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EXECUTIVE DYSFUNCTION AND PRESBYCUSIS IN OLDER PERSONS WITH AND WITHOUT MEMORY LOSS AND DEMENTIA

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Abstract

Objective—Determine the relation of age-related auditory processing dysfunction and executive functioning.

Background—Central auditory dysfunction is common in Alzheimer’s dementia but the mechanism is not established.

Method—Participants: 313 volunteers from the Adult Changes in Thought surveillance cohort with adequate peripheral hearing. Outcome measures (1) peripheral audition; (2) auditory-evoked potentials; (3) central auditory tests (Synthetic Sentence Identification with Ipsilateral Competing Message, Dichotic Sentence Identification, Dichotic Digits; (4) Executive Functioning: Trail Making; Clock Drawing, Stroop Color and Word, and subtests from the Cognitive Abilities Screening Instrument measuring mental concentration. A composite executive functioning score was created using item response theory.

Results—The composite executive functioning score was significantly associated with each central auditory measure, explaining 8–21% of the variance. Trails B was most strongly associated with the auditory outcomes, explaining 8–14% of the variance. The relation between executive functioning and central auditory function was still significant when participants diagnosed with memory impairment or dementia were excluded.

Conclusions—In elderly persons, reduced executive functioning is associated with central auditory processing, but not with primary auditory function. This suggests that central presbycusis and executive dysfunction may result from similar neurodegenerative processes.

Keywords

Executive functioning; Presbycusis; Central Auditory Function; Dementia

INTRODUCTION

Age-related hearing loss (presbycusis) is the most common cause of poor hearing. Presbycusis-induced communication errors strain interpersonal relationships and contribute to social-isolation and depression.¹ Presbycusis increases in prevalence as the population ages. Although degeneration of peripheral function is unarguably the primary pathology in

early presbycusis, central auditory processing dysfunction (i.e. central presbycusis) becomes an increasingly important factor in late presbycusis². Central presbycusis is typified by difficulty understanding speech in noisy situations and is implied by the lay term, “nerve deafness”. Central presbycusis is not remediable currently.

The neurological aspects of central presbycusis have received little attention, leaving many questions unanswered: 1) how is central presbycusis linked to cognitive decline and dementia? 2) what cognitive elements are involved? and 3) where is the locus of the abnormality? The present study was designed to examine these questions: the background for each is outlined next.

First, early research in auditory processing dysfunction excluded persons with cognitive dysfunction to avoid potential confounding from the effect of age on presbycusis and cognition.³ More recent studies demonstrate significant overlap of these processes. For example, central presbycusis and cognitive dysfunction often coexist, as they frequently do in Alzheimer’s dementia⁴, where it appears that auditory processing dysfunction precedes the onset of AD symptoms⁵ and becomes ubiquitous.⁶ These observations raised the possibility that central auditory dysfunction may be a sign of early, preclinical cognitive decline. Subsequently we demonstrated in the Framingham Heart Study cohort that poor central auditory function was a significant predictor of subsequent age-adjusted decline in the Mini Mental State Examination.⁷ We now extend those observations in a different cohort using similar methods while controlling for auditory pathway status and executive functioning.

Second, understanding speech against background noise is difficult at any age but especially in the elderly; adequate cochlear function and central auditory processing ability are both necessary. Altered executive functioning⁸, with deficits in selective and divided attention, is common in aging and early AD⁹, and these deficits coexist with central auditory dysfunction in AD cases.¹⁰ Executive functioning includes cognitive sub-domains, such as working memory, concept generation and comprehension, and ability to plan, initiate, maintain, switch, or inhibit behavioral responses¹¹ - skills also utilized in understanding speech-in-noise. Minor deficits in executive functioning might diminish performance on central auditory tasks even when other cognitive domains such as long-term memory or expressive language are normal.

Third, brainstem auditory pathways display typical postmortem histologic changes in advanced AD¹² but not in preclinical cases.¹³ Given that the histopathology of central presbycusis is unknown, we employed functional measures to assess the status of the primary auditory pathways, which, if found to be unrelated to cognitive status, would implicate by default auditory association areas as the site(s) of the abnormalities.

Justification for this study was two-fold. First, because central auditory processing involves rapidly-changing, time-linked stimuli that require complex attentional abilities, it may be more sensitive to subclinical deficits of cognitive function, specifically executive functioning, than are existing global cognitive screening tests. Thus, central auditory tests might have a place in the early clinical detection of cognitive deficits. Second, because auditory processing deficits severely limit the outcomes of current methods for rehabilitation, viewing central auditory dysfunction as a neurologic rather than an auditory disorder might stimulate the development of new approaches for remediation.

METHODS AND MATERIALS

Participants

Participants were volunteer members of the Adult Changes in Thought (ACT) study¹⁴, a population-based longitudinal study of aging and dementia that began in 1994. For the present study, potential participants were screened via telephone to exclude stroke, head trauma, or otologic problems. There were 313 participants: 232 cognitively normal, 60 memory-impaired, and 21 demented.

Informed consent was obtained using procedures approved by the human subjects committees of both the University of Washington and Group Health Cooperative. The study was conducted at the Virginia Merrill Bloedel Hearing Research Center at the University of Washington.

Twenty-four of the 337 volunteers were excluded because their peripheral hearing was not adequate for central auditory testing, i.e.: a) pure-tone threshold average (PTA) for 0.5, 1.0, 2.0 kHz that differed by more than 20 dB between ears, b) a PTA >48 dB HL in either ear, or >40 dB HL in both ears, and c) word recognition score of less than 70% in either ear. This left 313 participants.

Twenty-one participants had a consensus conference diagnosis of Alzheimer's disease using NINCDS-ADRDA criteria¹⁵; 19 were judged "probable" and 2 were judged "possible". The most recent annual Cognitive Abilities Screening Instrument (CASI) scores were used to determine whether the remainder were cognitively normal (CASI > 86, CASI memory subscale ≥ 11 , (N = 232)) or cognitively intermediate (N=60). The intermediate group included those with a CASI score ≤ 86 and normal CASI memory subscale (N=8), or a total CASI < 90 with a CASI memory subscale score ≤ 10 on their latest annual exam (N=52) but who had not been judged to be demented.

Peripheral Auditory Tests

Pure-tone behavioral thresholds and word recognition in quiet were determined bilaterally with equipment and methods that met ANSI S3.39 (1987) standards.¹⁶ Distortion-product otoacoustic emissions were obtained in the better hearing ear using a custom system. See Gates et al (2008) for details.

Auditory Evoked Potential (AEP) Test Battery

The integrity of the ascending auditory pathways and primary auditory cortex was assessed by an AEP battery using standard clinical paradigms measuring both amplitude and latency of the Auditory Brainstem Responses, Middle Latency Responses and Late Latency Responses. (See Gates et al. (2008) for technical details).

Central Auditory Processing Tests

The tests were (1) the Synthetic Sentence Identification test with ipsilateral competing message (SSI-ICM), a monaural test, and two binaural tests - (2) the Dichotic Sentence Identification test (DSI) in the free mode, and (3) the Dichotic Digits test (DDT). These tests are widely available, relatively easy to administer and take, have been validated^{17;18}, and were used in our earlier studies of AD and central auditory function¹⁹. The sequence of testing was randomized to prevent an order effect. The presentation level for each test was 50 dB above the participant's PTA. Insert earphones were used to enhance high-frequency audibility and avoid collapsing ear canals.

SSI-ICM requires selecting which one of 10 nonsense sentences was heard against a background of an interesting narrative presented by the same talker in the same ear. Training presentations were done at +10 dB signal-to-competition ratio and the actual test was done with the signal and competition at the same intensity level. One list of 10 sentences was presented for participants scoring 90% or better, two lists if the score was 80% or better, otherwise three lists were presented. Pauses between presentations were taken as needed for slow responders. Correct identification of 80% or more is considered normal.

DSI uses six of the same sentences as the SSI-ICM but presents a different sentence to each ear simultaneously. The participant selects from a printed list which two sentences were heard in either ear (free report).²⁰ In adults right ear scores are normally better than left ear scores, presumably due to age-related corpus callosum dysfunction.²¹ Normal adult scores are 80% and above.

DDT is widely used to screen for central auditory dysfunction.¹⁸ Five single digit dichotic pairs (numbers 1–10, excluding 7) followed by five double-digit dichotic pairs were presented for practice. Twenty-five sets of double-digit pairs were presented for a total of 50 digits per ear. If all numbers were recognized correctly, a score of 100% (50×2) was given. The DDT is not greatly affected by mild to moderate hearing loss²², and is commonly abnormal in people with AD.²³ Normal scores for adults are 90% or above.²⁴

Neuropsychological Testing

Conventional instruments and procedures were used: Trail Making (parts A and B); Clock Drawing, Stroop Color and Word test, and subtests from the CASI measuring mental concentration (digits backwards, serial 3s), and category fluency. Tests were chosen to measure multiple dimensions of executive control function including behavioral inhibition (Trails B, Stroop), concept generation (clock drawing, list fluency), and either verbal (list fluency, mental concentration) or visuospatial (Trails, Clock Drawing, Stroop) working memory.¹¹

Trail Making is a timed test that measures complex visual scanning, motor speed, and cognitive flexibility.²⁵ Subjects draw a line connecting randomly positioned numbers in consecutive order (i.e., 1–2–3 etc.) or alternating numbers and letters of the alphabet (A–B–C etc.). Scoring is based upon the total time of test completion and the difference score (Trails part B- part A), which correlates with severity of cognitive impairment.²⁶ Good norms have been established for its use with older adults.²⁷ In the present study, Trails was administered in the standard fashion but was discontinued once subjects reached 5 errors, or if the test was not completed within 5 minutes.

Clock Drawing is widely used as a screen for dementia²⁸ that measures visuospatial attention and motor skills, conceptualization, and planning.²⁹ The subject is asked to draw a clock face with the hands indicating 20 minutes to four. Scoring is standardized, with possible scores from 1–10.³⁰ Clock drawing has been found to be of value with both low educated elderly patients and multiethnic older adults.³¹

Stroop Color and Word Test is one of a family of Stroop tests measuring selective attention and response inhibition.³⁰ These timed tests are based on the observation that it takes longer to name colors than to read words, and longer still to name a color of ink that is used to print the name of a color that is different from the color of the ink. The usefulness of the Stroop test in differentiating levels of executive functioning among individuals with AD has been demonstrated.³² In the current study, 3 stimulus sheets were used: 1) a sheet of color words (i.e., Blue, Green, etc.) printed in Black ink, 2) a color naming sheet with meaningless symbols printed in colored ink (i.e., 'X' printed in Yellow ink), and 3) a word-color sheet

(interference trial), which combines the words from the first sheet and the colored ink from the second sheet in such a way that the word and the color do not match (i.e., the word 'Green' is printed in blue ink). The participant must look over each sheet and read the words or name the colors as quickly as possible. Difference scores in time of completion for the word-color interference trial and the color naming trial were computed.

The CASI is a 25-item global screening test that quantitatively assesses nine cognitive domains: attention, mental concentration, orientation, short-term memory, long-term memory, language abilities, visual construction, category fluency and abstraction and judgment.³³ CASI has been used to screen for dementia.³⁴ We used the mental concentration (digits backwards, serial 3s; score range 0–10) and category fluency subtests (range 0–10) for our executive functioning score.

Statistical Analysis

We used Parscale Version 4.1 (Scientific Software International, Chicago) to construct composite executive functioning scores with item response theory³³. We confirmed sufficient unidimensionality³⁴ with confirmatory factor analysis techniques in Mplus (Muthén & Muthén, Los Angeles). Timed tests (e.g. Trails, Stroop interference) were transformed into ordinal scores, and those with many errors for Trails were given the lowest score.

Gender differences were evaluated by the Kruskal-Wallis test for continuous variables and Fisher's exact for categorical variables. In the primary analyses, linear regression modeling was used to explore the relationship between auditory test scores and the composite executive functioning measure. Sex, age, education, and hearing threshold level in the worse ear were controlled for in all models. The results from the poorer ear were used for the primary analyses, as was done earlier where we observed notable asymmetry in central auditory function⁵. Results from the better ear were also examined.

Some models had problems with heteroskedasticity, so robust standard errors were used³⁵. For consistency, we report robust standard errors in all linear regression models. Other model assumptions were tenable for all regression models, and the effect of outliers was minimal. Including or excluding short term memory scores from the CASI did not affect the findings.

The percent of the variance in each hearing outcome explained by executive functioning was calculated as the difference in adjusted R^2 between the full model and the adjusted R^2 in the model without executive function. In secondary analyses, subjects with cognitive deficits were excluded.

We examined the combined effects of central auditory processing and executive functioning on the three cognitive categories (normal/cognitively intermediate/Alzheimer's disease) using ordinal logistic regression. The proportional odds assumption was assessed using the Brant test³⁶. In secondary analyses, subjects with cognitive deficits were excluded. In addition, the association of the individual executive functioning items with hearing was assessed, as was the potential confounding effect of short term memory scores from the CASI. Analyses were conducted in Stata v10 (StataCorp, 2007).

RESULTS

The demographic characteristics, executive functioning scores, and auditory test results are shown (Table 1). The age range of the participants was 71–96 years. Their audiograms showed the typical high-frequency loss pattern of presbycusis in 87% of cases, and, as

expected, the men had poorer mean hearing thresholds than did the women. Thus, the auditory characteristics of this group are similar to those of the general population.

The executive functioning score was significantly associated with the hearing threshold average in the worse ear, after controlling for sex, age and education. (Table 2) A one standard deviation (SD) poorer composite executive functioning score was associated with a 1.2 dB (95% confidence interval (CI) 0.1, 2.4) poorer hearing threshold. Executive functioning was not associated with the primary auditory pathway measures: one SD in executive functioning was associated with 0.0 (95% CI -0.0, 0.1) msec delay for ABR, -0.1 (95% CI -0.5, 0.3) msec delay for Pa latency and -0.3 (95% CI -2.4, 1.8) msec delay for P2 latency controlling for sex, age, education, and hearing threshold. Results were equivalent when amplitude was used instead of latency (data not shown).

In contrast, the executive functioning score was significantly associated with all three measures of central auditory processing. In adjusted models, a one SD poorer executive functioning score was associated with a 9.2% (95% CI 6.4, 11.9) percentage point difference in worse SSI-ICM, a 15.0% (95% CI 12.0, 18.0) percentage point difference in worse DSI, and a 8.4% (95% CI 6.4, 10.4) percentage point difference in worse DDT. Executive functioning explained 8% of the variance of worse SSI, 21% of worse DSI, and 16% of worse DDT (Table 2). Associations using the better ear were also significant with executive functioning explaining 7% of the variance in better SSI-ICM, 5% of better DSI, and 7% of better DDT. Distortion Product Otoacoustic Emission responses were not an independent predictor or a confounder of any of these outcomes.

Two of the central auditory processing tests were significantly associated with cognitive status (normal/intermediate/Alzheimer's disease) beyond the effects of executive functioning. In models controlling for executive functioning, age, education, and hearing thresholds, the odds ratios for decreased cognitive status were 1.52 (1.14, 2.03) for a 20-point poorer SSI-ICM in the worse ear, and 1.63 (1.27, 2.10) for a 20-point poorer DSI in the worse ear. The proportional odds assumptions were tenable overall ($p=0.29$ and 0.45 , respectively) and for each covariate ($p=0.17$ to 0.73).

In secondary analyses, executive functioning and the central auditory processing outcomes were associated in the cognitively normal participants, though the strength of the associations was attenuated. Executive functioning explained 4% of the variance in worse SSI-ICM, 11% of worse DSI, and 10% of worse DDT. In the better ears of the cognitively intact, the percents were 3%, 3%, and 2%, respectively. Of the individual cognitive tests, Trails B was most strongly associated with the auditory outcomes, explaining 8–14% of the variance in the full sample, and 3–8% in the cognitively normal participants (Table 2).

DISCUSSION

We affirm in this cohort, as in a prior cohort⁷, an association between age-related central auditory dysfunction (central presbycusis) and cognition, and extend those observations to implicate executive dysfunctioning as a putative mechanism. These findings argue against the hypothesis that central auditory dysfunction is distinct from cognitive dysfunction and suggest that difficulty understanding speech-in-noise – the hallmark of central presbycusis – may be an early manifestation of the processes that lead to dementia. The presence of executive dysfunction in both AD and central presbycusis suggests that similar pathologic processes may be involved. Of interest, the association between executive functioning and central presbycusis was not due solely to clinical dementia status as it persisted when only those with normal cognition were included.

We controlled our models for age and abnormalities in the peripheral and ascending auditory pathways, so our findings also argue against the hypothesis that difficulty understanding speech-in-noise is due to primary auditory pathway lesions. The anatomic area(s) involved in central presbycusis are not established. However, those areas where auditory association pathways and executive functioning overlap would seem to be likely candidates. Although the present methods were not capable of indicating whether the prefrontal or temporo-parietal cortices or both are involved, it is clear that the primary auditory pathways are not involved, as they are in advanced AD¹². The observed association between executive dysfunction and central presbycusis raises questions about commonality of mechanism and assessment overlap for future investigations to explore and resolve.

Performance on central auditory tests requires cognitive processing of auditory information in terms of short-term memory, task-shifting, and attention-to-task³⁷. The present data support the premise that central auditory testing could be regarded in part as a measure of cognitive function. When we added central auditory testing results to executive functioning scores, the amount of variation in cognitive impairment diagnoses explained was improved, suggesting that central auditory tests provide additional independent explanatory power for cognitive impairment and dementia beyond the executive functioning tests employed in this study.

In the present study we also noted abnormal central auditory results in 40%–45% of the older persons without cognitive impairment. We will re-examine these subjects in the future to determine if a poor result on central auditory testing predicts subsequent incident cognitive impairment in this group. When we compared incident cognitive decline using the Mini Mental State Examination (MMSE) with the SSI-ICM in another cohort (Framingham Heart Study) we found that unilaterally poor results on the SSI-ICM significantly predicted decline in the MMSE 6 years later.⁷ We also showed earlier that very poor results (<50% correct) on the SSI-ICM was a strong predictor for the subsequent diagnosis of clinical AD 3 to 10 years later.⁵

Difficulty understanding speech-in-noise is common among the elderly. Complainants typically receive a hearing test and a recommendation for amplification. However, our findings suggest that while this approach may be necessary in many cases, it may not be sufficient because hearing aids do not resolve deficits in cognition or executive functioning. Further research is indicated to determine whether cognitive training strategies might improve the ability of affected persons to understand speech-in-noise. Our results suggest that elderly patients with substantial central auditory dysfunction should be referred for neurologic evaluation and neuropsychologic assessment.

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Table 1Participant characteristics, by gender (mean $\pm$ SD or percent).

Characteristic	Men (n=119)	Women (n=194)	p-value *
Age (years + SD)	80.0 $\pm$ 5.6	79.7 $\pm$ 5.2	0.603
Education (years)	15.7 $\pm$ 3.2	14.2 $\pm$ 2.6	< 0.001
Hearing complaint	62%	53%	0.128
Hearing aid use	19%	7%	< 0.001
Exposure to loud noise	32%	3%	< 0.001
SSI-ICM Worse Ear (% correct)	69.8 $\pm$ 27.8	68.2 $\pm$ 28.0	0.621
SSI-ICM Better Ear (% correct)	81.5 $\pm$ 26.1	81.0 $\pm$ 25.1	0.552
DSI Worse Ear (% correct)	65.4 $\pm$ 28.8	68.7 $\pm$ 27.1	0.316
DSI Better Ear (% correct)	94.7 $\pm$ 8.6	94.0 $\pm$ 10.6	0.843
DDT Worse Ear (% correct)	71.2 $\pm$ 19.0	73.1 $\pm$ 17.0	0.521
DDT Better Ear (% correct)	89.1 $\pm$ 10.2	89.4 $\pm$ 9.8	0.960
PTA Worse Ear	29.0 $\pm$ 9.4	28.3 $\pm$ 9.6	0.581
PTA Better Ear	24.3 $\pm$ 8.8	24.1 $\pm$ 8.9	0.836
DPOE (average)	70.0 $\pm$ 9.4	67.5 $\pm$ 8.2	0.015
ABR Worse Ear	6.1 $\pm$ 0.3	5.8 $\pm$ 0.2	< 0.001
MLR Worse Ear	30.5 $\pm$ 2.5	30.9 $\pm$ 2.7	0.245
LLR Worse Ear	180 $\pm$ 12.4	174.3 $\pm$ 12.4	0.0005
Composite executive function score	0.1 $\pm$ 1.0	-0.1 $\pm$ 1.0	0.159

* P-values based on Kruskal-Wallis tests for continuous variables and Fisher's exact for categorical variables.

SSI-ICM – Synthetic Sentence Identification with Ipsilateral Competing Message

DSI – Dichotic Sentence Identification, free report mode

DDT – Dichotic Digits Test

PTA – average of behavioral thresholds at 1 2 3 kHz in dBHL

DPOEa – Distortion Product Otoacoustic Emission average at 1 2 3 kHz; were done only in the ear with better (i.e. lower) pure-tone thresholds..

ABR – latency in msec of wave V of the Auditory Brainstem Response

MLR - latency of poorer wave Pa

LLR - latency of poorer wave P2

Table 2

Percentage of the variance in central auditory processing explained by measures of executive functioning, controlling for age, education, gender, and worse pure tone average.

Central Auditory Processing	AR ^{2*}
<u>SSI-ICM Worse Ear</u>	
Composite score	8%
Trails B	8%
Clock drawing	3%
Stroop Color and Word	3%
Digits backwards (3 digits)	0%
Digits backwards (4 digits)	1%
Animal fluency	3%
Serial subtractions	2%
<u>DSI Worse Ear</u>	
Composite score	21%
Trails B	14%
Clock drawing	9%
Stroop Color and Word	8%
Digits backwards (3 digits)	4%
Digits backwards (4 digits)	4%
Animal fluency	5%
Serial subtractions	8%
<u>DDT Worse Ear</u>	
Composite score	16%
Trails B	13%
Clock drawing	0%
Stroop Color and Word	7%
Digits backwards (3 digits)	3%
Digits backwards (4 digits)	3%
Animal fluency	3%
Serial subtractions	5%

* Adjusted R²