Hearing Aids to Support Cognitive Functions of Older Adults at Risk of Dementia: the HearCog trial

Background

Hearing loss is the second highest cause of disability in the world, affecting 1.33 billion people,[6] with 90% of cases being due to age-related hearing loss (ARHL).[6] One in six Australian adults suffer from a hearing loss > 25dBHL and this number is projected to increase up to one in four by 2050.[7] Moreover, 88% of Australians aged 70 years or above have > 25 dBHL hearing loss in their worse ear.[7] There are two key components of the auditory system involved in processing incoming auditory stimuli: the peripheral and the central hearing systems.[8] The peripheral hearing system consists of the peripheral components of hearing, namely the cochlea, middle ear and outer ear.[8] The central hearing system encompasses the central auditory pathways and influences the way incoming auditory stimuli are perceived and understood, namely central auditory processing.[8] Peripheral hearing loss affects both the auditory processing of speech sounds and the higher-level cognitive functions required to process linguistically demanding sentences.[9] Evidence from both cross sectional[10] and longitudinal[11,12] studies confirmed the existence of an association between peripheral hearing impairment and cognitive impairment in older adults. Several recent studies have also reported an increase in the risk of incident dementia among older adults with ARHL,[11,12] as well as among those with central auditory dysfunction.[13]

According to currently available evidence, the incidence of all cases of dementia can be reduced by 9% if ARHL was eliminated, perhaps through hearing loss correction.[4] As an example of potential changes in outcome measures following hearing loss correction, we have recently reported that cochlear implant recipients performed substantially better on general measures of cognitive function compared with implant candidates on a waiting list.[14]

Whether the correction of ARHL can delay the onset of dementia remains to be determined. However, treatment of ARHL is an extremely low risk procedure that is associated with significant health, social and safety benefits. Hence, our study aims to investigate whether the correction of hearing loss through the use of HAs could decrease the 12-month rate of cognitive decline among older adults at risk of dementia. This project will allow us to investigate the effect of severity of impairment on cognitive outcomes.

Aims

1. This study will determine whether correction of hearing loss through the use of hearing aids (HA) decreases the 12-month rate of cognitive decline among older adults at risk of dementia.
2. We will also investigate whether the correction of hearing loss has a beneficial impact on memory and executive functions, anxiety and depressive symptoms, quality of life, physical health, and health-related costs over 12 months.
3 Whether the expected clinical gains achieved through the correction of hearing loss by 12 months can be sustained over an additional period of 12 months, and if losses experienced through the non-correction of hearing loss can be reversed with the fitting of HAs after 12 months (i.e., HAs fitting for controls at 12 months with follow up of 12 months).

Methods

Study design: Two-arm parallel randomised controlled trial.

Setting: Ear Science Institute Australia (ESIA) based in the Perth and Bunbury metropolitan regions, Western Australia.

Eligibility criteria:

- Participants will be older adults aged 70 years or older (cognitive decline is more pronounced later in life).
- Montreal Cognitive Assessment for the Hearing Impaired (MOCA-H)[15] ≥ 18 and < 26 (mild impairment).
- Better ear average hearing loss at 0.5, 1 & 2 kHz (3FAHL) > 23 dB or high frequency average hearing loss (2, 3 & 4 kHz) (HFAHL) ≥ 40dB as measured using air conduction pure-tone audiometry.[16] We have followed the HA fitting criteria recommended by OHS for older adults with ARHL.[16]
- Fluent English speakers

Exclusion criteria:

- Impaired instrumental activities of daily living (IADL)[17] due to cognitive deficits (requires assistance or is dependent in the use of telephone, shopping, housekeeping, laundry, transport, management of medications and finances) – i.e. has dementia or major neurocognitive disorder
- Meets clinical criteria for cochlear implantation (unaided bilateral sensorineural hearing loss ≥70 dBHL, and open-set sentence scores in quiet in the worse ear < 65% and in the better ear < 85% or open set phoneme scores in quiet in the worse ear < 45% and in the better ear < 65% with optimized HA fitting[18]
- Visual impairment that limits participant's ability to read Times New Roman font size 16 (a requirement for 2 sentences of MOCA-H)[15]
- Severe medical illness that limits the ability of the participant to attend appointments or sustain participation in the study for 24 months
- Plans to move away from the study area during the subsequent 24 months
- Unable or unwilling to provide written informed consent to participate
- Inability to complete the motor screening task (MOT) module of the Cambridge Neuropsychological Test Battery (CANTAB) due to visual impairment, inability to comprehend test instructions or inability to attend to the task due to dexterity problems.[19]

Recruitment: Participants will be recruited mainly from the ESIA Hearing Clinics. In addition, we will place advertisements in the local media and primary care networks inviting interested participants for screening. If the recruitment of participants is lower than predicted after 12 months, we will use the electoral roll list to select a random list of people aged ≥ 70 years living the study areas: they will receive information about the study and an invitation to contact the research office for screening if they believe they may potentially eligible (mail out is de-identified – i.e., investigators will not have access to the list). The research assistant will contact those who have expressed interest in taking part in the study and volunteers will complete a hearing and cognitive screening at the nearest ESIA Hearing Clinic.

Sample size: Based on DMS percent correct pilot test data, a total of 140 participants will be required (70 in each group; effect size d = 0.28, α = .05, power .90). To account for 25% of attrition over time, a total of 180 participants will be recruited.

Study measures:

1. Global cognitive abilities: Due to hearing impairment, the elderly may experience difficulty in following verbal instructions or completing tasks that heavily rely on hearing during

cognitive assessments. This may result in overestimation of cognitive impairment in such individuals.[10] Hence, we have used a non-verbal global cognitive measure that has been validated to use with the hearing impaired older adults.[15] The global cognitive abilities will be measured using Montreal Cognitive Assessment for the Hearing Impaired (MoCA-H).[15] No significant difference was observed for MOCA and MOCA-H scores in cognitively intact normal hearing participants and the test–retest reliability coefficient was 0.66.[15]

2. Nonverbal cognition assessment using Cambridge Neuropsychological Test Battery (CANTAB)[19] - This assessment does NOT rely on verbal communication:

- *Attention Switching task (AST):* is a test of executive functioning and provides a measure of cued attentional set shifting.[19] AST is based on the Stroop test and relies heavily on the functions of the anterior right hemisphere and medial frontal structures.
- *Delayed Matching Sample (DMS):* assesses participants' ability to recognize complex visual patterns at different time intervals.[19] It is primarily sensitive to medial temporal lobe dysfunction.
- *Paired Associates Learning (PAL):* PAL is a recall test of memory which assesses episodic visuospatial memory, learning and association ability.[19] PAL is primarily sensitive to the changes in medial temporal lobe functioning.
- *Spatial Working Memory (SWM):* measures the retention and manipulation of visuospatial information in areas such as non-verbal working memory, working visuospatial memory and strategy use.[19]

3. General physical & mental health: Participants will be asked to complete the following widely used and validated assessments:

- Cognitive reserve questionnaire to obtain information on participant age, gender, education, work history and leisure activities[20]
- Health status and Quality of life: Short form survey (SF-12)[21]
- Physical function: Functional Comorbidity Index (FCI)[22]
- Depressive symptoms: Patient Health Questionnaire (PHQ-9)[23]
- Anxiety symptoms: Geriatric Anxiety Inventory (GAI)[24]
- Function: Lawton & Brody Instrumental Activities of Daily Living (IADL)[25]
- Social Support and interaction: de Jon Gierveld social support questionnaire[26]
- Frailty: hand grip strength will be measured using a Jamar Analogue Hand Dynamometer [27]
- Psychological and social adjustment problems resulting from hearing loss: Hearing Handicap Inventory of the Elderly (HHIE)[28]
- Effectiveness of the HAs application: International Outcome Inventory for HAs (IOI-HA)[29].

4. Hearing Assessment: The assessment of hearing will consist of two parts:

- Peripheral hearing assessment will be based on tympanometry, which provides information about middle ear pathologies; pure-tone audiometry, which generates information on hearing thresholds across .25-8 kHz frequency range; and speech perception in quiet environment: CNC word [30] and City University of New York (CUNY) sentence test[31]

- Central hearing assessment will comprise of the following tests: Dichotic Digits Test (DDT),[32] Synthetic Sentence Identification with Ipsilateral Competing Message (SSI-ICM),[33] and Quick Speech in Noise (Quick-SIN).[34]

Procedures for the collection of study measures:
The procedure for the data collection will follow CONSORT guidelines. Participants who meet criteria for inclusion in the study will be randomly assigned to either the experimental (A) or control (B) group. Group A participants will receive intervention immediately after the baseline assessment, whereas group B participants will receive intervention 12 months later (Figure 5). All participants will be informed that if they get randomly allocated to group B, they will have to wait 12 months to receive the treatment. Those who prefer to receive HA immediately without having to wait 12 months will be given the option to opt out from the study. Cognition, mental health and QoL assessments will be carried out separately to the hearing assessments and HA fitting.

Group A will complete hearing assessment, cognition, mental health and QoL assessment at the baseline, 12 and 24 months.

Group B will complete hearing assessment, cognition, mental health and QoL assessment at the baseline and 12 months. (Figure 5).

Timeline:

Task	Dates
Ethics application	June-July 2018
Participant recruitment & Screening	August 2018- August 2019
Baseline assessment	October 2018- October 2019
Intervention Group A	October 2018-October 2019
52 week analysis	October 2019-October 2020
Intervention Group B	October 2019-October 2020
Follow up 104 weeks	October 2020-October 2021
Data management	October 2020-October 2021
Data analysis	November 2021-March 2022
Manuscript preparation and submission	March 2022- December 2022

<u>Intervention</u>:
The intervention consist of three parts: (i) hearing assessment and HA discussion, (ii) HA fitting, verification and validation and (iii) HA review following daily use of HAs.
The intervention will be carried out by a qualified audiologist according to the Australian Audiological Society Standards in a standardised sound proof booth.

Part I: Hearing assessment and HA discussion
Duration 1.15 hours.
During the first appointment, the participant will complete (1) a comprehensive case history that contains information on medical and hearing history, ear infections, ear surgeries, head trauma, noise exposure, ototoxic drug exposure, visual and dexterity problems, tinnitus, vertigo, and cognition. (2) Client Oriented Scale of Improvement (COSI) goals[35] for everyday listening situations and a standard hearing assessment. Finally, we will discuss with

participants currently available technology of HAs that include suitable type and style of HAs and their cost, as well as participant's daily listening expectations. The choice of hearing aid will be based on hearing loss, subject preference and ease of management. An explanation on what are hearing aids and how they work, what they are used for, how to use them, and questions and answers will be provided. Study participants receiving the intervention will also be given an educational booklet summarizing the topics presented.

A HA is a device designed to improve hearing by amplifying and acoustically modifying the sound to suit a person's hearing loss. Current HA technology uses digital signal processing techniques to improve speech intelligibility and provide comfort for the user.

Part II: HA fitting, real-ear verification and validation -immediately following appointment part I.

Duration: 1 hour.

The audiologist will program the HA and carry out the real-ear verification using real ear insertion gain (REIG) to ensure that appropriate amplification is provided to a person with hearing loss.[36] The HA program will be fine-tuned to fit the participants' every day listening demands using NAL-NL2 formula[36]. Following, HA out-put verification, validation tasks will be carried out to determine that the participant is benefitting from the HAs. Validation includes asking the patient about sound quality, ear balance, comfort of the devices and finally a speech in quiet assessment using AB word list[37] will also be carried out to determine that the participants is benefitting from the HAs. Adjustments can be made to the devices so that the patient is comfortable with the devices.

Part III: HA review: 2 weeks after the HA fitting.

Duration: 30 minutes.

HA data logging information recorded in the software of the HA is analysed to ensure that the HA program provides the best solutions to the listening demands of the participant. Based on COSI goals, data logging information and feedback received from the participants, changes are made to the HA program.

HA review appointments at 12 and 24 months after HA fitting:

Duration: 1 hour.

These appointments are similar to Part II and III of the HA fitting appointments. During these appointments, a standard pure-tone audiometric assessment to obtain hearing thresholds, reprogramming of the HA according to the current hearing loss and finally REIG to ensure that the HA is programmed according to the current hearing loss of the participant will be carried out.

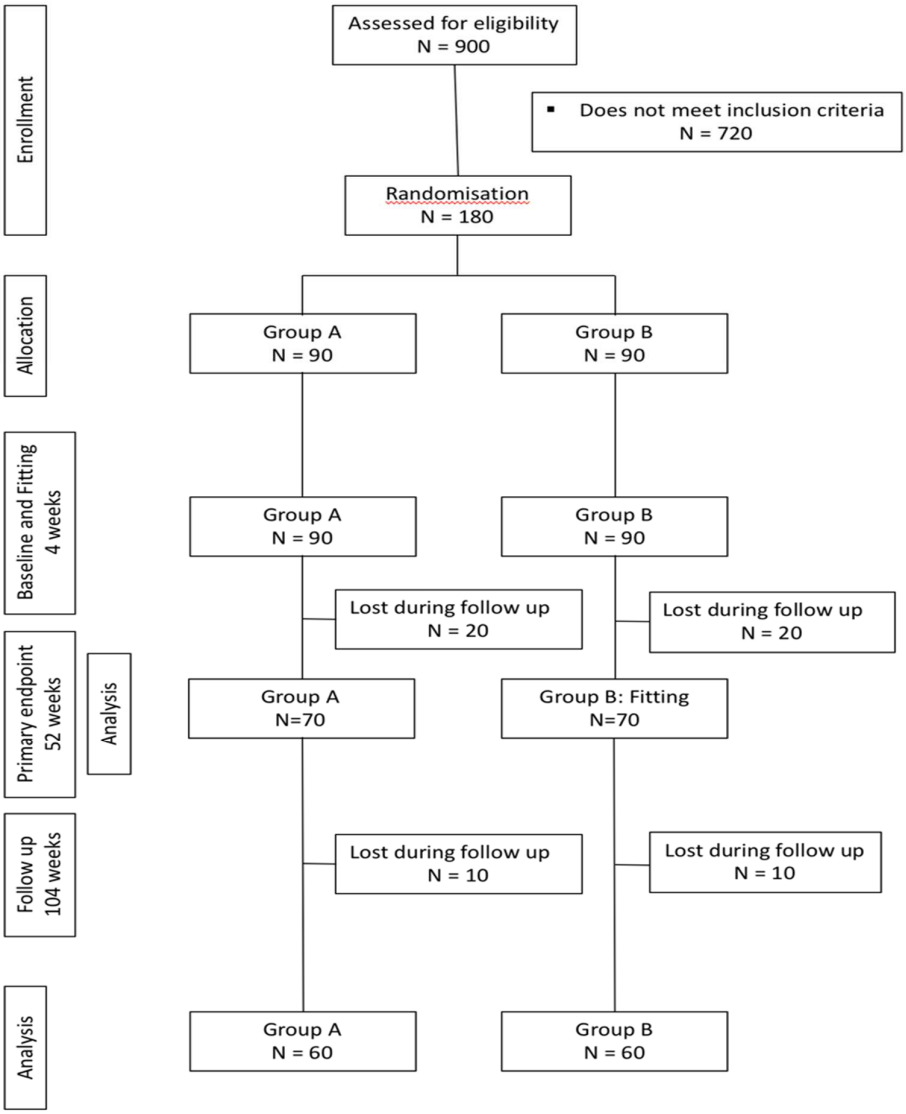

Figure 5: Flow of participants from the time of recruitment to the final collection of endpoints.

Measuring adherence with treatment: Current HAs have a "log in" feature that records both the average number of hours and different listening environments in which the participant has used the HA. These data can be retrieved when the HA is connected to the program software, which will be done at all assessments. In addition, the participant will be asked to maintain a daily listening diary in which s/he records the number of hours the HA worn.

Randomisation, concealment and blinding: This trial will be registered with the Australian and New Zealand Clinical Trials Registry before recruitment commences (http://www.anzctr.org.au). The computer generated randomisation sequence will be stratified by the severity of the hearing loss (mild to moderate vs severe) based on the results of the hearing assessment. Each stratification block will be associated with a random sequence of numbers assigned to the intervention and control groups in random permuted blocks of 6, 8 or 10. This sequence will be stored in a password-protected server housed at the University of Western Australia and will be managed by a biostatistician not involved in this project (A/Prof

Kieran McCaul). Once a participant consents and is enrolled, s/he will be automatically ascribed a number and group membership (intervention or control).

Due to the nature of the intervention, participants will know their group assignment, but research staff involved in the assessment of cognitive function, quality of life, mood and physical function will remain blind to treatment allocation. This will be achieved by directing participants to **NOT**: (i) discuss any aspects of the intervention during the assessments, (ii) wear their HAs during assessment. Binaural hearing amplifiers will be used to facilitate the communication between participants and research staff during all assessment visits (including the 12 and 24-month visits).

Statistical methods: All analyses will follow CONSORT guidelines. We will use standard descriptive statistics to compare basic sociodemographic and clinical data across treatment arms. We will use multilevel mixed models to investigate changes in cognitive and other scale scores over time. Mixed models provide estimates that are 'intention-to-treat' and allow for the investigation of interactions between group and time effects, as well as for the adjustment of possible imbalances between the groups following the randomisation. We will use imputed chain equations if loss to follow up exceeds 25%. All probability tests will be two-tailed.

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