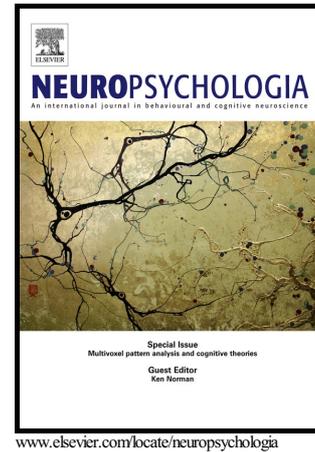


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Restoration of sensory input may improve cognitive and neural function*

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Abstract

Age-related hearing loss is one of the most prevalent health conditions among the elderly. Hearing loss may lead to social isolation, depression, and cognitive decline in older adults. The mechanistic basis for the association between hearing loss and decreased cognitive function remains unknown as does the potential for improving cognition through hearing rehabilitation. To that end, we asked whether the restoration of sensory input through the use of hearing aids would improve cognitive and auditory neural function. We compared a group of first-time hearing aid users with a hearing-matched control group after a period of six months. The use of hearing aids enhanced working memory performance and increased cortical response amplitudes. Neurophysiologic changes correlated with working

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memory changes, suggesting a mechanism for decreased cognitive function with hearing loss. These results suggest a neural mechanism for the sensory-cognitive connection and underscore the importance of providing auditory rehabilitation for individuals with age-related hearing loss to improve cognitive and neural function. Our findings of improved cognitive function with hearing aid use may lead to increased adoption of hearing loss remedies.

Keywords: Amplification, hearing aids, cortical auditory evoked potentials, older adults, hearing loss, age-related hearing loss

1. Introduction

Individuals with even mild hearing loss are more likely to experience reduction in cognitive performance than individuals with normal hearing (Lin, 2011), and those with more severe degrees of hearing loss experience steeper declines in mental function (Lin, et al., 2013). It is therefore important to address this association between hearing loss and cognitive decline, and to determine whether hearing rehabilitation can induce improvement in cognitive function.

Adult aging brings special challenges for speech comprehension due to age-related hearing loss (ARHL) (Fitzgibbons & Gordon-Salant, 2010), which is associated with declines in episodic memory (Wingfield & Kahana, 2002), processing speed (Salthouse, 1996), and working memory resources (Salthouse, 1994). Age-related changes in the auditory periphery degrade the speech signal delivered to the central nervous system for cognitive and linguistic processing; therefore, speech understanding problems of older listeners may represent the combined effects of peripheral, central-auditory, and cognitive factors (Humes, et al., 2012). Cognitive processing speed was found to be associated with speech in noise perception and improved signal processing of hearing aids (Yumba, 2017). Sensory devices such as hearing aids could reduce the effects of sensory loss, by restoring some aspects of sensory functioning (Gil & Iorio, 2010; Lavie, et al., 2015). However, sensory loss has effects that extend beyond the sensory system and related brain functions, with distinct effects on central neurological and higher order neurocognitive functioning (Kral, et al., 2016). Yet, it remains unknown whether sensory management can overcome these declines.

The brain is a dynamic self-organizing system that develops based on reciprocal experiences between neural activity and stimulation from the environment (Hübener & Bonhoeffer, 2014; Kral, et al., 2016). Auditory experience provides temporal patterns to the developing brain (Tallal, 2013) that are important for developing cognitive abilities such as pattern detection, memory, and sustained attention (Conway, et al., 2009). Working memory, specifically, is commonly defined as a limited capacity, temporary storage mechanism for holding information for further processing (Daneman & Hannon, 2007). However, even moderate declines in peripheral auditory acuity lead to a systematic downregulation of neural activity during the processing of higher-level aspects of speech (Pelle, et al., 2011), affecting working memory resources (Salthouse, 1994). This connection between hearing loss and decreased higher level speech processing motivated us to examine whether increased audibility through the use of hearing aids can positively affect or offset cognitive declines.

Cortical auditory evoked potentials (CAEPs) are characterized by three main peaks in adults: a positive P1 peak that occurs around 50 milliseconds (ms) after stimulation, a negative peak (N1) at around 100 ms, and another positive wave (P2) at around 200 ms (Martin, et al., 2007). The P1-N1- P2 complex has been used extensively to examine the effects of auditory stimulation on evoked neural activity and can be recorded in individuals while wearing hearing aids (Dawes, et al., 2014; Tremblay, et al., 2006). Recent studies have investigated the effects of hearing aid use on CAEPs after a period of four to twelve weeks. Dawes et al. (2014) did not find any changes in P1, N1, or P2 peaks of the cortical response after 12 weeks of hearing aid use. However, Rao et al. (2017) found a significant reduction in P3a amplitude in older adults with mild to moderate hearing loss after four weeks of hearing aid use. The differing results between the two studies might be attributed to the cortical measures and methodology employed in the studies; the P3a peak was obtained through an odd ball procedure and is linked to attention; therefore, effects of amplification may be more evident when there is a direct link to cognitive resources within the methodology used. Here, we aimed to examine both cognitive and neuroplastic changes following six months of hearing aid use. We hypothesized that the use of hearing aids increases access to the auditory signal, thus diminishing the resources needed to encode auditory input that is inaudible or degraded. These neural resources can then be redirected to higher levels of the auditory system to improve cognitive performance. We therefore expected to find that hearing aid use leads

to improvements in higher order neurocognitive functioning that are related to changes in CAEPs.

2. Materials and Methods

2.1. Study Population

Older adults were recruited from the Washington, D.C. metro area through flyers, presentations to senior living communities, and Craigslist advertisements. A power analysis based on auditory training data indicated that 32 participants were needed for an alpha level of 0.05. Given the demands of this study we assumed an attrition rate of 10% and planned to enroll 36 participants who met the inclusionary criteria of age 60-84 years, mild-to-moderate sensorineural hearing impairment with no neurologic disorders, English as a first language and no history of hearing aid use. A final number included thirty-two adults (19 females) aged 62-82 years (mean [SD] age, 72.65 [6.21] years) who completed the study (Figure 1).

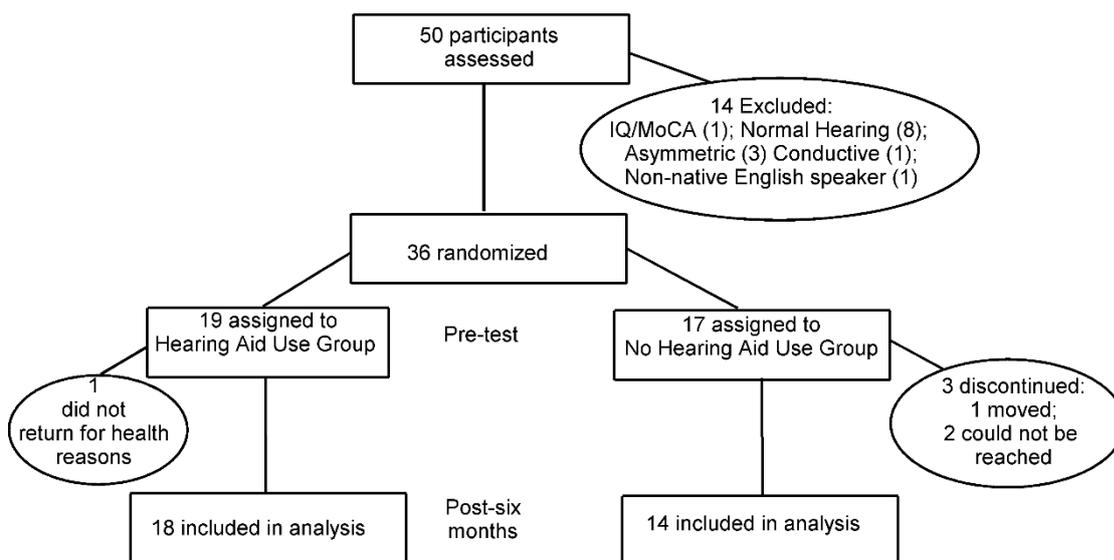


Figure 1. Flowchart. Flow of participants randomly assigned to Hearing Aid Use or No Hearing Aid Use groups.

All procedures were approved by the Institutional Review Board of the University of Maryland. Participants provided informed consent and were compensated for their time. Pure-tone air conduction audiometric thresholds were obtained bilaterally at octave and interoctave frequencies from 250-8000 Hz and for bone conduction at octave frequencies 250-4000 Hz. Participants had symmetrical hearing thresholds ranging from mild to severe, with pure-tone averages ≥ 25 dB HL from 500-4000 Hz, no pure-tone

thresholds ≥ 90 dB HL at any frequency, no air-bone gaps ≥ 15 dB HL at two or more adjacent frequencies, and no interaural asymmetries ≥ 15 dB HL or greater at two or more frequencies. All participants had expected click-evoked auditory brainstem response (click-ABR) latencies for age and hearing loss (wave V < 6.8 ms; Otto & McCandless, 1982), measured by a 100- μ s click stimulus presented at 80 dB SPL (peak equivalent) at a rate of 21.1 Hz (inset, Figure 2). All participants had normal IQs (≥ 89) as evaluated using the Wechsler Abbreviated Scale of Intelligence (mean [SD], 113.05 [14.76]; WASI; Zhu & Garcia, 1999) and were screened for dementia using a criterion score of 22/30 on the Montreal Cognitive Assessment (mean [SD], 25.74 [2.27]; MOCA; Nasreddine, et al., 2005).

2.2. Study design

The study used a randomized and controlled design. All participants underwent cognitive tests and electrophysiological tests (detailed below) in the initial pre-testing session (pre-test), then the experimental group was given their newly fitted hearing aids and wore them for at least eight hours per day for a period of six months. The control group were not provided with hearing aids during the six-month period. After the completion of the study, both groups were provided the option of purchasing hearing aids for a reduced price. Six months after the pre-test, all participants underwent another identical post-test session (Average days between sessions: Experimental: mean = 179.5 days \pm 10.7; Control: mean = 180.1 days \pm 7.6). As shown in Figure 1, 32 participants were included in the analysis. As shown in Table 1, both groups were matched on all demographic criteria. Independent samples *t* tests were conducted to confirm that the two groups did not differ statistically in terms of age, sex, hearing, intelligence (IQ assessed by WASI) and dementia (screened by MOCA). Pre- and post-test measures included cognitive and electrophysiological measures, as listed below. The participants were tested with the following cognitive measures from the National Institutes of Health (NIH) Toolbox (www.nihtoolbox.org): List Sort Working Memory (Tulsky, et al., 2013), Pattern Comparison Processing Speed Test, and the Flanker Test. These were chosen because of previous studies showing that working memory, processing speed, and attention play a role in performance with improved signal processing through amplification (Foo, 2007; Lunner & Sundewall-Thorén, 2007; Souza & Sirow, 2014; Yumba, 2017). Group average audiograms are shown in Figure 2.

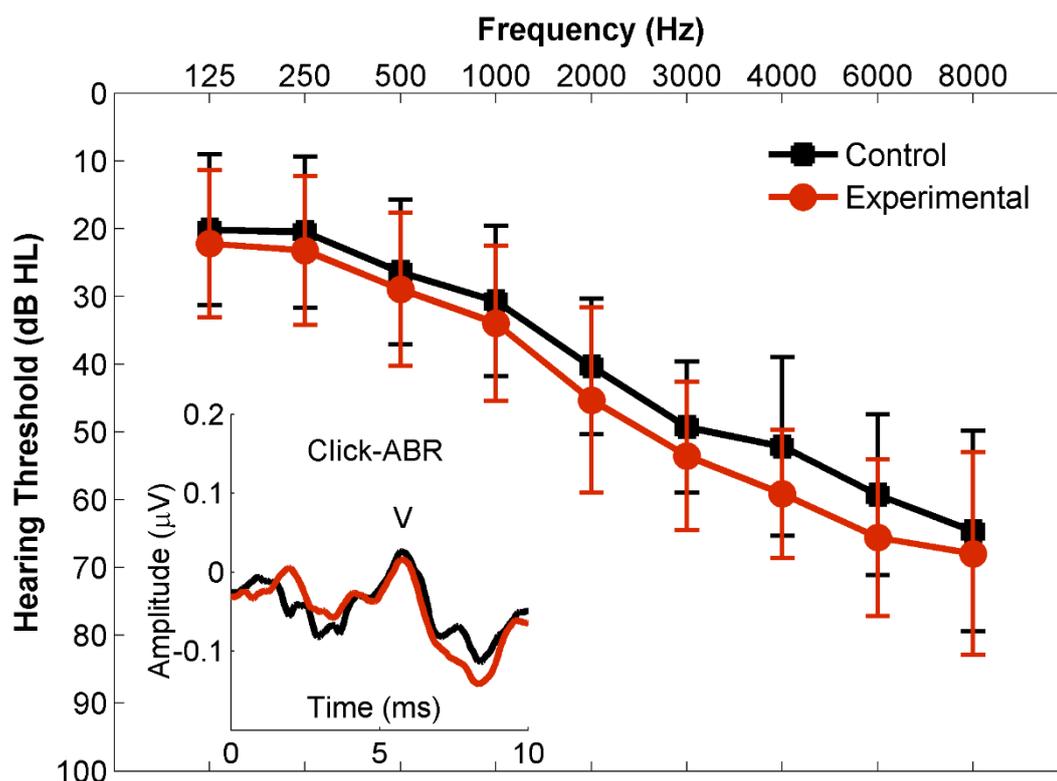


Figure 2. Audiogram. Mean unaided air conduction hearing thresholds across ears and participants are plotted for the experimental (red) and control (black) groups. Error bars represent standard deviations (SDs). Inset: Click-Auditory Brainstem Response (Click-ABR) grand average is also shown for the experimental (red) and control (black) groups.

2.3. Hearing aid fitting

All participants were fit bilaterally with Widex Dream 440 receiver-in-the-canal hearing aids with size M receivers and open domes (pure-tone air-conduction thresholds for 250-500 Hz < 30 dB HL) or tulip domes (pure-tone air-conduction thresholds for 250-500 Hz \geq 30 dB HL). The hearing aid fitting took place in the lab on the first day of testing immediately following the audiologic examination. The Widex Dream 440 Fusion hearing aids accommodate hearing losses up to 85 dB HL from 125-8000 Hz when coupled with M receivers. Open domes were used to facilitate patient comfort and compliance with wearing the aids for eight hours per day when appropriate. The hearing aid use (average hours/day) was monitored through the hearing aid data logging function, which was calculated and displayed by the manufacturer's hearing aid fitting software (group average = 9.4 hours/day \pm 2 hours). Only one automatic program was used for the study and the participants were unable to alter the hearing aid gain to minimize variability. This program had an extended input dynamic range of 113 dB SPL, 15 frequency channels, wide

dynamic range compression, directional microphones, and noise reduction technology. The hearing aids were linked using ear-to-ear communication technology for compression, speech enhancement, and feedback cancellation. Real-ear measurements were performed to verify the fitting. Real-ear-to-coupler differences were first obtained, and then the hearing aids were adjusted to match NAL-NL2 prescriptive targets for International Speech Test Signal stimuli (Holube, et al., 2010) presented at 55 dB SPL, 65 dB SPL, and 75 dB SPL.

2.4. Cognitive measures

The National Institutes of Health (NIH) Toolbox was used to assess whether the use of hearing aids leads to cognitive changes, specifically working memory, attention and processing speed. The tests are described below (further details about the development of the test instruments and reliability and validity data are available in Weintraub, et al., 2013).

2.4.1. Working Memory

The NIH Toolbox List Sorting Working Memory Test (Tulsky, et al., 2013) was used to assess working memory change. The Toolbox List Sorting Working Memory Test is a sequencing task requires sorting and sequence information. Items are presented both visually and auditorily. The participants are presented with a series of illustrated pictures, each depicting an item on the computer, along with their auditory names. Participants are instructed to repeat the stimuli verbally to the examiner in size order, from smallest to largest. The number of objects in a series increases on successive items, thereby taxing the working memory system. Furthermore, the task starts with a “1-list” version in which the participants have to sequence one type of stimuli (e.g., “animals” or “food”) according to size order and then switches to a “2-list” version in which two types of stimuli have to be sequenced, each in size order. In the 2-list version, the working memory load is increased substantially as the stimuli are presented from two categories (animals and food) and this “dual” tracking and processing information increases the working memory load of the task. The prototype task was validated previously in an elderly sample (Mungas, et al., 2005; Mungas, et al., 2011). The testing was conducted while the participants were wearing their hearing aids both during the initial and final testing sessions. The List Sorting task requires approximately seven minutes to administer. Test scores consist of

total correct items across all trials. Age-adjusted test scores were compared between groups and within each session (pre and post).

2.4.2. Attention

The NIH Toolbox Flanker Inhibitory Control and Attention Test (Flanker Test) was used to assess changes in attention and executive function. The Flanker test measures attention and inhibition through assessment of the participant's ability to suppress distracting response cues. On each trial, a central directional stimulus is flanked by similar stimuli on the left and right. The task is to indicate the direction of the central stimulus (in Weintraub, et al., 2013, page S56). In the present study, arrow stimuli were used (which are the chosen stimuli for adults), pointing to the left and right, and participants were asked to determine the direction of the central arrow as quickly as possible. The testing was conducted while the participants were wearing their hearing aids both during the initial and final testing sessions. Test scores consist of total correct items across all trials. Age-adjusted test scores were compared between groups and within each session (pre and post).

2.4.3. Processing Speed

The NIH Toolbox Pattern Comparison Processing Speed Test (Processing Speed) was used to assess changes in speed of processing changes. This test was modeled after Salthouse's Pattern Comparison Task (Salthouse, et al., 1991). Participants are asked to identify whether two visual patterns are the "same" ("Yes" button) or "not the same" ("No" button) (in Weintraub, et al., 2013, page S57). The testing was conducted while the participants were wearing their hearing aids both during the initial and final testing sessions. Test scores consist of total correct items across all trials. Age-adjusted test scores were compared between groups and within each session (pre and post).

2.5. Electrophysiological measures

Electrophysiological recordings were conducted in aided and unaided conditions, and the speech syllable was presented in quiet and noise (+10 signal to noise ratio (SNR) six-talker babble noise) conditions. The amplitudes of the CAEP P1, N1 and P2 peaks were measured.

2.5.1. Electrophysiology Acquisition and Analysis

All of the recording sessions were conducted in the same sound-treated, electrically-shielded booth with the lights off to reduce electrical interference. During recordings, participants watched a silent movie with subtitles playing on a projector screen to promote relaxation and a state of calm wakefulness and to minimize head movement. The participants were seated 2 meters in front of an Interacoustics SP90 speaker at 0° azimuth. This position was pre-measured and marked so that each participant sat in the same place for each visit. A speech syllable /ga/ was presented through the speaker via Presentation software (Neurobehavioral Systems, Inc.). The stimulus was presented through sound field to allow processing through the hearing aid microphones and to simulate ecologically valid listening conditions. During the recording session, participants were seated in an upright position so that the microphones of the hearing aids were in the same plane as the speaker at a relative angle elevation of 0 degrees.

Stimuli. A 170-ms speech syllable /ga/ synthesized with a Klatt-based synthesizer (Boersma & Weenink, 2009) at 20 kHz was the chosen stimulus. The stimulus was characterized by a 10-ms onset burst followed by a 50-ms consonant-vowel transition and a steady-state vowel region from 60 to 170 ms. Voicing was constant for the duration of the stimulus with a fundamental frequency of 100 Hz. The transition region was characterized by rapidly changing formants: the first formant rose from 400 Hz to 720 Hz, the second formant fell from 2480 Hz to 1240 Hz, and the third formant fell from 2580 Hz to 2500 Hz; all three formants stabilized for the steady-state region of the syllable. The fourth through sixth formants remained constant over the entire duration of the syllable at 3300, 3750, and 4900 Hz, respectively.

Conditions. The /ga/ was presented in two listening conditions: 1) 80 dB SPL in quiet; and 2) 80 dB SPL in the presence of 70 dB SPL 6-talker babble (+10 dB Signal to noise ratio (SNR), noise condition). The 6-talker babble was taken from the Words-in-Noise sentence lists (Wilson, et al., 2003) and was continually played on a 4.6 second loop. Prior to each recording session, the /ga/ and noise stimuli were calibrated to within ± 1 dB of the desired stimulus level using a Larson Davis System 824 sound level meter at ear level. Electrophysiological responses were recorded in two amplification conditions: 1) aided (while wearing hearing aids) and 2) unaided (without wearing hearing aids). Note that the control group wore the hearing aids while being tested but did not again wear the hearing aids until they returned for repeat testing six months later.

Recording. The /ga/ stimulus was presented at a rate of 1 Hz, and responses were recorded using the Biosemi Active-Two acquisition system (BioSemi B.V., Amsterdam,

Netherlands), at a sampling frequency of 2048 Hz, using a 32-channel electrode cap that incorporated a subset of the International 10-20 system (Jasper, 1958), with all offsets $< 50 \mu\text{V}$ and average earlobes (A1 and A2) serving as references. A criterion of $\pm 100 \mu\text{V}$ was used for off-line artifact rejection, and 600 artifact-free sweeps were collected for each condition.

Data Processing and Analyses. Responses were offline bandpass filtered from 1-30 Hz with a 4th order Butterworth filter. Eye movements were removed from filtered data using a regression-based electrooculography reduction method (Romero, et al., 2006; Schlögl, et al., 2007). The time window for each sweep was -100 to 400 ms referenced to the stimulus onset. A final average response was extracted with the first 500 artifact-free sweeps.

Data analysis. Responses were processed using MATLAB (MathWorks, version R2011b). Mean response amplitudes at the Cz electrode were calculated for the expected time region for each of the prominent cortical peaks: P1 (35-75 ms), N1 (80-150 ms), and P2 (160-250 ms) in the quiet condition and P1 (35-75 ms), N1 (150-200 ms), and P2 (225-275 ms) in the noise condition.

2.6. Statistical analyses

All statistical analyses were conducted in SPSS version 23. Based on two-tailed independent samples *t* test analysis, there were no significant differences between the experimental and the control groups in the electrophysiological measures in any of the amplification and stimulus conditions ($t(30) \leq 1.603$, $P \geq 0.119$), or the working memory and speed processing pre-test measures ($t(30) \leq 1.183$, $P \geq 0.246$). However, one significant pre-test difference was observed between both groups in the Flanker pre-test scores ($t(30) = 2.742$, $P = 0.01$). Shapiro-Wilk tests were used to confirm that the data were normally distributed within each group ($P > 0.170$). In addition, Levene tests confirmed that variances were homogeneous across groups within each analysis ($P > 0.180$). Results were considered significant when $P < 0.05$.

To determine whether the use of hearing aids resulted in greater pre- to post-test changes in the experimental than in the control group, pre- and post-test performance on each of the measures was compared between groups using a repeated measures ANOVA with group (experimental vs. control) as the between-subject factor, and time (pre vs. post) as the main within-subject factor, in addition to other within-subject factors depending on the data being analyzed. Within-subject factors are described in detail below. When

significant interactions were observed, univariate ANOVAs and pairwise comparisons were conducted.

Cognitive Statistical Analysis. To determine if use of hearing aids resulted in improved performance, NIH Toolbox List Sorting Working Memory, Flanker, and Processing Speed Tests' Age Adjusted scores were compared between groups using a repeated measures ANOVA with one between-subject factor (group: experimental, control) and one within-subject factor (time: pre-test, post-test), followed by paired samples *t* test analyses.

Electrophysiological Statistical Analysis. To test hearing aid use effects on CAEP amplitudes, an omnibus repeated measures ANOVA for amplitude was performed with one between-subject factor (group: experimental vs. control) and four within-subject factors (time: pre, post; amplification: aided, unaided; stimulus: quiet, noise; peak: P1, N1, P2). When significant interactions were observed, univariate ANOVAs for each peak separately were conducted with one between-subject factor (group: experimental vs. control) and three within-subject factors (time, pre, post; amplification, aided, unaided; stimulus: quiet, noise), followed by *t* test paired samples analyses to determine the direction of the effects. Table 2 represents mean amplitudes for each group, across sessions, listening conditions and peaks. Only time \times group interactions were presented and discussed. There were significant effects of stimulus conditions, such as aided vs. unaided and quiet vs. noise. Such effects were not a focus of interest in the present study, and shall not be discussed further. These effects have been well-documented previously (Billings, et al., 2015; Jenkins, et al., 2017; Kuruvilla-Mathew, et al., 2015; M. Sharma, et al., 2014).

Correlations between cortical and cognitive measures. The relationship between the cortical physiological responses and cognitive performance was assessed. Physiological pre-to-post response changes in the aided quiet and noise conditions were correlated with the improvement on cognitive performance. Correlations were pooled across all participants using Pearson correlations. We focused on N1 and P2 measures because they have been related to auditory sensory memory (Picton, 2013) and are thought to be markers of auditory learning (Ross, et al., 2013; Tremblay, et al., 2001).

3. Results

3.1. Cognitive scores

Working memory scores significantly increased after six months of hearing aid use. Repeated measures analysis of variance showed a significant time \times group interaction ($F(1,30) = 4.691, P = 0.038, \eta^2_p = 0.131$). This interaction was driven by improvement in working memory performance in the experimental group (108.10 [11.71] vs. 116.25 [8.99], $t(17) = 2.950, P = 0.008$) that was not observed in the control group (109.75 [13.01] vs. 107.43 [13.91], $t(13) = 0.537, P = 0.601$) after six months (see Figure 3, Table 3). This result suggests that the use of hearing aids may improve working memory in people with age-related hearing loss. While working memory scores were affected by the use of hearing aids, attention scores and speed of processing were not affected by hearing aid use. Repeated measures ANOVA did not show a time \times group interaction ($F(1,30) = 1.436, P = 0.242$) for the attention scores reflected by the Flanker Inhibitory Control and Attention Test or for processing speed ($F(1,30) = 0.051, P = 0.823$) reflected by the Pattern Comparison Processing Speed Test (Table 3).

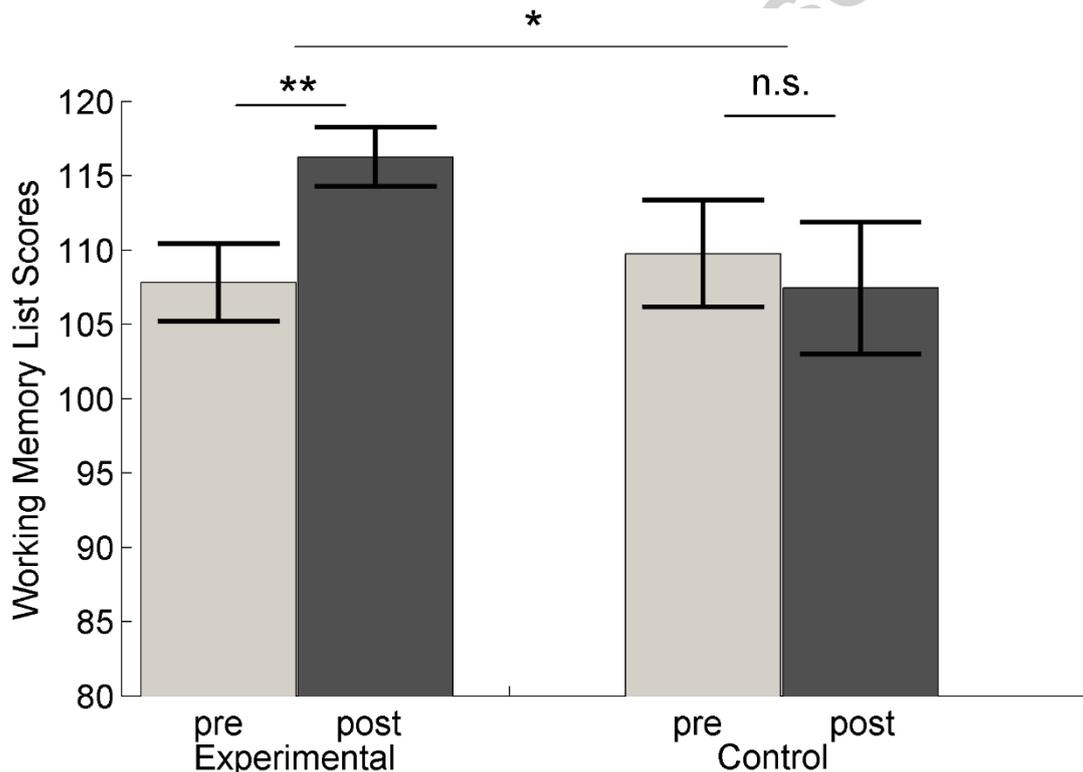


Figure 3. Working memory scores. Pre (light grey) and post (dark grey) working memory mean scores for the experimental and control groups. Error bars represent standard error of the mean. ** $P < 0.01$, * $P < 0.05$. n.s: not significant.

3.2. Cortical auditory evoked responses

An omnibus repeated measures multivariate ANOVA was conducted to compare changes from pre- to post-test sessions in cortical peak amplitudes across listening conditions (stimulus: quiet and noise; amplification: unaided and aided) between experimental and control groups. A significant time \times stimulus \times amplification \times group interaction was observed ($F(1,26) = 6.431$, $P = 0.018$, $\eta_p^2 = 0.211$). Each cortical peak was then analyzed separately to determine the direction of the interaction. In general, these analyses show that N1 and P2 amplitudes were enhanced after six months of hearing aid use in the experimental group, mainly in the aided quiet conditions. These changes are demonstrated in Figures 4, 5 and 6. Topographic maps provided in Figure 7 show the amplitude distribution across electrodes and also demonstrate an overall increase in amplitude for N1 and P2 amplitudes in quiet in the experimental group. No significant time \times group interactions were observed for P1 amplitudes (Figures 4, 5), suggesting that P1 is not a biological marker for hearing aid plasticity in adults ($P > 0.21$), although it appears to be a biomarker for developmental plasticity in newly-implanted children (A. Sharma, et al., 2005).

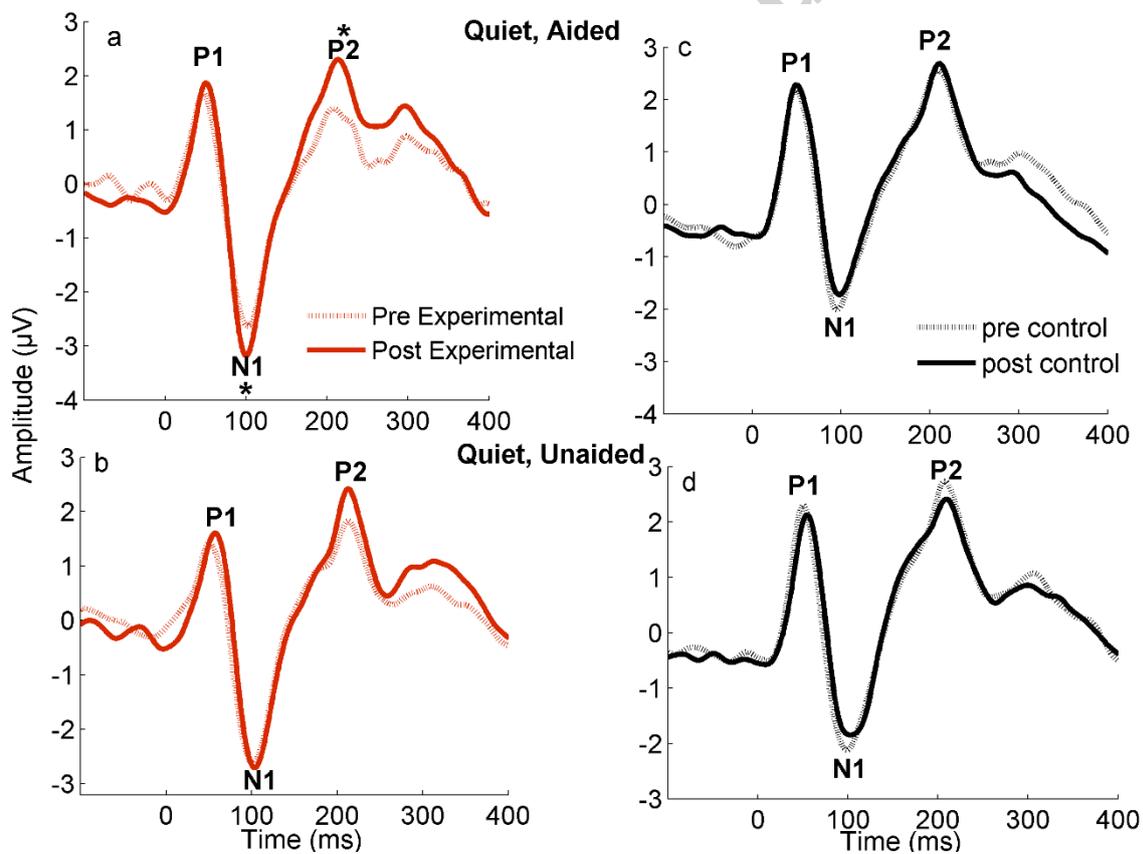


Figure 4. Grand average waveforms for the Quiet Condition. Response waveforms for the experimental (red) and control (black) groups from pre (dashed lines) and post session

(solid lines), measured at Cz for peaks P1 (~50 ms), N1 (~100 ms), P2 (~200 ms). Responses are shown for the quiet aided (a,c) and unaided (b,d) conditions. Significant increases in amplitude from pre to post were noted for N1 and P2. * $P < 0.05$.

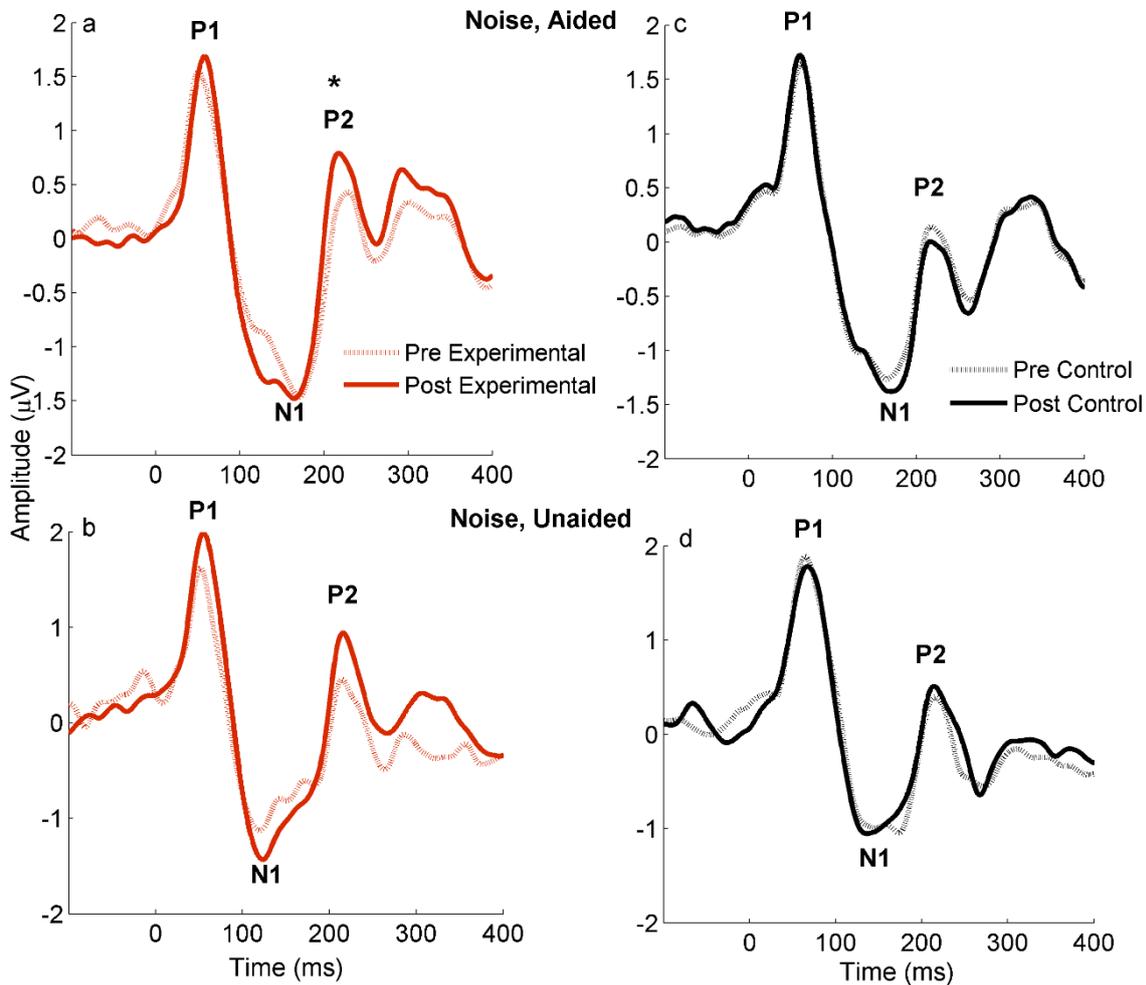


Figure 5. Grand average waveforms for the Noise Condition. Response waveforms for the experimental (red) and control (black) groups from pre (dashed lines) and post session (solid lines), measured at Cz for peaks P1 (~50 ms), N1 (~100 ms), P2 (~200 ms). Responses are shown for the noise aided (a,c) and unaided (b,d) conditions. Significant increases in amplitude from pre to post were noted for P2 in the experimental group only. * $P < 0.05$.

However, a significant time \times stimulus \times amplification \times group interaction was observed for N1 amplitude ($F(1,26) = 6.201$, $P = 0.020$, $\eta_p^2 = 0.205$). There was a significant time \times amplification \times group interaction effect in the quiet condition ($F(1,26) = 4.492$, $P = 0.040$, $\eta_p^2 = 0.152$), that was driven by increased amplitudes of the N1 peak in the aided condition in the experimental group (-2.92 [1.57] vs. -3.58 [1.53], $t(13) = 2.273$, $P = 0.042$) that was not observed in the control group (-2.71 [1.94] vs. -2.30 [2.69], $t(13) =$

1.102, $P = 0.290$) (see Figure 4 and Figure 6a). No significant time \times group interactions were observed in noise ($P > 0.06$, Table 2, Figure 5 and Figure 6c).

P2 amplitudes were also enhanced after the use of hearing aids. Paired sample t test analysis showed a significant change in P2 experimental amplitudes specifically in aided conditions for the quiet (2.38 [1.27] vs. 2.79 [1.33], $t(13) = 2.267$, $P = 0.041$, $\eta^2_p = 0.301$ Figure 4 and Figure 6b) and noise (0.73 [0.69] vs. 1.14 [0.63], $t(16) = 2.234$, $P = 0.040$, $\eta^2_p = 0.238$, Figure 5 and Figure 6d) but not in unaided conditions ($P > 0.147$). However, repeated measures ANOVAs did not show a significant time \times group interaction ($P = 0.073$), probably due to large individual variance. No significant changes were observed in any of the peaks for the control group ($t(13) < 1.657$, $P > 0.121$).

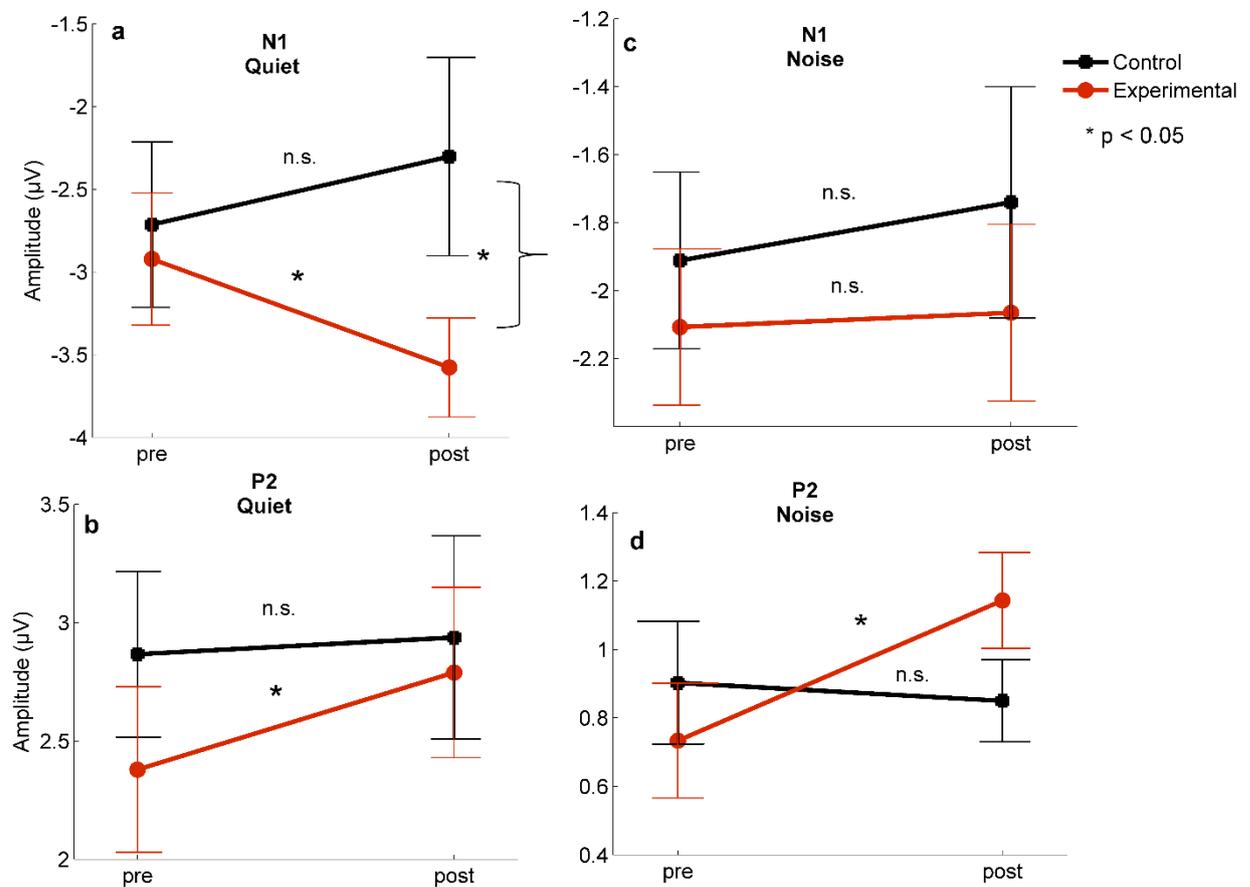


Figure 6. Response amplitudes. N1 and P2 mean amplitudes for the experimental (red) and control (black) groups across pre and post-test sessions in aided quiet and noise conditions. Error bars represent standard error of the mean. * $P < 0.05$. n.s.: not significant.

These amplitude increases suggest that hearing aid use may alter cortical processing, but the results contrast with those of a previous study by Dawes et al. (2014) that did not find changes in CAEPs following 12 weeks of hearing aid use. The different outcomes between the current study and that of Dawes et al. might suggest that more than

12 weeks of hearing aid use are necessary to observe neuroplastic changes. Alternatively, study design differences between ours and the previous study may have also affected the results. In particular, the Dawes et al. study presented pure-tones to both ears via insert earphones while the current study presented speech stimuli via sound field in unaided and aided conditions.

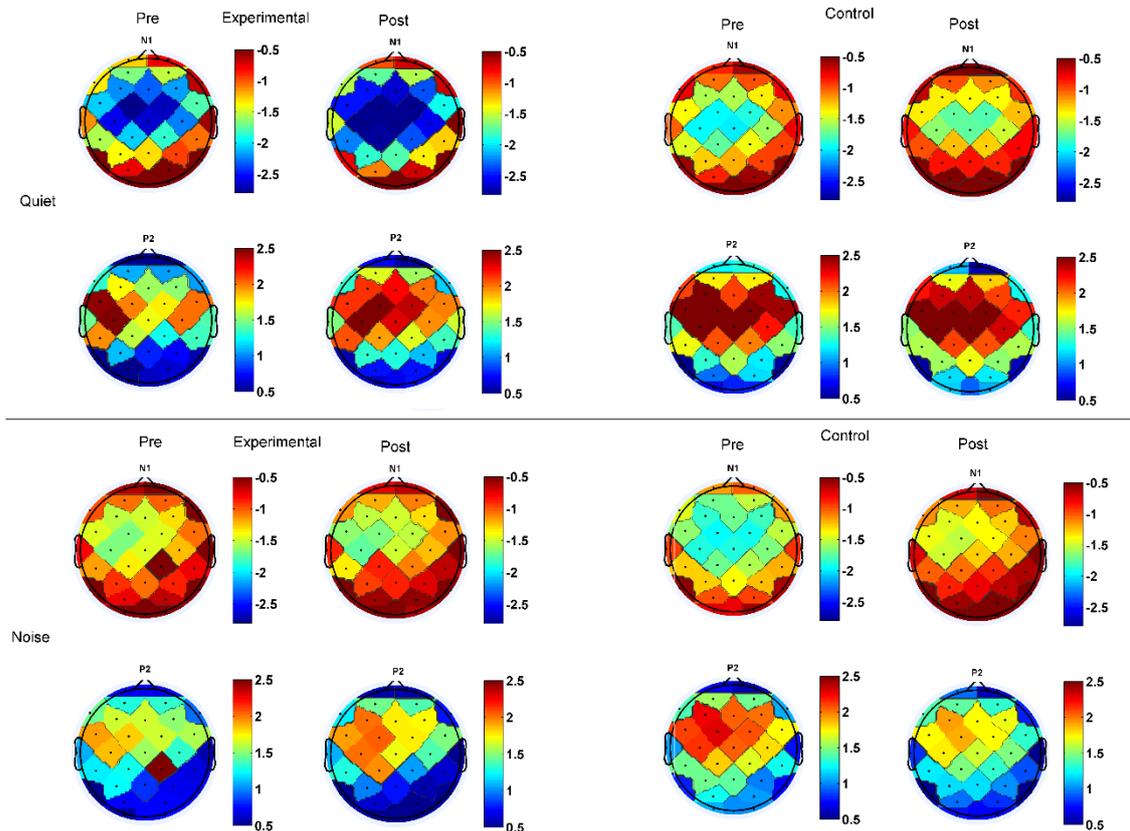


Figure 7. Topographic representation of N1 and P2 mean amplitudes (μV) for the experimental (left panels) and control (right panels) groups across pre and post-test sessions in Aided Quiet (top panels) and Aided Noise (lower panels) conditions.

3.3 Correlations among cognitive and physiological measures

We focused on cognitive measures that showed time \times group interactions. i.e. working memory was correlated with physiological changes. Because the N1-P2 complex is a marker of sensory memory (Picton, 2013) and auditory learning plasticity (Ben-David, et al., 2011; Ross, et al., 2013; Tremblay, et al., 2001), correlations among physiological N1 and P2 response changes and working memory changes were assessed and are shown in Figure 8. Working memory improvement was related to higher P2 peak amplitudes in quiet ($r = 0.409$, $P = 0.047$, Figure 8c), but did not relate to P2 amplitude

changes in noise ($r = 0.174$, $P = 0.280$, Figure 8d) or to N1 amplitudes in quiet or noise ($r = -0.244$, -0.128 , $P > 0.250$).

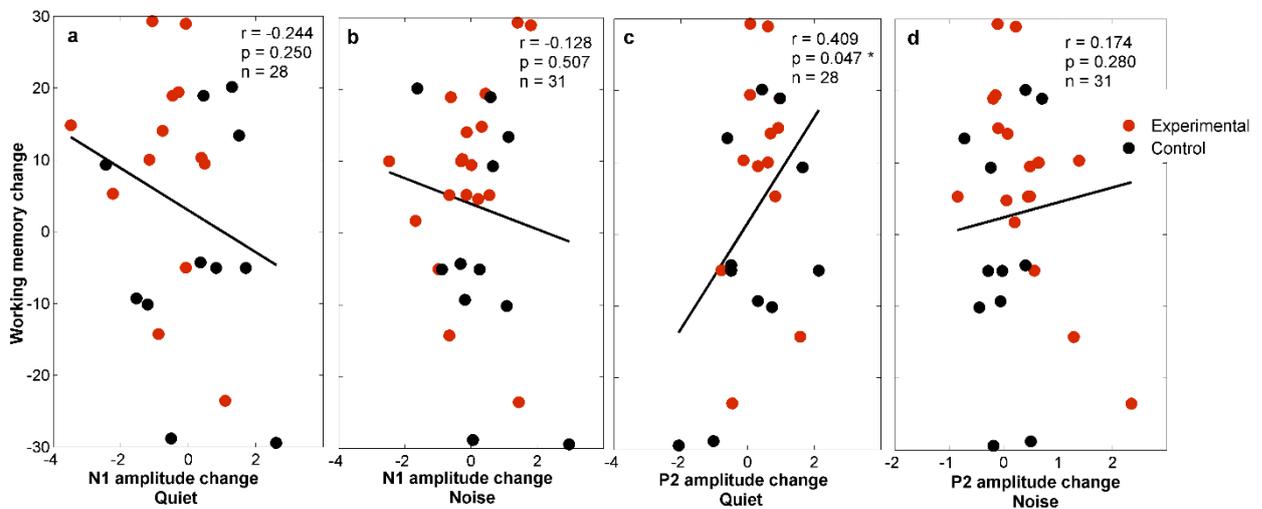


Figure 8. Correlations between cortical and cognitive measures. Pearson correlations between response amplitude changes and working memory change pooled across all participants are shown for N1 and P2 amplitudes in quiet and noise listening conditions. The experimental (red circles) and control (black squares) data points are shown on each graph. Pearson's correlation coefficients (r), P values and number of participants (n) are shown on each graph (n does not equal 32, because some of the cortical files were corrupted).

In addition, we tested whether the changes in working memory performance and cortical auditory evoked responses correlate with the number of hours that the participants wear their hearing aids. These relationships were studied using Pearson correlations pooled across the participants of the experimental group. The average number of hours for each participant was correlated with 1) post minus pre working memory score differences 2) post minus pre N1 amplitude value differences in the aided quiet condition and 3) post minus pre P2 amplitude value differences in aided quiet condition. Pearson correlation coefficients were small ($r < 0.45$) and did not reach statistical significance ($P > 0.07$). Because we required that the participants wear the hearing aids for a minimum of eight hours per day, there was a restricted range of logged hours, limiting the likelihood of finding a correlation.

4. Discussion

Restoration of sensory input resulted in three key findings: 1) improvement in working memory, 2) enhanced cortical processing of speech stimuli, and 3) correlations among increases in working memory and increases in cortical amplitudes.

Larger N1 peak amplitudes were observed after the use of hearing aids, especially when recorded in aided quiet listening conditions. The N1 component is believed to reflect early triggering of attention to auditory signals (Čeponien, et al., 2002; Näätänen, 1990).

Therefore, this finding suggests that increased auditory experience through hearing aid use gained during the 24-week period enabled increased attentional resources to the signal. Although we did not find similar N1 amplitude increases in the noise condition, perhaps a longer period of hearing aid use is necessary to engender enhanced N1 amplitudes in challenging listening conditions, such as in background noise.

N1 changes did not correlate with working memory changes. This lack of correlation might be attributed to the fact that N1 reflects initial storage of sensory information (Näätänen & Winkler, 1999), or lower-level sensory processing, and working memory changes may be more tightly connected to higher level representations (such as P2) than lower-level sensory processing.

P2 amplitudes were more robust after the use of hearing aids, and changes in amplitude were related to improvement in working memory. The P2 peak occurs at approximately 200 ms, when stimulus features have been integrated into a consciously identified auditory object (Näätänen & Winkler, 1999; Ross, et al., 2013). This 200-ms time window includes the time required for bottom-up processing of acoustic information, creating the auditory object representation reflected by P2 (Ross, et al., 2013). Neuroimaging studies in humans have linked auditory object representation to the anterior auditory cortex (Leaver & Rauschecker, 2010). Specifically, P2 sources were localized in anterior auditory association cortex, part of the antero-ventral pathway for object identification, suggesting that P2 amplitude may represent facilitation of implicit memory for an auditory object (Ross, et al., 2013). Animal models have shown that complex stimuli are processed in the anterior temporal plane (Kravitz, et al., 2013) and then are projected to memory-related areas (Suzuki & Amaral, 1994). Previous studies have shown that perceptual learning induces changes in the P2 cortical component (e.g. Atienza, et al., 2002; Shahin, et al., 2003, Tremblay & Kraus, 2002). This experience-dependent enhancement in P2 underlies the acquisition of improved perception (Atienza, et al., 2002). P2 enhancement is also associated with improved behavioral performance, suggesting that experience leads to fast pre-attentive access to perceptual representations (Tong, et al., 2009). A possible mechanistic association between auditory perception and working memory was demonstrated in the current study.

While improvements were observed in working memory outcomes due to the use of hearing aids, the present study did not demonstrate direct correlations between the use of hearing aids and improved attention or processing speed. The lack of improvement in attention or processing speed may suggest that these cognitive functions are not

remediated with bottom-up signal processing strategies but perhaps would benefit from top-down auditory-based cognitive training as has been demonstrated in previous studies (Anderson, et al., 2013; Anderson, et al., 2014). Rao et al. (2017) did not find behavioral changes in selective attention tasks (using the behavioral oddball paradigm) following four weeks of hearing aid use. However, they reported that selective attention improved after adding four weeks of auditory training to eight weeks of the hearing aid rehabilitation process. These results might suggest the importance of using auditory-based cognitive training to engender improvements in top-down processing and subsequent changes in higher order cognitive processes. It is also possible that changes would be seen after a longer period of hearing aid use. Lin (2011) reported that 13 individuals who used their hearing aids daily for at least one year showed improvements in performance on the Digit Symbol Substitution Scores (Wechsler, 1997), a measure of speed of processing, executive function, and attention.

In addition, we noted large P1 amplitudes in all conditions, consistent with previous findings (e.g. Alain, et al., 2014). Alain et al. suggested that the larger P1 amplitudes in older adults with mild hearing loss may arise from compensatory cortical mechanisms – specifically, decreased inhibitory neurotransmission leading to increased neural excitability in auditory cortices. Hearing aid use for a period of 6 months did not affect P1 amplitudes. Further research is important to assess whether a more prolonged period would affect components of P1.

One limitation of our study was the difference in frequency of contact between the two groups: the control group was a no-contact group and their testing was performed only twice, while the experimental group was seen for four additional sessions throughout the study to ensure that the participants were complying with hearing aid use and to obtain additional electrophysiological recordings. The experimental group participants may have become accustomed to the lab environment and may therefore have had better performance in the final session. Therefore, in future studies an active control group with an alternate type of sensory management should be used in order to account for familiarity effects.

Our findings suggest that enhanced auditory experience enables better access to details in sensory representation (reflected by CAEPs), which in turn permits the correct identification of auditory objects and potentially improves projections to working memory sources.

5. Conclusions

Our results suggest a neural basis for the link between cognitive and sensory decline. We demonstrated that age-related declines in sensory-cognitive function may not be permanent but rather may be malleable in response to changes in acoustic experience. The boost in sensory audibility for six months improved working memory performance and also increased cortical neural processing. This study suggests that the benefits of auditory rehabilitation through the use of hearing aids may extend beyond increased audibility and may include improved cognitive skills and enhanced cortical speech processing.

We strongly believe our findings will be of significant interest to practitioners who provide service to the geriatric population. Our findings of improved cognitive function with hearing aid use may lead to increased adoption of hearing loss remedies.

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Author contribution:

S.A. designed the study. K.J. and S.A. collected the data. H.K. analyzed the data. H.K. and S.A. interpreted the results and wrote the manuscript. All authors approved the final version of the manuscript.

All data required to reach the stated conclusions are presented in the paper. Additional data related to this paper may be requested from the authors.

Declarations of interest: none

8. References

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Table 1. Demographic. Groups were matched on all demographic criteria. Means (SDs) are displayed for age, sex distribution, hearing, IQ, and Montreal Cognitive Assessment (MOCA) scores. Number of participants in each group (N), t values with degrees of freedom and P values of the group comparison are also shown.

	Experimental	Control	$t(30)$	P
N	18	14		
Age (years)	75 (6.52)	74 (5.79)	0.751	0.459
Male/female	8/10	5/9	0.903	0.374
Pure-tone average hearing (0.5–4 kHz; dB HL)	42.58 (7.15)	40.21 (8.37)	0.863	0.395
High-frequency hearing (6–8 kHz; dB HL)	66.52 (11.88)	60.98 (13.47)	1.235	0.226
IQ	113.18 (9.23)	112.72 (6.94)	1.673	0.120
MOCA	26.72 (1.77)	25.24 (2.45)	1.866	0.076

Table 2. Cortical Amplitudes. Means (μV) and (SDs) are shown for pre- and post-amplitudes across amplification and stimulus conditions for each peak (P1, N1, P2) for the experimental and control groups.

Peak	Amplification	Experimental				Control			
		Quiet		Noise		Quiet		Noise	
		pre	post	pre	post	pre	post	pre	post
P1	Unaided	2.478	2.743	1.857	2.045	2.766	1.997	2.126	1.956
		(1.73)	(1.42)	(1.16)	(1.02)	(1.68)	(0.96)	(1.25)	(1.25)
	Aided	2.360	2.371	1.760	1.845	2.701	2.770	2.142	1.982
		(1.18)	(1.12)	(1.04)	(0.88)	(1.33)	(1.62)	(1.11)	(1.00)
N1	Unaided	-3.488	-	-	-	-	-	-	-
			2.854	1.538	1.839	2.272	2.619	1.817	1.465
	Aided	(2.54)	(1.73)	(1.22)	(0.89)	(1.86)	(1.56)	(1.10)	(1.08)
		-2.922	-	-	-	-	-	-	-
P2	Unaided		3.577	2.107	2.065	2.714	2.302	1.911	1.740
		(1.57)	(1.53)	(0.83)	(0.97)	(1.94)	(2.69)	(0.99)	(1.28)
	Aided	2.245	2.137	1.048	1.258	2.825	2.537	1.180	0.987
		(1.23)	(1.14)	(0.87)	(0.95)	(1.56)	(1.22)	(0.92)	(0.58)
Aided	2.3785	2.789	0.734	1.143	2.866	2.937	0.859	0.808	
	(1.27)	(1.33)	(0.69)	(0.63)	(1.33)	(1.61)	(0.67)	(0.47)	

Table 3. Cognitive Measures. Means and (SDs) are shown for pre- and post-scores for the List Sort Working Memory, Flanker Inhibitory Control and Attention Test (Flanker) and Pattern Comparison Processing Speed (Processing Speed) Tests for the experimental and control groups. Paired samples t -values with degrees of freedom and P -values of session comparisons are also shown for the experimental and control groups.

	Experimental				Control			
	Pre	Post	$t(17)$	P	Pre	Post	$t(13)$	P
Working Memory	108.10 (11.71)	116.25 (8.99)	2.950	0.008	109.75 (13.01)	107.43 (13.91)	0.537	0.601
Flanker	109.75 (10.57)	110.99 (13.35)	0.547	0.591	99.82 (10.86)	106.30 (13.07)	1.612	0.151
Processing Speed	96.90 (19.60)	100.48 (15.23)	1.047	0.308	88.75 (18.01)	91.02 (19.45)	0.549	0.598

Highlights

- Restoration of sensory input improves working memory in older adults with age-related hearing loss.
- The use of hearing aids for six months enhances cortical processing of speech stimuli.
- Improved cognitive function with hearing aid use may lead to increased adoption of hearing loss remedies.

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