralateral acoustic noise used to produce suppression (i.e., 60 dB SPL). These results might suggest that the involvement of stapedius muscle reflex was relatively controlled in this study. However, stapedius muscle may affect cochlear input and output at levels of stimulation that are well below those that cause a change in middle ear impedance (Eliasson & Gisselson, 1955; Simmons & Beatty, 1962). In fact, recent work on auditory reflexes suggest that middle ear muscle reflect can be elicited on an average 12 to 13.7 dB below (for 1 and 2 kHz tonal activators) the auditory reflex threshold measured using a 226 Hz probe tone in adults (Feeney et al., 2003; Mishra & Lutman, 2014). Therefore, it is not possible to completely rule out the contribution of auditory reflexes on MOC-induced TEOAE suppression for both the right and left ears.

Moreover, middle ear muscle reflex could also be elicited by the clicks that are used to record OAEs (Guinan 2006). According to Guinan et al. (2003) click stimuli used to record TEOAE presented at 60 to 70 dB SPL are potent elicitors of efferent activity. In the present study, click stimuli used to record TEOAE were presented at 80 dB SPL, as opposed to previous studies in young adults that have found significant ear differences by recording TEOAE in the RE and LE using click stimuli at 60 dB SPL (Khalfa & Collet, 1996; Khalfa et al., 1998; Bidelman & Bhagat, 2015). This might suggest that the present results were not entirely free from probe-induced

efferent effects. Then, if the click sounds used in this study elicited some MOC activity, theoretically, it could have contributed to imprecise estimation of the MOC suppression magnitude in both the RE and the LE. A similar effect could have also been observed in the results reported by Tadros et al. (2005) since they recorded TEOAE using click stimuli presented at 84 dB SPL. Thus, the high level of evoking clicks may have elicited the middle ear acoustic reflex thereby affecting the results for MOC-induced TEOAE suppression in both ears. Altogether, these methodological issues may possibly account for the absence of significant right/left MOC-induced TEOAE suppression differences among older adults. Finally, although individually older adults exhibited ID in MOC-induced TEOAE suppression, it is possible that a strong laterality pattern should have not been expected among this population. While there is evidence demonstrating stronger auditory efferent activity in the RE than the LE among young adults (Khalifa & Collet, 1996; Khalifa et al., 1998; Philibert et al., 1998; Bidelman & Bhagat, 2015), there are several studies showing opposite results demonstrating an absence of significant ear effects on MOC-induced TEOAE suppression (e.g., Graham and Hazell, 1994; Garinis et al., 2011; Stuart & Butler, 2012; Stuart & Cobb, 2015; Stuart & Kerls, 2018). These contradicting results among young adults suggest that a clear pattern of MOC-induced TEOAE suppression laterality may be still unknown. Future studies should be conducted to confirm if the MOC functionality is indeed asymmetrical and whether this laterality pattern changes as a function of age.

In frank contrast to the results obtained for the peripheral auditory measures, a strong pattern of subcortical laterality for sound encoding emerged among older adults (see First article). On the one hand, the results from the click-ABR analysis showed symmetrical responses (e.g., amplitude and latency) between the right and left ear presentation. These results are consistent with previous research in young (Rowe, 1978; Hornickel et al., 2009; Vander Werff & Burns, 2011) and older

adults (Johansen & Lehn, 1994; Vander Werff & Burns, 2011; Peng et al., 2016; Van Yper et al., 2016) demonstrating no ID in auditory brainstem processing for click stimuli. On the other hand, for speech-like stimuli (e.g., /da/syllable), temporal and frequency-related (i.e., fundamental frequency) components of speech were clearly lateralized at the brainstem level among older adults. These results are also in accordance with previous studies conducted in young adults indicating lateralized subcortical processing for speech components (e.g., Hornickel et al., 2009; Sinha & Basavaraj, 2010; Vander Werff & Burns, 2011; Ahadi et al., 2014). Thus, the present results support the hypothesis that older adults exhibit significant ID in sensory processing at lower (i.e., subcortical) levels of the auditory system.

As discussed earlier (First article), differences in the laterality pattern of subcortical processing between click and speech stimuli might be the consequence of pervasive exposure to and active engagement with speech and not click stimuli (Hornickel et al., 2009). Hearing speech sounds (unlike click sounds), which have environmental relevance, leads to the extraction of significant information about encoding of the time-varying aspect of sounds, which may potentially shape the auditory system to react differently when encoding complex (i.e., speech) versus non-complex (i.e., click) sounds (Johnson et al., 2008). Consistent with this idea, it has been shown that brainstem encoding of sound might be shaped by linguistic experience (Krishnan et al., 2004, 2005). In addition, it has been proposed that neural populations at the brainstem level (particularly the inferior colliculus) might adjust their firing patterns improving coding accuracy for sounds (i.e., speech) occurring most commonly (Dean et al., 2005). Thus, considering that humans have little exposure to clicks and that clicks have little linguistic importance, then it should not be expected that the brainstem would process such an irrelevant stimulus asymmetrically. The results from this thesis (i.e., no lateralization for nonrelevant click sounds and lateralization for relevant speech

acoustic components) along with previous studies (e.g., Hornickel et al., 2009; Sinha & Basavaraj, 2010; Vander Werff & Burns, 2011) support this claim. Moreover, the present results reinforce the maintenance of a clear pattern of brainstem asymmetry for acoustic features of speech among older adults.

In summary, the results obtained across peripheral and subcortical auditory measures partly support the hypothesis of increased ID in sensory processing at lower levels of the auditory system among older adults. At a peripheral level, although individual results showed that older adults exhibit ID in sensory processing, as a group, they do not demonstrate a consistent (statistically significant) pattern of laterality for peripheral auditory processing as young adults do. Certainly, the present results suggest a trend of a right ear advantage for all peripheral auditory measures which is consistent with the plethora of evidence suggesting enhanced auditory processing in the RE relative to the LE. However, as discussed above, the absence of a strong ear effect (rightward laterality effect) among older adults could be possibly attributed to several concerns including the number of participants, gender related differences in auditory function, and measurement matters (MOC inhibitory effects). Future studies, controlling for the above-mentioned issues, should reexamine the effects of ear in peripheral auditory processing among older adults. Conversely, at the brainstem level, older adults clearly show a laterality pattern of brainstem encoding for speech acoustic features as young adults do. Moreover, based on the results it seems that ID in subcortical processing is further increased in older compared to young adults. Although these differences cannot be statistically tested with the current data, since young adults did not participate in this study, interaural neural timing differences for transient and sustained components of speech appear to be larger in older adults relative to young adults (see Table 4, first article). These results may

support the hypothesis that a greater age-related decline in the LE pathway would further increase ID in sensory processing at lower levels of the auditory system, at least at the brainstem level.

7.2 ID in sensory processing at lower levels of the auditory system and their effect on the magnitude of the REA for DL.

It was hypothesized that the magnitude of the ID in sensory processing at lower portions of the auditory system explained in part the increased magnitude of the REA for DL observed among older adults. The results from the present study support this hypothesis by demonstrating that ID in sensory processing at lower levels (i.e., peripheral) of the auditory system significantly contributed to the variance of the magnitude of the REA for DL among older adults. It should be recalled that individual results clearly identified ID in sensory processing at lower levels of the auditory system among older adults albeit the fact that as a group there was not a strong (statistically significant) pattern of peripheral auditory lateralization. Specifically, regression analyses indicated that ID in audibility along with ID in MOC-induced TEOAE suppression significantly accounted for the increased magnitude of the REA for DL among older adults. Unexpectedly, ID in neural timing for speech-ABR did not account for the increased REA (see discussion section, second article).

Particularly interesting is the association between ID in audibility and the REA. This is the first study to report that small ID in audibility, despite the lack of significant audibility difference between ears, in older adults with age-appropriate hearing could be implicated on the pronounced magnitude of the REA for DL tasks. Based on these results, it was proposed that ID in audibility could have either increased or reduced the external redundancy (i.e., acoustic features) of the speech stimuli, which in turn either enhanced or diminished the neural representation of the speech

stimuli. Indeed, higher (or lower) auditory inputs from either ear might result in a stronger (or weaker) neural signal from the ear exposed to the louder (or softer) stimulus (Boudreau & Tsuchitani, 1968). Accordingly, this effect may either increase or decline auditory speech processing, ultimately leading to improved (or reduced) performance during DL tasks. Consistent with this idea, it would be reasonable that an increased ID in audibility in favor of the RE may have led to a larger REA for DL. Speech processing in the RE is already more efficient due to the direct access to the left hemisphere (Kimura, 1961a,b). In addition, small changes in intensity in favor of the RE significantly enhances the REA in young and older adults (Hugdahl et al., 2008; Westerhausen et al., 2009; Passow et al., 2012). Thus, increased RE audibility would likely improve RE processing ultimately increasing the REA for DL (Westerhausen, 2019).

However, it should be kept in mind that an increased ID in audibility favoring the RE also implies reduced audibility in the LE. A much closer inspection of the results showed that RE audibility was not significantly correlated with improved performance in the RE for DL in either the nonforced ($r = .031$, $p = .799$) or the forced attention ($r = .008$, $p = .948$) paradigms. Conversely, LE audibility was significantly correlated with worse LE performance in DL in both the nonforced ($r = -.279$, $p = .023$) and forced attention ($r = -.280$, $p = .023$) paradigms (see Supplementary Tables 1 and 2, second article). These results indicate that changes in the magnitude of the REA due to ID in audibility were driven by reduced LE audibility rather than by better RE audibility. These results also imply that even in the absence of significant audibility differences between both ears, the LE auditory pathway seems to depend more on audibility than the RE pathway to process speech stimuli. In fact, previous studies in young and older adults have shown that the LE requires around 6 to 9 dB extra (while keeping the RE intensity constant) to perform as similar as the RE in DL tasks (i.e., no ear advantage), and around 9 to 15 dB extra to overcome the REA, shifting to a LE

advantage (Hugdahl et al., 2008; Westerhausen et al., 2009; Passow et al., 2012, 2014). Thus, taking the above-mentioned studies into account along with the results from this thesis (i.e., an association between audibility in the LE and worse DL performance in the LE), it may be concluded that among older adults the LE pathway depends more on audibility (i.e., external redundancy) than the RE to process speech, at least in competing situations such as DL.

It should also be mentioned that the effects of ID in audibility might be more evident on DL tasks that use speech stimuli with low lexical content. This might occur because reducing contextual cues (e.g., lexical) forces subjects to strongly rely on the acoustic features (i.e., external redundancy) of the auditory signal to enable accurate processing (Findlen & Roup, 2011). Thus, it may be possible that ID in audibility (e.g., reduced external redundancy) would further decline processing of the speech signal in the weaker ear (i.e., LE), leading to a larger interaural asymmetry for DL performance. The results from this study support this premise. Conversely, increasing contextual cues in the speech stimuli could attenuate the effect of ID in audibility on speech processing in DL tasks among older adults. During competing acoustic situations (e.g., dichotic listening), older adults strongly rely on lexical cues and top-down processing for the recognition of speech stimuli (Findlen & Roup, 2016). For example, Jerger et al. (1994) found that ID in audibility explained only 5% of the REA for DL in older adults with presbycusis (with ID in audibility of around 30 dB), as opposed to the approximately 16% reported by this study. Jerger et al. used the dichotic sentence identification test (DSI; Fifer et al., 1983) to evaluate DL performance in older adults, and sentences have relatively more lexical and phonetic content as opposed to other speech stimuli (Findlen & Roup, 2011). Thus, even in the presence of compromised bottom-up processing (i.e., increased ID in audibility of around 30dB), older adult's ability to rely on lexical cues and top-down processing may have compensated for potential speech processing difficulties

attributed to increased ID in audibility during DL stimulation. Therefore, the use of CV syllables could serve to minimize (or to avoid) the lexical effects of top-down processes in older adults during DL tasks. This might be useful to define whether age-related declines in DL performance among older adults (e.g., larger REA or reduced overall scores) might be the result of bottom-up (auditory processing) or top-down (cognitive processing) difficulties, or a combination of both.

Regarding the MOC efferent strength, results from the present thesis demonstrated that ID in MOC-induced TEOAE suppression significantly contributed to the magnitude of the REA for DL. This association suggest that MOC efferent reflex (suppression) could be involved in DL performance, although its exact role is unknow. The MOC efferent system has been related to selective attention, protection of the ear from acoustic trauma, and reduction of the effects of masking noise (Guinan, 2006). About the latter, several studies have found that the MOC efferent system enhances the encoding of speech signals in the presence of competing noise (Kumar & Vanaja, 2004; Kalaiah et al., 2017). The auditory efferent system seems to improve the signal to noise ratio for complex stimuli throughout an “anti-masking” effect (Mukari et al., 2020). It has been proposed that this anti-masking effect arises because the MOC system increases the neural activity measured in challenging acoustic conditions (e.g., competing noise), thereby improving the audibility of speech sounds (Guinan, 2006; Garinis et al., 2008). It is thus possible that during DL stimulation, the simultaneous presentation of the CV-syllable in the contralateral ear could be considered as competing noise. Accordingly, the MOC system may have been activated with the aim to reduce the effects of the noise (contralateral speech stimuli) improving speech processing. Thus, the ear with a more effective MOC system may have been able to exert more suppression reducing the competing stimuli from the contralateral ear, increasing speech processing in the same ear (with a more efficient MOC system). The present results showed that MOC-induced TEOAE suppression

did not significantly differ between both ears among older adults. These results suggest that MOC functionality was, in average, similar between the RE and the LE among older adults. However, individual results indicated that older adults exhibited clear ID in MOC induced TEOAE suppression, showing differences in MOC efferent suppression ranging from ± 0 to 5.5 dB SNR between both ears. This ID in MOC-induced TEOAE suppression observed across individual results, and not as a group, could have been functionally enough to improve speech processing in one ear versus the other. This view is consistent with the significant association between ID in MOC-induced TEOAE suppression in favor of the RE (i.e., less TEOAE suppression in the LE) and the larger REA for DL found among older adults.

In summary, the results from the present study support the hypothesis that ID in sensory processing at lower levels of the auditory system explain, at least in part, the increased magnitude of the REA for DL among older adults. Specifically, ID in peripheral (i.e., pure-tone thresholds, TEOAE and MOC-induced TEOAE suppression) auditory processing, even in the absence of statistically significant differences, seem to play an important role on DL performance among older adults, particularly on the LE. The role of the MOC efferent system on DL is less clear. However, the fact that there was a significant association between TEOAE suppression and DL performance suggests that age-related declines across several levels of the ascending and descending auditory pathways may contribute to the increased magnitude of the REA for DL among older adults. Results from the study showed significantly delayed neural timing encoding for speech-ABR in the LE compare to the RE in older adults, but ID in neural timing for speech-ABR measures were not significantly associated with the REA's magnitude for DL. These results were rather unexpected considering that interaural latency differences for click-ABR (i.e., peak V and interpeak I-V) have been

significantly correlated with the magnitude of the REA in DL to CV-syllables in young adults (Hu & Lau, 2017). Moreover, decreased DL scores in the RE have been significantly correlated with increased latencies for speech-ABR onset (i.e., V-A) components in young adults (Lotfi et al., 2019). We speculate that top-down attentional control may have influenced neural timing encoding of speech sounds thereby attenuating any potential effects due to ID in neural timing at the brainstem level on DL performance and ultimately on the magnitude of the REA. While there was no any significant correlation between the REA's magnitude and ID in speech-ABR neural timing, these results are not interpreted as indicating that subcortical neural conduction time does not contribute to DL performance among older adults. Future studies should be carried out to elucidate the role of subcortical neural conduction time in DL tasks among older adults.

7.3 ID in sensory processing at lower levels of the auditory system and their effect on SIN performance.

It was hypothesized that the magnitude of ID in peripheral and subcortical auditory processing would account for SIN performance among older adults. The results demonstrated that ID in peripheral (i.e., TEOAE) and subcortical (speech-ABR neural timing encoding) auditory processing contributed to SIN difficulties among older adults. However, these effects were only true for SIN scores in the HINT LE condition, whereby speech and noise were spatially separated. In a way, this result was expected considering that ID in sensory processing were consistently in disfavor of the LE overall suggesting that the LE pathway was weaker than the RE pathway for speech segregation amidst background noise. This result is in accordance with previous studies in older adults demonstrating significantly worse SIN performance in the LE than the RE among older adults (e.g., Divenyi and Haupt, 1997; Mukari et al., 2014; Behtani et al., in press).

However, ID in peripheral and subcortical processing did not contribute to SIN performance in the HINT NF condition, where the target speech and noise were coming directly from the same direction (e.g., 0-degree azimuth). This result indicates that small ID in sensory processing may not affect overall SIN performance among older adults with age-appropriate hearing, particularly when there is a more efficient auditory pathway (i.e., RE) to process (i.e., extract) the speech signal in the presence of background noise. This result is consistent with some evidence showing that even individuals with asymmetric hearing loss (without a hearing impairment in the best ear) may exhibit high SIN performance because the speech signal coming from the better hearing ear may be still successfully processed in the auditory cortex (Ostler & Crandell, 2001; Barona et al., 2019). In addition, older adult with increased working memory capacity may be able to deploy more cognitive resources to process speech stimuli in adverse listening situations (Gordon-Salant & Cole, 2016). Thus, small ID in peripheral and subcortical auditory processing that may probably affect accurate speech intelligibility particularly in the presence of background noise may be easily compensated by top-down mechanisms such as working memory.

In summary, the result from the present study partly supports the hypothesis that the magnitude of ID in peripheral and subcortical auditory processing accounts for SIN performance among older adults. However, these effects are only evident under competing listening conditions (i.e., HINT LE) whereby the weaker auditory pathway is forced to segregate the speech signal from background noise.

7.4 Implications of the study

From a neuroscientific perspective, the results from the present study are important because the source of variability accounting for the substantial increase in the REA for DL among older adults, which ranges between 10% and 30% (Jerger et al., 1994; Bellis & Wilber, 2001; Strouse & Wilson, 1999, 2001; Roup et al., 2006, 2011; Kam and Keith, 2010), has been mostly attributed to declines in cognitive functions (e.g., working memory, attention) and reduced callosal thickness. Therefore, the current results may help explain some of the performance variability in DL experienced by older adults. In addition, these results might increase our understanding of why older adults usually present reduced capacity to segregate and/or integrate binaural information.

From a clinical perspective, providing evidence that increased interaural asymmetry in DL performance among older adults might also have peripheral and subcortical origins would support the utilization of clinical training programs specifically designed to restore the DL deficit by implementing strategies oriented to improve the processing along the weaker auditory pathway reducing the asymmetry between ears.

Moreover, the fact that DL and SIN might share some of their underlying auditory mechanisms (Martin and Jerger, 2005; Walden & Walden, 2005; Bhatt & Wang, 2019), along with the evidence showing that an increased REA for DL may contribute to older adult's ability to understand speech in the presence of background noise (Lavie et al., 2013; Mukari et al., 2020) might bolster the notion that DL tests could potentially serve as a reliable clinical predictor of SIN difficulties among older listeners.

7.5 Limitations of the study

Several limitations of the work need to be acknowledged:

First, participants were mainly selected from a registry of participants who are actively involved in research. In addition, they all had normal hearing according to their age and sex; normal cognitive function and none of them had a history of language or neurological disorders. According to Schoof and Rosen (2016) these participants may be entitled as “super-agers”. While their biological characteristics (e.g., audibility and cognition) may be considered as a strength in this exploratory study, the results of this thesis may not accurately represent the general population of older adults. Further research investigating older adults with and without hearing loss along with other age-related declines such as cognition should be carried to elucidate whether these results may replicate in a more general population of older adults.

Second, some of the speech-ABR neural responses showed patterns of complex morphology. This may be attributed to background noise contamination or muscle artifact. In fact, some participants were excluded from the analysis due to large postauricular muscle response in at least one ear. Thus, techniques such as assessing in a soundproof booth may help reduce contamination noise when recording speech-ABR in older adults. Also, placing the electrodes to the earlobes may help reduce muscle artifact. Moreover, it has been shown (e.g., Akhoun et al., 2008) that even with insert earphone use, possible stimulus artifact contamination may emerge in normal hearing adults during speech-ABR recordings, which can be difficult to identify because of the similarity between stimulus and response. This possibility was minimized in the present study by presenting the speech stimulus using alternating polarities (Skoe & Kraus, 2010). However, futures studies should also

use electromagnetically shielded insert earphones to further increase the chances of removing the possibility of stimulus artifact contamination (Akhoun et al., 2008; Skoe & Kraus, 2010).

Third, the role of subcortical processing on DL performance may have been limited by the 40-ms /da/ syllable chosen to examine neural representation of temporal aspects of speech at the brainstem level. For example, no associations between the magnitude of the REA in DL and speech-ABR neural timing responses for transient peaks were found. Other speech-ABR components may be more useful to explain changes in the magnitude of the REA for DL. For example, it has been shown that the subcortical differentiation of contrastive speech sounds, such as the stop consonant components of the CV-syllables used in the DL task, do not occur in the onset response but manifest later in the formant transition portion of the syllable (Hornickel et al., 2009; Johnson et al., 2008). Specifically, the second and the third formant frequencies which are the primary cues for distinguishing stops consonants (Chodroff & Wilson, 2014) are represented by latency shifts during the formant structure (Johnson et al., 2008). However, this could not be tested with the current data because to investigate subcortical differentiation, speech-ABR should have been recorded using more than one CV-syllable as speech stimulus. Futures studies should investigate whether disparities in subcortical differentiation of stop consonant sounds (e.g., /ba/-/da/-/ga/) between right and left auditory pathways might explain changes in the REA's magnitude in DL among older adults.

Fourth, the suppression effect was based upon the difference between the average TEOAE responses across frequencies (1-4 kHz) with and without contralateral acoustic stimulation. Suppression effects are frequency specific, with the greatest amount of suppression observed within the 1.0–4.0 kHz range. MOC-induced TEOAE suppression was not measured in a

frequency-specific manner and thus, their effect may have been underestimated. Analysis of time-varying changes in MOC activity (suppression) may provide larger estimates of contralateral acoustic stimulation induced MOC activation than averaging across the entire epoch window (Bidelman & Bhagat, 2015). Moreover, MOC-induced TEOAE suppression was measured using the non-linear click method (Kemp et al., 1986), which may fail to represent the entire magnitude of the MOC inhibitory response (Guinan, 2006). A linear click method which captures both the linear and nonlinear part of the MOC inhibitory response (Mishra & Lutman, 2013) should be used for futures studies.

Fifth, SIN performance was measured with the HINT, which uses highly redundant sentences rich with semantic and syntactic context which provides contextual cues decreasing the reliance of the listener on acoustic cues. Thus, the potential effect of ID in peripheral and subcortical processing on SIN performance may have been obscured by older adult's ability to take considerable advantage of contextual cues to improve speech understanding in challenging acoustic situation (Pichora-Fuller et al., 1995). Future studies should evaluate SIN ability using a speech-in-noise test which minimizes the effects of working memory and linguistic context on recognition performance thereby forcing listeners to rely specially on acoustic cues. For example, the Test de Mots Dans le Bruit (Lagacé, 2010) may be considered as a good measure of basic auditory function because the effects of linguistic context (i.e., semantic) and working memory are minimized (Wilson et al., 2007).

7.6 Future directions

Several questions have come to light from the findings of the current work and warrant further investigation. For example, results from the first article revealed evidence of symmetric auditory brainstem processing for click stimuli among older adults. Although these results are consistent with previous studies in young and older adults (e.g., Hixson & Mosko, 1978; Rowe, 1978; Lauter & Karzon, 1990; Hornickel et al., 2009; Vander Werff & Burns, 2011; Peng et al., 2016), there is compelling evidence indicating a clear pattern of subcortical lateralization for click encoding in children and some young adults (e.g., Eldredge & Salamy, 1996; Sininger et al., 1998; Sininger & Cone-Wesson, 2006; Van Yper et al., 2016). Future studies should address this issue by investigating (A) if click or other simple (e.g., tones) stimuli are indeed asymmetrically processed at the brainstem level across the lifespan; and (B) if the pattern of brainstem lateralization is modified as a function of age. These analyses could also be extended to more complex and ecologically valid stimuli such as speech.

In addition, results from the first article demonstrated evidence of subcortical laterality of speech encoding among older adults. These results agreed with previous studies in young adults (e.g., Ahadi et al., 2014; Hornickel et al., 2009; Sinha and Basavaraj 2010). However, a novel result that has not previously been reported in either younger or older adults emerged. Older adults exhibited a larger spectral F0 amplitude for LE presentation than RE presentation as opposed to the studies in young adults demonstrating a rightward laterality or even no laterality for F0 encoding. In the discussion section of the first article, it was hypothesized that bilingualism may have accounted for the different results between this study and previous studies carried out in young adults. This hypothesis was based on current evidence suggesting that bilingualism produces better neural encoding of acoustic elements of complex sounds, based on speech-ABR studies (Kraus &

Anderson, 2014; Krishnan & Gandour, 2009, Krishnan et al., 2012; Krizman et al., 2012; Skoe et al., 2017). However, with the current data, this hypothesis could not be tested as the degree of bilingualism in each participant was not determined since the effect of bilingualism was beyond the scope of this thesis. Future studies should investigate whether bilingualism is associated with asymmetric speech-ABR between right-and left-ear stimulation among older adults.

The findings from the second article suggest that ID in speech-ABR neural timing encoding of transient (onset and offset) components may not play a role in the REA for DL. This was unexpected considering that interaural latency differences for click-ABR and increased latencies for speech-ABR transient components have been significantly correlated with DL results (Hu & Lau, 2017; Lotfi et al., 2019), suggesting that neural conduction time might influence DL performance. To explain these results, it was suggested that top-down corticofugal influences enhanced brainstem representation of selective features of speech sounds during DL and reduced any effect attributed to ID in neural timing for speech encoding. Future studies should investigate speech-ABR using dichotic stimulation with CV syllables with controlled attention to right or left ear to test whether attention might modulate neural conduction time at the brainstem level.

Results from the third article revealed that ID in subcortical processing (speech-ABR neural timing encoding) were significantly associated with SIN performance among older adults. These results are consistent with previous studies in young and middle-aged adults showing significant correlations between speech-ABR neural timing and SIN performance (Parbery-Clark et al., 2011, 2012). Moreover, previous studies in older adults have shown that pitch cues, such as the fundamental frequency, significantly contribute to SIN performance (Anderson et al., 2011; Jain et al., 2019), especially in listening situations whereby speech and noise are not spatially separated

(Anderson et al., 2011). As previously mentioned, older adults exhibited a larger spectral F0 amplitude for LE presentation than RE presentation. However, ID in frequency encoding (e.g., F0) were not calculated in the current work. It would be of interest to investigate whether subcortical differences in fundamental frequency encoding between right and left auditory pathways contribute to SIN difficulties among older adults.

7.7 Conclusion

The objective of this doctoral thesis was three-fold: to investigate if older adults exhibited ID in peripheral and subcortical auditory processing, and whether the magnitude of these ID in sensory processing at lower levels of the auditory system were associated with the magnitude of the REA for DL and with SIN performance. The results from the present study show that older adults exhibit ID in peripheral auditory processing. However, as a group, they do not demonstrate a clear pattern of peripheral laterality as young adults do. Conversely, at the brainstem level, older adults demonstrate a clear pattern of laterality for the encoding of frequency and temporal acoustic components of speech like the pattern observed among young adults.

Moreover, results of the current thesis provide novel evidence suggesting that changes in the magnitude of the REA for DL among older adults could even originate from small (not statistically relevant) ID in sensory processing occurring at lower (i.e., peripheral) portions of the auditory system. Specifically, the present findings indicate that differences in sensory processing between right and left auditory pathways may affect DL performance, particularly by declining LE processing, at a preattentive bottom-up sensory stage of auditory processing. These results particularly complement with the structural model of DL proposed by Kimura (1967) by suggesting

that age-related declines preferentially targeting the LE pathway contribute to the enhanced magnitude of the REA for speech stimuli usually observed in older adults.

The effects of ID in peripheral and subcortical processing extend to other complex perceptual processes such as understanding speech in the presence of background noise. However, this effect is particularly evident under competing binaural listening conditions whereby the weaker auditory pathway (i.e., LE) is forced to process (segregate) the speech signal from background noise. ID in peripheral and subcortical auditory processing do not affect overall SIN performance among older adults. This result suggests that age-related changes in the peripheral and central auditory system would have a greater impact on the LE pathway significantly declining speech processing in the presence of background noise in the LE than the RE.

In addition, the present results support the link of cognitive function in DL and SIN performance among older adults. Result from this thesis support the hypothesis that the increased REA's magnitude in DL with advancing age may originate from age-related changes in cognitive abilities (Bellis & Wilber, 2001; Hällgren et al., 2001; Hommet et al., 2010). Specifically, the present findings indicate that both speed of processing and cognitive flexibility contribute to the enlarged REA among older adults. Also, results from this thesis bolster the role of working memory as a top-down mechanism for speech understanding during challenging listening conditions where the speech signal is further degraded as result of reduced sensory processing attributed to a weaker auditory pathway (i.e., LE).

References

- Ahadi, M., Pourbakht, A., Jafari, A. H., & Jalaie, S. (2014). Effects of stimulus presentation mode and subcortical laterality in speech-evoked auditory brainstem responses. *International journal of audiology*, 53(4), 243-249.
- Akhoun, I., Moulin, A., Jeanvoine, A., Ménard, M., Buret, F., Vollaie, C., ... & Thai-Van, H. (2008). Speech auditory brainstem response (speech ABR) characteristics depending on recording conditions, and hearing status: an experimental parametric study. *Journal of Neuroscience Methods*, 175(2), 196-205.
- Allen, L., Richey, M., Chai, Y., & Gorski, R. (1991). Sex differences in the corpus callosum of the living human being. *Journal of Neuroscience*, 11, 933-942.
- Anderson, S., Parbery-Clark, A., White-Schwoch, T., & Kraus, N. (2012). Aging affects neural precision of speech encoding. *Journal of Neuroscience*, 32(41), 14156-14164.
- Anderson, S., Parbery-Clark, A., Yi, H. G., & Kraus, N. (2011). A neural basis of speech-in-noise perception in older adults. *Ear and hearing*, 32(6), 750.
- Anderson, S., White-Schwoch, T., Parbery-Clark, A., & Kraus, N. (2013). A dynamic auditory-cognitive system supports speech-in-noise perception in older adults. *Hearing research*, 300, 18-32.
- Andersson, M., Reinvang, I., Wehling, E., Hugdahl, K., & Lundervold, A. J. (2008). A dichotic listening study of attention control in older adults. *Scandinavian journal of psychology*, 49(4), 299-304.
- Barona, R., Vizcaíno, J. A., Krstulovic, C., Barona, L., Comeche, C., Montalt, J., ... & Polo, C. (2019). Does Asymmetric Hearing Loss Affect the Ability to Understand in Noisy Environments? *The Journal of International Advanced Otology*, 15(2), 267.
- Behtani, L., Fuente, A., Ianiszewski, A., Al Osman, R., Hickson, L. (in press). Right-ear advantage for unaided and aided speech perception in noise in older adults. *The Journal of International Advanced Otology*.
- Bellis, T. J., & Wilber, L. A. (2001). Effects of aging and gender on interhemispheric function. *Journal of Speech, Language, and Hearing Research*.

Ben-David BM, Tse VY, Schneider BA. (2012). Does it take older adults longer than younger adults to perceptually segregate a speech target from a background masker? *Hear Res.* 290 (1–2):55–63

Bhatt, I. S., & Wang, J. (2019). Evaluation of dichotic listening performance in normal-hearing, noise-exposed young females. *Hearing research*, 380, 10-21.

Bidelman, G. M., & Bhagat, S. P. (2015). Right-ear advantage drives the link between olivocochlear efferent ‘antimasking’ and speech-in-noise listening benefits. *Neuroreport*, 26(8), 483-487.

Bless, J. J., Westerhausen, R., Arciuli, J., Kompus, K., Gudmundsen, M., & Hugdahl, K. (2013). “Right on all occasions?”—On the feasibility of laterality research using a smartphone dichotic listening application. *Frontiers in Psychology*, 4, 42.

Boudreau, J. C., & Tsuchitani, C. (1968). Binaural interaction in cat superior olive S segment. *Journal of Neurophysiology*, 31, 442–454.

Bryden, M.P. (1988) An overview of the dichotic listening procedure and its relation to cerebral organization. In: Hugdahl, K. (Ed.), *Handbook of Dichotic Listening: Theory, Methods and Research*. Wiley and Sons, New York, pp. 1- 44

Bryden, M. P., Munhall, K., & Allard, F. (1983) Attentional biases and the right-ear effect in dichotic listening. *Brain and Language*, 18, 236–248.

Bryden, M. P. & Murray, J. E. (1985). Toward a model of dichotic listening performance. *Brain and Cognition*, 4, 241-257.

Broadbent, D. E. (1954). The role of auditory localization in attention and memory span. *Journal of Experimental Psychology*, 47, 191-196.

Broadbent, D. E. (1958). *Perception and communication*. New York: Oxford University Press.

Bruder, G. E. (1991). Dichotic listening: New developments and applications in clinical research. *Annals of the New York Academy of Sciences*, 620, 217-232.

Carter, A. S., Noe, C. M., & Wilson, R. H. (2001). Listeners who prefer monaural to binaural hearing aids. *Journal of the American Academy of Audiology*, 12(5), 261-272.

Chandrasekaran, B., & Kraus, N. (2010). Music, noise-exclusion, and learning. *Music Perception*, 27(4), 297-306.

Chao, L. L., & Knight, R. T. (1997). Prefrontal deficits in attention and inhibitory control with aging. *Cerebral Cortex*, 7(1), 63–69.

Chodroff, E., & Wilson, C. (2014). Burst spectrum as a cue for the stop voicing contrast in American English. *The Journal of the Acoustical Society of America*, 136(5), 2762-2772.

Chung, D. Y., Willson, G. N., & Gannon, R. P. (1983). Lateral differences in susceptibility to noise damage. *Audiology*, 22(2), 199-205.

Colbourn, C. J. & Lishman, W. A. (1979). Lateralization of function and psychotic illness: A left hemisphere deficit? In Gruzeliier, J. & Flor-Henry, P (Eds.), *Hemispheric Asymmetries of Function in Psychopathology* (pp. 539-559). Amsterdam, The Netherlands: Elsevier.

Cruickshanks, K. H., Wiley, T. L., Tweed, T. S., Klein, B. E., Klein, R., Mares-Perlman, J. A., & Nondahl, D. M. (1998). Prevalence of hearing loss in older adults in Beaver Dam, Wisconsin. The epidemiology of hearing loss study. *American Journal of Epidemiology*, 148, 879–886.

Dean, I., Harper, N. S., & McAlpine, D. (2005). Neural population coding of sound level adapts to stimulus statistics. *Nature neuroscience*, 8(12), 1684-1689.

Desmette, D., Hupet, M., Schelstraete, M. A., & Van der Linden, M. (1995). Adaptation en langue française du « Reading Span Test » de Daneman et Carpenter (1980). *L'année Psychologique*, 95(3), 459-482.

Divenyi, P. L., & Haupt, K. M. (1997). Audiological correlates of speech understanding deficits in elderly listeners with mild-to-moderate hearing loss. I. Age and lateral asymmetry effects. *Ear and hearing*, 18(1), 42-61.

Dolcos, F., Rice, H. J., & Cabeza, R. (2002). Hemispheric asymmetry and aging: Right hemisphere decline or asymmetry reduction. *Neuroscience & Biobehavioral Reviews*, 26(7), 819–825.

Doraiswamy, P., Figiel, G., Husain, M., McDonald, W., Shah, S., Boyko, O., Jr, E. E., & Krishnan, K. (1991). Aging of the human corpus callosum: Magnetic resonance imaging in normal volunteers. *Journal of Neuropsychiatry and Clinical Neuroscience*, 3, 392-397.

Dubno, J. R., Ahlstrom, J. B., & Horwitz, A. R. (2002a). Spectral contributions to the benefit from spatial separation of speech and noise.

Dubno, J. R., Horwitz, A. R., & Ahlstrom, J. B. (2002b). Benefit of modulated maskers for speech recognition by younger and older adults with normal hearing. *The Journal of the Acoustical Society of America*, 111(6), 2897-2907.

Eldredge, L., & Salamy, A. (1996). Functional auditory development in preterm and full-term infants. *Early human development*, 45(3), 215-228.

Emmerich, D. S., Harris, J., Brown, W. S., & Springer, S. P. (1988). The relationship between auditory sensitivity and ear asymmetry on a dichotic listening task. *Neuropsychologia*, 26(1), 133-143.

Feeney, M. P., Keefe, D. H., & Marryott, L. P. (2003). Contralateral acoustic reflex thresholds for tonal activators using wideband energy reflectance and admittance. *Journal of Speech, Language, and Hearing Research*.

Fifer R, Jerger J, Berlin C, Tobey E, Campbell J. (1983). Development of a dichotic sentence identification test for hearing-impaired adults. *Ear Hear* 4:300-305.

Findlen, U. M., & Roup, C. M. (2011). Dichotic speech recognition using CVC word and nonsense CVC syllable stimuli. *Journal of the American Academy of Audiology*, 22(1), 13-22.

Findlen, U. M., & Roup, C. M. (2016). The Effect of Lexical Content on Dichotic Speech Recognition in Older Adults. *Journal of the American Academy of Audiology*, 27(1), 13-28.

Fischer, M. E., Cruickshanks, K. J., Nondahl, D. M., Klein, B. E., Klein, R., Pankow, J. S. et al. (2017). Dichotic digits test performance across the ages: results from two large epidemiologic cohort studies. *Ear and hearing*, 38(3), 314.

Fling BW, Chapekis M, Reuter-Lorenz PA, Anguera J, Bo J, Langan J, et al. (2011). Age differences in callosal contributions to cognitive processes. *Neuropsychologia*, 49(9): 2564-2569

Foundas, A. L., Corey, D. M., Hurley, M. M., & Heliman, K. M. (2006). Verbal dichotic listening in right and left-handed adults: laterality effects of directed attention. *Cortex*, 42(1), 79-86.

Füllgrabe, C., Moore, B. C., & Stone, M. A. (2015). Age-group differences in speech identification despite matched audiometrically normal hearing: contributions from auditory temporal processing and cognition. *Frontiers in aging neuroscience*, 6, 347.

Gadea, M., Marti-Bonmatí, L., Arana, E., Espert, R., Casanova, V., & Pascual, A. (2002). Dichotic listening and corpus callosum magnetic resonance imaging in relapsing-remitting multiple sclerosis with emphasis on sex differences. *Neuropsychology*, 16(2), 275.

Garinis, A. C., Glatcke, T., & Cone-Wesson, B. K. (2008). TEOAE suppression in adults with learning disabilities. *International journal of audiology*, 47(10), 607-614.

- Garinis, A. C., Glatcke, T., & Cone, B. K. (2011). The MOC reflex during active listening to speech. *Journal of Speech, Language, and Hearing Research*.
- Gates, G., & Cooper JC Jr. (1991). Incidence of hearing decline in the elderly. *Acta Oto-Laryngologica*. 111; (2): 240-248
- Gates GA, Cooper JC, Kannel WB, Miller NJ. (1990) Hearing in the Elderly: The Framingham Cohort, 1983-1985. Part I. Basic Audiometric Test Results. *Ear Hear*. 11: 247–256.
- Gates, G. A., & Mills, J.H. (2005). Presbycusis. *The Lancet*, 366(9491), 1111-1120.
- Glorig, A., Grings, W., & Summerfield, A. (1958). Hearing loss in industry. *The Laryngoscope*, 68(3), 447-465.
- Goldstein, S. G., & Braun, L. S. (1974). Reversal of expected transfer as a function of increased age. *Perceptual and Motor Skills*, 38, 1139-1145.
- Goldstein, G., & Shelly, G. (1981). Does the right hemisphere age more rapidly than the left? *Journal of Clinical Neuropsychology*, 3, 65–78.
- Gootjes, L., Bouma, A., Van Strien, J. W., Van Schijndel, R., Barkhof, F., & Scheltens, P. (2006). Corpus callosum size correlates with asymmetric performance on a dichotic listening task in healthy aging but not in Alzheimer's disease. *Neuropsychologia*, 44(2), 208-217.
- Gootjes, L., Scheltens, P., Van Strien, J. W., & Bouma, A. (2007). Subcortical white matter pathology as a mediating factor for age-related decreased performance in dichotic listening. *Neuropsychologia*, 45(10), 2322-2332.
- Gootjes, L., Van Strien, J. W., & Bouma, A. (2004). Age effects in identifying and localising dichotic stimuli: a corpus callosum deficit. *Journal of clinical and experimental neuropsychology*, 26(6), 826-837.
- Gordon, H. W. (1980). Degree of ear asymmetries for perception of dichotic chords and for illusory chord localization in musicians of different levels of competence. *Journal of Experimental Psychology. Human Perception and Performance*, 6, 516-527.
- Gordon-Salant, S. (2005). Hearing loss and aging: New research findings and clinical implications. *Journal of Rehabilitation Research and Development*, 42(4 suppl 2), 9-24.

- Gordon-Salant, S., & Cole, S. S. (2016). Effects of age and working memory capacity on speech recognition performance in noise among listeners with normal hearing. *Ear and Hearing*, 37(5), 593-602.
- Gosselin, P. A., & Gagné, J. P. (2011). Older adults expend more listening effort than young adults recognizing audiovisual speech in noise. *International journal of audiology*, 50(11), 786-792.
- Graham, R. L., & Hazell, J. W. P. (1994). Contralateral suppression of transient evoked otoacoustic emissions: intra-individual variability in tinnitus and normal subjects. *British journal of audiology*, 28(4-5), 235-245.
- Guinan Jr, J. J. (2006). Olivocochlear efferents: anatomy, physiology, function, and the measurement of efferent effects in humans. *Ear and hearing*, 27(6), 589-607.
- Guinan Jr, J. J. (2018). Olivocochlear efferents: Their action, effects, measurement and uses, and the impact of the new conception of cochlear mechanical responses. *Hearing research*, 362, 38-47.
- Guinan, J. J., Backus, B. C., Lilaonitkul, W., & Aharonson, V. (2003). Medial olivocochlear efferent reflex in humans: otoacoustic emission (OAE) measurement issues and the advantages of stimulus frequency OAEs. *Journal of the Association for Research in Otolaryngology*, 4(4), 521-540.
- Hällgren, M., Larsby, B., Lyxell, B., & Arlinger, S. (2001). Cognitive effects in dichotic speech testing in elderly persons. *Ear and Hearing*, 22(2), 120-129.
- Heine, C., & Browning, C. J. (2002). Communication and psychosocial consequences of sensory loss in older adults: overview and rehabilitation directions. *Disability and rehabilitation*, 24(15), 763-773.
- Hirnstein, M., Westerhausen, R., Korsnes, M. S., & Hugdahl, K. (2013). Sex differences in language asymmetry are age-dependent and small: A large-scale, consonant–vowel dichotic listening study with behavioral and fMRI data. *Cortex*, 49(7), 1910-1921.
- Hiscock, M., & Kinsbourne, M. (2011). Attention and the right-ear advantage: What is the connection? *Brain and cognition*, 76(2), 263-275.
- Hixson, W. C., & Mosko, J. D. (1979). Normative bilateral brainstem evoked response data for a naval aviation student population: group statistics (No. NAMRL-1262). Naval Aerospace Medical Research Lab Pensacola Fl.

Hommet, C., Mondon, K., Berrut, G., Gouyer, Y., Isingrini, M., Constans, T., & Belzung, C. (2010). Central auditory processing in aging: the dichotic listening paradigm. *The journal of nutrition, health & aging*, 14(9), 751-756.

Hornickel, J., Skoe, E., Nicol, T., Zecker, S., & Kraus, N. (2009). Subcortical differentiation of stop consonants relates to reading and speech-in-noise perception. *Proceedings of the National Academy of Sciences*, 106(31), 13022-13027.

Hornickel, J., Skoe, E., & Kraus, N. (2009). Subcortical laterality of speech encoding. *Audiology and Neurotology*, 14(3), 198-207.

Hu, X. J., & Lau, C. C. (2017). Central conduction time in auditory brainstem response and ear advantage in dichotic listening across menstrual cycle. *PloS one*, 12(11).

Hugdahl, K. (2003). Dichotic listening in the study of auditory laterality. In K. Hugdahl & R. J. Davidson (Eds.), *The Asymmetrical Brain* (pp. 441-475). Cambridge, MA: The MIT Press.

Hugdahl, K. & Andersson, L. (1986). The “forced-attention paradigm” in dichotic listening to CV-syllables: A comparison between adults and children. *Cortex*, 22, 417-432.

Hugdahl, K., Carlsson, G., & Eichele, T. (2001). Age effects in dichotic listening to consonant-vowel syllables: interactions with attention. *Developmental neuropsychology*, 20(1), 445-457.

Hugdahl, K., & Helland, T. (2013). Central auditory processing as seen from dichotic listening studies. In Musiek, F. & Chermak, G. (Eds.). (2013). *Handbook of central auditory processing disorder, volume I: Auditory Neuroscience and Diagnosis* (Vol. 1). Plural Publishing.

Hugdahl, K., Westerhausen, R., Alho, K., Medvedev, S., & Hamalainen, H. (2008). The effects of stimulus intensity on the right ear advantage in dichotic listening. *Neuroscience Letters*, 431(1), 90-94.

Hugdahl, K., Westerhausen, R., Alho, K., Medvedev, S., Laine, M., & Hämäläinen, H. (2009). Attention and cognitive control: Unfolding the dichotic listening story. *Scandinavian Journal of Psychology*.

Hugdahl, K., & Westerhausen, R. (2016). Speech processing asymmetry revealed by dichotic listening and functional brain imaging. *Neuropsychologia*, 93, 466-481.

Humes LE. (1996). Speech understanding in the elderly. *J Am Acad Audiol*. 1996; 7:161–167.

Humes, L. E., Coughlin, M., & Talley, L. (1996). Evaluation of the use of a new compact disc for auditory perceptual assessment in the elderly. *Journal-American Academy of Audiology*, 7, 419-427.

Humes L. E, Christopherson LA. (1991). Speech identification difficulties of hearing-impaired elderly persons: the contributions of auditory processing deficits. *J Speech Hear Res.* 34: 686–693.

Humes, L. E., Dubno, J. R., Gordon-Salant, S., Lister, J. J., Cacace, A. T., Cruickshanks, K. J., ... & Wingfield, A. (2012). Central presbycusis: a review and evaluation of the evidence. *Journal of the American Academy of Audiology*, 23(8), 635-666.

Humes, L. E., Lee, J. H., & Coughlin, M. P. (2006). Auditory measures of selective and divided attention in young and older adults using single-talker competition. *The Journal of the Acoustical Society of America*, 120(5), 2926-2937.

Humes LE, Roberts L. (1990). Speech recognition difficulties in hearing-impaired elderly: the contributions of audibility. *J Speech Hear Res.* 33:726–735.

Humes LE, Watson BU, Christensen LA, Cokely CG, Halling DC, Lee L (1994). Factors associated with individual differences in clinical measures of speech recognition among the elderly. *J Speech Hear Res.* 37; 465–474.

International Organization for Standardization. (2000) *Acoustics Statistical Distribution of Hearing Thresholds as a Function of Age*. ISO 7029. Geneva: ISO.

Jerger, J. (1970) Clinical Experience with impedance audiometry. *Arch Otolaryng*, 92, 311-324

Jerger, J., Alford, B., Lew, H., Rivera, V., & Chmiel, R. (1995). Dichotic listening, event-related potentials, and interhemispheric transfer in the elderly. *Ear and hearing*, 16(5), 482-498.

Jerger, J., Chmiel, R., Allen, J., & Wilson, A. (1994). Effects of age and gender on dichotic sentence identification. *Ear and hearing*, 15(4), 274-286.

Jerger, J., Jerger, S., & Pirozzolo, F. (1991). Correlational analysis of speech audiometric scores, hearing loss, age, and cognitive abilities in the elderly. *Ear and Hearing*, 12(2), 103-109.

Jerger, J., & Martin, J. (2006). Dichotic listening tests in the assessment of auditory processing disorders. *Audiological Medicine*, 4(1), 25-34.

Johnson, K. L., Nicol, T., Zecker, S. G., Bradlow, A. R., Skoe, E., & Kraus, N. (2008). Brainstem encoding of voiced consonant–vowel stop syllables. *Clinical Neurophysiology*, 119(11), 2623-2635.

Johnson, K. L., Nicol, T., Zecker, S. G., & Kraus, N. (2008). Developmental plasticity in the human auditory brainstem. *Journal of Neuroscience*, 28(15), 4000-4007.

Kalaiah, M. K., Nanchirakal, J. F., Kharmawphlang, L., & Noronah, S. C. (2017). Contralateral suppression of transient evoked otoacoustic emissions for various noise signals. *Hearing, Balance and Communication*, 15(2), 84-90.

Kam, A.C. S., & Keith, R. W. (2010). Aging effect on dichotic listening of Cantonese. *International journal of audiology*, 49(9), 651-656.

Kannan, P. M., & Lipscomb, D. M. (1974). Bilateral hearing asymmetry in a large population. *Journal of the Acoustical Society of America*, 55, 1092–1094.

Kemp, D. T. (1986). Otoacoustic emissions, travelling waves and cochlear mechanisms. *Hearing research*, 22(1-3), 95-104.

Keppler, H., Dhooge, I., Corthals, P., Maes, L., D’haenens, W., Bockstael, A., ... & Vinck, B. (2010). The effects of aging on evoked otoacoustic emissions and efferent suppression of transient evoked otoacoustic emissions. *Clinical Neurophysiology*, 121(3), 359-365.

Khalfa, S., & Collet, L. (1996). Functional asymmetry of medial olivo-cochlear system in humans. Towards a peripheral auditory lateralization. *Neuroreport* 7, 993-996.

Khalfa, S., Micheyl, C., Veuillet, E., & Collet, L. (1998). Peripheral auditory lateralization assessment using TEOAEs. *Hearing Research*, 121, 29–34.

Khalfa, S., Morlet, T., Micheyl, C., Morgon, A., & Collet, L. (1997). Evidence of peripheral hearing asymmetry in humans: clinical implications. *Acta Oto-Laryngologica*, 117(2), 192-196.

Kim, S., Frisina, R. D., & Frisina, D. R. (2006). Effects of age on speech understanding in normal hearing listeners: Relationship between the auditory efferent system and speech intelligibility in noise. *Speech communication*, 48(7), 855-862.

Kimura, D. (1961a). Some effects of temporal-lobe damage on auditory perception. *Canadian Journal of Psychology*, 15, 156-165.

- Kimura, D. (1961b). Cerebral dominance and the perception of verbal stimuli. *Canadian Journal of Psychology*, 15, 166-171.
- Kimura, D. (1967). Functional asymmetry of the brain in dichotic listening. *Cortex*, 3, 163-168.
- Kimura, D. (2011) From ear to brain. *Brain and Cognition*, 76(2), 214-217.
- Kinsbourne, M. (1970). The cerebral basis of lateral asymmetries in attention. *Acta Psychol* (33), 193-201.
- Kramer, A. F., Humphrey, D. G., Larish, J. F., Logan, G. D., & Strayer, D. L. (1994). Aging and inhibition: Beyond a unitary view of inhibitory processing in attention. *Psychology and Aging*, 9(4), 491-512.
- Krishnan, A., & Gandour, J. T. (2009). The role of the auditory brainstem in processing linguistically relevant pitch patterns. *Brain and language*, 110(3), 135-148.
- Krishnan, A., Gandour, J. T., & Bidelman, G. M. (2012). Experience-dependent plasticity in pitch encoding: from brainstem to auditory cortex. *Neuroreport*, 23(8), 498.
- Krishnan, A., Gandour, J. T., Ananthakrishnan, S., Bidelman, G. M., & Smalt, C. J. (2011). Functional ear (a) symmetry in brainstem neural activity relevant to encoding of voice pitch: A precursor for hemispheric specialization? *Brain and language*, 119(3), 226-231.
- Krishnan, A., Xu, Y., Gandour, J. T., & Cariani, P. A. (2004). Human frequency-following response: representation of pitch contours in Chinese tones. *Hearing research*, 189(1-2), 1-12.
- Krishnan, A., Xu, Y., Gandour, J., & Cariani, P. (2005). Encoding of pitch in the human brainstem is sensitive to language experience. *Cognitive Brain Research*, 25(1), 161-168.
- Kraus, N., & Anderson, S. (2014). Bilingualism enhances neural speech encoding. *The Hearing Journal*, 67(7), 40.
- Krizman, J., Marian, V., Shook, A., Skoe, E., & Kraus, N. (2012). Subcortical encoding of sound is enhanced in bilinguals and relates to executive function advantages. *Proceedings of the National Academy of Sciences*, 109(20), 7877-7881.
- Kumar, U. A., & Vanaja, C. S. (2004). Functioning of olivocochlear bundle and speech perception in noise. *Ear and hearing*, 25(2), 142-146.
- Lagacé, J. (2010). Développement du test de mots dans le bruit: mesure de l'équivalence des listes et données préliminaires sur l'effet d'âge. *Canadian Acoustics*, 38(2), 19-30.

- Lauter, J. L., & Karzon, R. G. (1990). Individual Differences in Auditory Electric Responses III. A Replication, with Observations of Individual vs. Group Characteristics. *Scandinavian audiology*, 19(2), 67-72.
- Lavie, L., Banai, K., & Attias, J. (2013). Dichotic listening: A predictor of speech-in-noise perception in older hearing-impaired adults? In *Proceedings of the International Symposium on Auditory and Audiological Research* (Vol. 4, pp. 357-364).
- Levine, R. A., Liederman, J., & Riley, P. (1988). The brainstem auditory evoked potential asymmetry is replicable and reliable. *Neuropsychologia*, 26(4), 603-614.
- Levine, R. A., & McGaffigan, P. M. (1983). Right-left asymmetries in the human brain stem: auditory evoked potentials. *Electroencephalography and clinical neurophysiology*, 55(5), 532-537.
- Lisowska, G., Namyslowski, G., Orecka, B., & Misiolek, M. (2014). Influence of aging on medial olivocochlear system function. *Clinical interventions in aging*, 9, 901-914.
- Lotfi, Y., Moossavi, A., Javanbakht, M., & Zadeh, S. F. (2019). Speech-ABR in contralateral noise: A potential tool to evaluate rostral part of the auditory efferent system. *Medical hypotheses*, 132
- MacPherson, S. E., Phillips, L. H., & Della Sala, S. (2002). Age, executive function, and social decision making: A dorsolateral prefrontal theory of cognitive aging. *Psychology and Aging*, 17(4), 598-609.
- Markevych, V., Asbjørnsen, A. E., Lind, O., Plante, E., & Cone, B. (2011). Dichotic listening and otoacoustic emissions: Shared variance between cochlear function and dichotic listening performance in adults with normal hearing. *Brain and cognition*, 76(2), 332-339.
- Martin, J. S., & Jerger, J. F. (2005). Some effects of aging on central auditory processing. *Journal of Rehabilitation Research & Development*, 42(4 Suppl 2), 25-44.
- McFadden, D. (1993). A speculation about the parallel ear asymmetries and sex differences in hearing sensitivity and otoacoustic emissions. *Hearing Research*, 68, 143-151.
- McFadden, D., Loehlin, J. C., & Pasanen, E. G. (1996). Additional findings on heritability and prenatal masculinization of cochlear mechanisms: click-evoked otoacoustic emissions. *Hearing Research*, 97(1-2), 102-119.
- McFadden, D., & Mishra, R. (1993). On the relation between hearing sensitivity and otoacoustic emissions. *Hearing research*, 71(1-2), 208-213.

- Mishra, S. K. (2014). Medial efferent mechanisms in children with auditory processing disorders. *Frontiers in human neuroscience*, 8, 860.
- Mishra, S. K., & Lutman, M. E. (2013). Repeatability of click-evoked otoacoustic emission-based medial olivocochlear efferent assay. *Ear and hearing*, 34(6), 789-798.
- Mishra, S. K., & Lutman, M. E. (2014). Top-down influences of the medial olivocochlear efferent system in speech perception in noise. *PLoS One*, 9(1), e85756.
- Moncrieff, D. W., Jorgensen, L., & Ortmann, A. (2013). Psychophysical auditory tests. *Handbook of Clinical Neurophysiology: Disorders of Peripheral and Central Auditory Processing*, Elsevier BV, Amsterdam, 217-234.
- Moore, D. R., Edmondson-Jones, M., Dawes, P., Fortnum, H., McCormack, A., Pierzycki, R. H., & Munro, K. J. (2014). Relation between speech-in-noise threshold, hearing loss and cognition from 40–69 years of age. *PloS one*, 9(9), e107720.
- Mukari, S. Z. M. S., Wahat, N. H. A., & Mazlan, R. (2014). Effects of ageing and hearing thresholds on speech perception in quiet and in noise perceived in different locations. *Korean journal of audiology*, 18(3), 112
- Mukari, S. Z. M. S., Yusof, Y., Ishak, W. S., Maamor, N., Chellapan, K., & Dzulkifli, M. A. (2020). Relative contributions of auditory and cognitive functions on speech recognition in quiet and in noise among older adults. *Brazilian journal of otorhinolaryngology*, 86(2), 149-156.
- Musiek, F. E. (1983). The evaluation of brainstem disorders using ABR and central auditory tests. Educational Services Division of Instrumentation Associates Incorporated.
- Musiek, F. E., Chermak, G. D., Weihing, J., Zappulla, M., & Nagle, S. (2011). Diagnostic accuracy of established central auditory processing test batteries in patients with documented brain lesions. *Journal of the American Academy of Audiology*, 22(6).
- Nasreddine, Z., Phillips, N., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Chertkow, H. (2005) The Montreal Cognitive Assessment, MoCA- A Brief Screening Tool for Mild Cognitive Impairment. *Journal of American Geriatrics Society*, 53(4), 695-699.
- Nilsson, M., Soli, S. D., & Sullivan, J. A. (1994). Development of the Hearing in Noise Test for the measurement of speech reception thresholds in quiet and in noise. *The Journal of the Acoustical Society of America*, 95(2), 1085-1099.

Oldfield, R. (1971) The assessment and analysis of handedness the Edinburgh inventory. *Neuropsychologia*, 9, 97-113.

Ostler, D. A., & Crandell, C. C. (2001). The effects of symmetrical and asymmetrical sensorineural hearing loss on speech perception in noise. *The Journal of the Acoustical Society of America*, 109(5), 2503-2503.

Parthasarathy, T. K. (2001). Aging and contralateral suppression effects on transient evoked otoacoustic emissions. *Journal of the American Academy of Audiology*, 12(2), 80-85.

Passow, S., Westerhausen, R., Hugdahl, K., Wartenburger, I., Heekeren, H. R., Lindenberger, U., & Li, S. C. (2014). Electrophysiological correlates of adult age differences in attentional control of auditory processing. *Cerebral Cortex*, 24(1), 249-260.

Passow, S., Westerhausen, R., Wartenburger, I., Hugdahl, K., Heekeren, H. R., Lindenberger, U., & Li, S.-C. (2012). Human aging compromises attentional control of auditory perception. *Psychology and Aging*, 27(1), 99–105.

Peng, L., Yu, S. L., Jing, Y., Chen, R. C., & Liang, J. P. (2016). Diffusion tensor imaging of the central auditory system in the elderly. *Lin chuang er bi yan hou tou jing wai ke za zhi= Journal of clinical otorhinolaryngology, head, and neck surgery*, 30(8), 637-640.

Philibert, B., Veuille, E., & Collet, L. (1998). Functional asymmetries of crossed and uncrossed medial olivocochlear efferent pathways in humans. *Neuroscience letters*, 253(2), 99-102.

Pichora-Fuller, M. K., Schneider, B. A., & Daneman, M. (1995). How young and old adults listen to and remember speech in noise. *The Journal of the Acoustical Society of America*, 97(1), 593-608.

Pollmann, S., Maertens, M., von Cramon, D. Y., Lepsien, J., & Hugdahl, K. (2002). Dichotic listening in patients with splenial and non-splenial callosal lesions. *Neuropsychology*, 16, 56-64.

Profant, O., Tintěra, J., Balogova, Z., Ibrahim, I., Jilek, M., & Syka, J. (2015). Functional changes in the human auditory cortex in ageing. *PLoS One*, 10(3).

Rimol, L., Eichele, T., & Hugdahl, K. (2006). The effect of voice-onset-time on dichotic listening with consonant–vowel syllables. *Neuropsychologia*, 44, 191-196.

Roup, C. M., Wiley, T. L., & Wilson, R. H. (2006). Dichotic word recognition in young and older adults. *Journal of the American Academy of Audiology*, 17(4), 230-240; quiz 297-238.

Roup, C. M. (2011). Dichotic word recognition in noise and the right-ear advantage. *Journal of Speech, Language, and Hearing Research*.

Rowe III, M. J. (1978). Normal variability of the brain-stem auditory evoked response in young and old adult subjects. *Electroencephalography and Clinical Neurophysiology*, 44(4), 459-470.

Schneider, B. A., Pichora-Fuller, K., & Daneman, M. (2010). Effects of senescent changes in audition and cognition on spoken language comprehension. In *The aging auditory system* (pp. 167-210). Springer, New York, NY.

Schoof, T., & Rosen, S. (2014). The role of auditory and cognitive factors in understanding speech in noise by normal-hearing older listeners. *Frontiers in aging neuroscience*, 6, 307.

Schoof, T., & Rosen, S. (2016). The role of age-related declines in subcortical auditory processing in speech perception in noise. *Journal of the Association for Research in Otolaryngology*, 17(5), 441-460.

Sidtis, J. J. (1981). The complex tone test: Implications for the assessment of auditory laterality effects. *Neuropsychologia*, 19, 103-111.

Simmons, F. B., & Beatty, D. L. (1962). A theory of middle ear muscle function at moderate sound levels. *Science*, 138(3540), 590-592.

Sinha, S. K., & Basavaraj, V. (2010). Lateral asymmetry in speech processing at the brainstem: evidence from speech evoked ABR. *Journal of the All India Institute of Speech & Hearing*, 29(1).

Sininger, Y. S., Cone-Wesson, B., & Abdala, C. (1998). Gender distinctions and lateral asymmetry in the low-level auditory brainstem response of the human neonate. *Hearing Research*, 126(1-2), 58-66.

Sininger, Y. S., & Cone-Wesson, B. (2004). Asymmetric cochlear processing mimics hemispheric specialization. *Science*, 305(5690), 1581-1581.

Sininger, Y. S., & Cone-Wesson, B. (2006). Lateral asymmetry in the ABR of neonates: evidence and mechanisms. *Hearing research*, 212(1-2), 203-211.

Skoe, E., Burakiewicz, E., Figueiredo, M., & Hardin, M. (2017). Basic neural processing of sound in adults is influenced by bilingual experience. *Neuroscience*, 349, 278-290.

Skoe E. & Kraus, N. (2010). Auditory brainstem response to complex sounds: A tutorial. *Ear Hear*, 31, 302.

Soli, S. D., & Wong, L. L. (2008). Assessment of speech intelligibility in noise with the Hearing in Noise Test. *International Journal of Audiology*, 47(6), 356-361.

Sparks, R. & Geschwind, N. (1968). Dichotic listening in man after section of neocortical commissures. *Cortex*, 4, 3-16.

Springer, S. P., & Gazzaniga, M. S. (1975). Dichotic testing of partial and complete split-brain subjects. *Neuropsychologia*, 13(3), 341-346.

Strouse, A., Wilson, R. H., & Brush, N. (2001). Effect of order bias on the recognition of dichotic digits in young and elderly listeners. *Audiology*, 39(2), 93-101.

Stuart, A., & Butler, A. K. (2012). Contralateral suppression of transient otoacoustic emissions and sentence recognition in noise in young adults. *Journal of the American Academy of Audiology*, 23(9), 686-696.

Stuart, A., & Cobb, K. M. (2015). Reliability of measures of transient evoked otoacoustic emissions with contralateral suppression. *Journal of Communication Disorders*, 58, 35-42.

Stuart, A., & Kerls, A. N. (2018). Does contralateral inhibition of transient evoked otoacoustic emissions suggest sex or ear laterality effects? *American journal of audiology*, 27(3), 272-282.

Sullivan EV, Pfefferbaum A, Adalsteinsson E, Swan GE, and Carmelli D. (2002). Differential rates of regional brain change in callosal and ventricular size: A 4-year longitudinal MRI study of elderly men. *Cerebral Cortex*, 12: 438-445

Tadros, S. F., Frisina, S. T., Mapes, F., Kim, S., Frisina, D. R., & Frisina, R. D. (2005). Loss of peripheral right-ear advantage in age-related hearing loss. *Audiology and Neurotology*, 10(1), 44-52.

Takio, F., Koivisto, M., Jokiranta, L., Rashid, F., Kallio, J., Tuominen, T., ... & Hämäläinen, H. (2009). The effect of age on attentional modulation in dichotic listening. *Developmental Neuropsychology*, 34(3), 225-239.

Tervaniemi, M., & Hugdahl, K. (2003). Lateralization of auditory-cortex functions. *Brain research reviews*, 43(3), 231-246.

Thomsen, T., Specht, K., Hammar, Å., Nytingnes, J., Ersland, L., & Hugdahl, K. (2004). Brain localization of attentional control in different age groups by combining functional and structural MRI. *Neuroimage*, 22(2), 912-919.

- Tremblay, K. L., Piskosz, M., & Souza, P. (2003). Effects of age and age-related hearing loss on the neural representation of speech cues. *Clinical Neurophysiology*, 114(7), 1332-1343.
- Vander Werff, K. R., & Burns, K. S. (2011). Brain stem responses to speech in younger and older adults. *Ear and hearing*, 32(2), 168-180.
- Van Yper, L. N., Vermeire, K., De Vel, E. F., Beynon, A. J., & Dhooge, I. J. (2016). Age-related changes in binaural interaction at brainstem level. *Ear and hearing*, 37(4), 434-442.
- Vincent, G. K., & Velkoff, V. A. (2010). The next four decades: The older population in the United States: 2010 to 2050 (No. 1138). US Department of Commerce, Economics and Statistics Administration, US Census Bureau.
- Walden, T. C., & Walden, B. E. (2005). Unilateral versus bilateral amplification for adults with impaired hearing. *Journal of the American Academy of Audiology*, 16(8), 574-584.
- Weihing, J., & Atcherson, S. R. (2014). Dichotic listening tests. In *Handbook of central auditory processing disorder*. San Diego: Plural Publishing, 369-404.
- Weihing, J., & Musiek, F. (2014). The influence of aging on interaural asymmetries in middle latency response amplitude. *Journal of the American Academy of Audiology*, 25(4), 324-334.
- Westerhausen, R. (2019). A primer on dichotic listening as a paradigm for the assessment of hemispheric asymmetry. *Laterality: Asymmetries of Body, Brain and Cognition*, 24(6), 740-771.
- Westerhausen, R., Bless, J., & Kompus, K. (2015). Behavioral Laterality and Aging: The Free-Recall Dichotic-Listening Right-Ear Advantage Increases with Age. *Developmental Neuropsychology*, 40(5), 313-327.
- Westerhausen, R., & Hugdahl, K. (2008). The corpus callosum in dichotic listening studies of hemispheric asymmetry: a review of clinical and experimental evidence. *Neurosci Biobehav Rev*, 32(5), 1044-1054.
- Westerhausen, R., Moosmann, M., Alho, K., Medvedev, S., Hämäläinen, H., & Hugdahl, K. (2009). Top-down and bottom-up interaction: Manipulating the dichotic listening ear advantage. *Brain Research*, 1250, 183-189.
- Wilson, R. H. (2003). Development of a speech-in-multitalker-babble paradigm to assess word-recognition performance. *Journal of the American Academy of Audiology*, 14(9), 453-470.

Wilson, R. H., & Leigh, E. D. (1996) Identification performance by right- and left-handed listeners on dichotic CV materials. *J Am Acad Audiol*. 7;(1): 1-6.

Wilson, R. H., McArdle, R. A., & Smith, S. L. (2007). An evaluation of the BKB-SIN, HINT, QuickSIN, and WIN materials on listeners with normal hearing and listeners with hearing loss. *Journal of Speech, Language, and Hearing Research*.

Yueh, B., Shapiro, N., MacLean, C. H., & Shekelle, P. G. (2003). Screening and management of adult hearing loss in primary care: scientific review. *Jama*, 289(15), 1976-1985.