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Validation of a cognitive screening tool for hearing-impaired older adults

A Thesis Presented for the Degree of

Doctor of Philosophy in

Neuroaudiology and Audiovestibular Medicine

By

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Declaration

I, Nattawan Utoomprurkporn confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

All participating subjects gave informed consent and all work was carried out with the approval of National Health Service (NHS) Ethics Committee, according to guidelines established by the Declaration of Helsinki.

The work was done under the guidance and supervision of Professor Doris-Eva Bamiou at the Audio-vestibular medicine department, Royal National Throat Nose Ear Hospital and the UCL Ear Institute, and Dr Sergi Costafreda Gonzalez at Division of Psychiatry, Faculty of Brain Sciences, and Dr Joshua Stott at Division of Psychology & Language Sciences, Faculty of Brain Science.

Signature:

Date:

Abstract

(300 words)

Dementia usually starts in individuals aged over 65, and one-third of people in this age group have disabling hearing impairment. Moreover, older adults with hearing impairment are nearly 2 times more likely to develop dementia compared with their normal-hearing peers. This makes early and accurate screening for mild cognitive impairment (MCI) among this population even more important.

The Montreal cognitive assessment (MoCA) is a commonly used cognitive screening tool to early identify the individuals at risk of MCI. However, the tool relies on verbal administration of the instructions and target words/sentences which as shown in a previous meta-analysis could be a disadvantage for the hearing-impaired population, making the screening inaccurate.

The MoCA for hearing-aid users (MoCA-HA) was developed and validated. The development phase was done with feedback from professionals and the older adult hearing-aid users, the tool's final target population. The appropriate cut-point score of below 26 out of 30 is proposed for an onward cognitive assessment referral which yields a similarly high sensitivity to the traditional MoCA. It had an excellent discrimination property and correlated well with other existing cognitive measures. The MoCA-HA is suitable to be used in hearing aid centres for early screening for potential mild cognitive impairment.

Despite measuring with the visually presented tool such as MoCA-HA, the information encoding ability was slightly reduced in the hearing-impaired cohort. The information retrieval ability was well preserved among the hearing-impaired population but was reduced when they had additional mild cognitive impairment. This also affected their performance and reliability of the self-reported hearing difficulty questionnaires.

The visuospatial ability of the hearing-impaired population was better than the norms. With additional MCI, the ability was decreased but still comparable to the norms. These considerations could formulate better and holistic care plans for the hearing-impaired population with potential cognitive impairment.

Statement of impact

(500 words-research and clinical)

Most cognitive screening tools rely on verbal administration of instructions and tasks dependent on verbal memory. However, one-third of older adults with aged over 65 who are at higher risk of dementia have a hearing impairment, that may impact on implementation and interpretation of the cognitive screening tool results. Therefore, cognitive screening tools tailored to the needs of this population is needed.

The Montreal cognitive assessment tool for hearing aid users (MoCA-HA) was developed and validated with feedback from healthcare professionals and the older adult hearing aid users who would be the final target population of the tool to ensure the practicality and effectiveness. As a result, the MoCA-HA has an excellent discrimination property similar to the traditional MoCA and correlated well with other existing visually based cognitive measures.

Even when overcoming auditory difficulty with MoCA-HA, a slightly lower memory sub-category score was still found in the normal cognition with hearing impairment group. The analysis of memory index score (MIS), a verbal fluency task of MoCA-HA and visually presented graded naming test score showed a preserved information retrieval pathway. This indicated that the problem may lie on the information encoding pathway.

The encoding problem was previously studied among the hearing-impaired population with MoCA, however, unlike in this study, the effect could not previously be demonstrated as clearly with traditional auditory presented MoCA when an encoding problem can also stem from mishearing the target words or increasing listening effort. This study reveals that the encoding ability of the hearing impaired brain, regardless of the stimulus presentation mode, suffers from a permanent negative effect of hearing impairment as previously described by the sensory deprivation theory (Husain et al., 2011).

This study also included participants with both hearing and mild cognitive impairment. This helps to explore the interaction between hearing and cognition which has only been speculated in previous literature. Additional information retrieval problems on top of the information encoding difficulty were found among these participants, which may interfere with their abilities to report/recall their difficulties in various situations. The commonly used self-reported hearing-related questionnaires such as the Modified Amsterdam Inventory for Auditory Disability (mAIAD) and The Speech, Spatial and Qualities of Hearing Scale (SSQ) may not be able to capture their hearing difficulties, despite their having a deficit in

auditory processing test. Therefore, hearing evaluation and test interpretation among this population should be done carefully.

Older adults hearing aid users may have a slight decrease in their memory encoding ability to store the information which could interfere with their memory. However, their compensated visuospatial ability in remembering the visual target in space becomes better. Even with additional mild cognitive impairment, their visuospatial ability is still comparable to their peers. They could potentially benefit by auditory rehabilitation programmes through facial cues and lip-reading.

Mild cognitive impairment can be a “hidden” population in any hearing-aid clinic. This study provides a screening tool for early detection of these individuals and insight into their cognitive and auditory abilities which could potentially improve their cares.

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Abbreviations

AUC	Area under curve
CI	Confidence interval
GNT	Graded naming test
HL	Hearing loss
ICD	International Classification of Disease
mAIAD	Modified Amsterdam Inventory for Auditory Disability
MCI	Mild cognitive impairment
MIS	Memory index score
MoCA	Montreal cognitive assessment
MoCA-HA	Montreal cognitive assessment-Hearing aids
MoCA-HI	Montreal cognitive assessment-Hearing impaired
PPI	Patient-public involvement
ROC	Receiver Operating Characteristic
ROCFT	Rey Osterrieth Complex figure test
SSQ	Speech, Spatial and Qualities of Hearing Scale
WHO	World Health Organization

1. Chapter 1: Introduction- Accurate identification of mild cognitive impairment (MCI) in hearing loss population/hearing aids users

In this chapter, hearing problems and their effects toward cognitive assessments were addressed. Currently available cognitive screening tools which do not take into account these effects would fail to accurately capture the hearing impairment population's cognitive status. Potential problems of traditional cognitive screening tools in this population were discussed in more detail.

The importance of the newly developed cognitive screening tool or the adaptation of existing tool that could be delivered visually and do not depend on hearing ability hence the primary aim of this research was emphasised. Despite, having high face validity, this novel tool needs to be validated to confirm it's diagnostic property, which is the secondary aim of this research.

1.1. The burden of hearing loss in the older population

Age-related hearing loss is prevalent in older adults. Hearing ability is continuous, so the prevalence of diagnosed hearing loss depends on the diagnostic threshold used to define the condition. The world health organisation (WHO) defines disabling hearing loss as the hearing level greater than 40 dB HL in the better-hearing ear (WHO, 2012, WHO, 2018). According to this definition, almost one in every three adults aged over 65 years suffering from disabling hearing loss.

Since the global population is ageing, the burdens associated both with older age and hearing loss are on the increase. Currently, in the UK, there are over 12 million people who are over 65 and over 4 million older adults with disabling hearing loss (Park, 2018). This population requires not only hearing care but also that the rest of their healthcare takes into account the high prevalence of hearing impairment in this population.

1.2. Hearing loss associated with cognition

There is evidence of an association between impaired hearing and poorer cognition. Several hypotheses have been proposed to account for this association (Wayne and Johnsrude, 2015). Combination of one or more of these hypotheses listed below may be needed to fully explain the relationship (Wong et al., 2019).

1.2.1. Sensory degradation hypothesis

This hypothesis postulates that the relationship is explained by perceptual degradation of the auditory input during various cognitive tasks including the cognitive assessment. Participants with hearing loss tended to have increase listening effort even with appropriate amplification which affected their abilities to perform cognitive tasks (Rakerd et al., 1996). Moreover, miss hearing the instruction and target words during the assessments can also negatively impact cognitive test scores (Yeok Leng Lim and Loo, 2018).

Therefore, the apparent cognitive performance decline may be due to listening fatigue or miscommunication. This effect may be reversible with clearer communication. Previous research of personal assistive listening devices in the geriatric ward showed that the cognitive assessment score improved within 24 hours after the device implementation (MacDonald et al., 2012).

This theory suggests that we need better and more accurate cognitive assessment tools for the hearing-impaired older adult population, that can differentiate between the potentially reversible effects of sensory degradation and permanent cognitive impairment. Accurate cognitive assessment is needed for the diagnosis and treatment of clinically significant cognitive impairment and dementia.

1.2.2. Sensory deprivation hypothesis

This hypothesis postulates that there are permanent effects of hearing loss on cognition via changes in neural structure and organisation of the central nervous system. A brain imaging study of hearing-impaired participants showed a decrease of overall volume especially in the auditory cortex and associated areas (Husain et al., 2011). With these permanent brain changes, even with auditory amplification, the cognitive function decline may not be reversed.

In addition to the decrease in the neural activity in auditory cortex, when listening in a noisy background, as a compensatory mechanism, older adults with hearing loss tend to have increased neural activity in brain area subserving working memory and attention namely the prefrontal and precuneus regions (Wong et al., 2009) along with the medial temporal lobe (MTL) region (Griffiths et al., 2020). These areas are also affected in many patients with Alzheimer type dementia (Yokoi et al., 2018). The increased neural activity is suggested to further aggravate the pathological neural change (excitotoxic cell death) in these patients (Griffiths et al., 2020).

A consequence of this hypothesis is that altered neural activities would be permanent for the hearing loss population and the cognitive decline may still be evident when assessed via another modality i.e. the visually instead of auditory.

1.2.3. Cognitive load hypothesis

This model postulates that the cognitive decline is causing a burden on neural systems responsible for sensory input perception including hearing. Therefore, people with cognitive decline would perform worse on hearing assessment (Kiely et al., 2012) and seemingly have hearing problems.

Previous research showed that even among confirmed diagnosed dementia patients, an audiogram could be accurately obtained when performed with care (Lemke, 2011). This means that cognitive decline should not be interfering with the audiological performance of older adults at least when measuring pure-tone audiograms. However, with listening in real-life noisy situations, cognitive decline may cause hearing difficulty due to listening attention problems (Hardy et al., 2016). As a result, older adults with cognitive decline may still struggle in everyday listening situations, despite their normal pure-tone audiogram. Auditory tests which simulate speech in everyday background noise along with hearing difficulty related questionnaires may be able to reveal their particular hearing problems.

1.2.4. Common cause hypothesis

This hypothesis proposes that the neuronal changes associated with the ageing brain are the common cause that contributes to both the auditory decline and the cognitive decline (Baltes and Lindenberger, 1997). In addition to the auditory modality, other sensory modalities such as visual, vestibular were also found to deteriorate in older adults (Lin et al., 2004, Lindenberger and Baltes, 1994). This deterioration may, therefore, result from the common neurodegenerative changes that affect the ageing brain.

An accurate cognitive assessment is thus required for the hearing-impaired population to rule out the sensory degradation and cognitive load component in order to disentangle the dilemma of this common cause hypothesis.

If this hypothesis was true, early intervention of hearing loss would not result in improved cognition. However, research has suggested that hearing intervention can decrease the cognitive decline rate among hearing-impaired older adults and could even improve cognitive performance (Sarant et al., 2020).

1.2.5. Social isolation and depression mediated hypothesis

Hearing loss can interfere with an individual ability to communicate and participate in social activities which can lead to depression (Boi et al., 2012). Several previous research studies showed that depression is a risk factor for cognitive decline (Suciu and Miclutia, 2020).

This hypothesis proposes that the association between hearing and cognition would not be direct but mediated through an additional factor such as social isolation and depression, which are also recognised risk factors for cognitive impairment (Dawes et al., 2015). This indicates that if we can offer early intervention to prevent these consequences, we may see a partially less negative effect of hearing loss on cognition.

Therefore, this theory not only emphasises the importance of early hearing screening and intervention for older adults but also early screening for cognitive decline among the hearing-impaired population to avoid further damage.

1.3. Hearing loss may be the highest modifiable risk factor for cognitive impairment

Several studies have emphasised the correlation between hearing loss and abnormal results in cognitive assessments in older adults. Older adults with moderate or higher degrees of hearing loss perform worse on the Mini-Mental Status Evaluation (MMSE) than those with normal to mildly raised hearing thresholds (Jupiter, 2012). A drop of 1.2 dB (95% confidence interval 0.1-2.4 dB) in hearing threshold can be associated with a decrease of up to 1 standard deviation (SD) on a composite executive functioning score computed using Item response theory from the Trail Making, Clock Drawing, Stroop Color and Word, and subtests from the Cognitive Abilities Screening Instrument (Gates et al., 2010).

There is also evidence that hearing loss increases the risk of cognitive decline. In the Baltimore longitudinal study of Aging, incident dementia risk increased by a factor of approximately 1.27 for every 10 dB decrease of average speech frequency hearing thresholds after adjustment for sex, age, race, education, diabetes, smoking, and hypertension (Lin et al., 2011). A decrease in hearing thresholds has also been shown to accelerate the rate of cognitive deterioration by up to 30-40% (Lin et al., 2013a).

Furthermore, a recent meta-analysis showed that hearing loss is a significant risk factor for dementia, with a pooled relative risk of 1.94 (95% CI [1.38-2.73]) (Livingston et al., 2017). Moreover, as it is also one of the most common dementia risk factors found in older adults with a prevalence of up to 31.7%, it was reported to be the most important modifiable risk factor for dementia, with an estimated 9% Population Attributable Fraction (PAF) (Livingston et al., 2017). These findings indicate that older adults

with hearing loss may be a higher-risk population for dementia. While there is ongoing research on what explains the association of hearing loss with cognition, attention now is shifting on whether an early hearing intervention can decrease the dementia risk.

1.3.1. Why are an accurate screening and early diagnosis of cognitive impairment needed?

Screening for cognitive impairment needs to be done accurately to facilitate a prompt onward referral and appropriate diagnosis. Screening tool performance is defined by their sensitivity and specificity as illustrated in Figure 1 below.

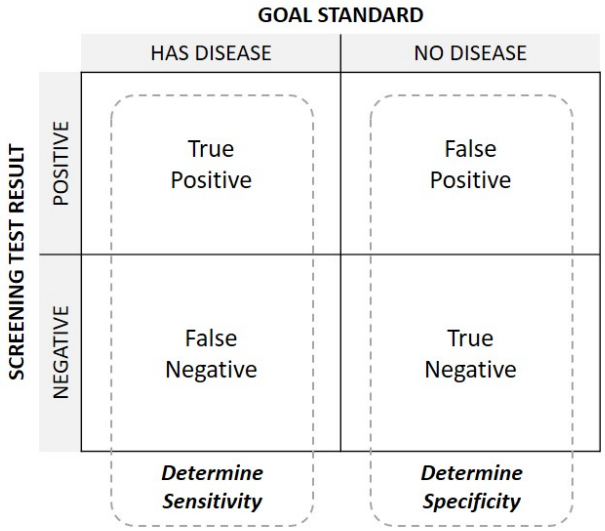

Figure 1 the sensitivity and specificity of a screening tool

Sensitivity is the rate of true-positives actually identified as such by the test among all people with the condition, while specificity is the rate of true-negative cases (without the disease) identified by the test. For a good screening test, high sensitivity is required to ensure that a large proportion of cognitive impairment cases are captured with this tool for onward assessment. Acceptable specificity is also necessary so that only a small number of cases are falsely declared as positives preventing unnecessary

over referral and excessive stress for the older adults who fail the test. Sensitivity and specificity are conditional on the cut-point establishing whether a test is declared positive or negative for the condition.

Establishing a timely diagnosis of dementia is critical in promoting positive patients outcomes as described in the World Alzheimer report in 2011 (Prince et al., 2011). Only after diagnosis, will older adults with dementia be able to access pharmacological and non-pharmacological treatment and intervention. Moreover, with early diagnosis, these older adults, along with their families, would be able to gradually adapt and prepare for the health-related care/support that they would need.

The World Alzheimer report also emphasises the importance of family and social support for the patients. Communication with family and community may be even more troublesome when hearing loss is present (Schulz et al., 2017), therefore, this group of patients need additional support and attention.

1.3.2. Who should be the targets?: Levels of hearing loss warranting cognitive intervention

According to the British Society of Audiology(BSA), a pure-tone average (PTA) of more than 20 dB HL, is classified as a mild hearing loss. However, not every case with PTA >20 dB HL would require intervention. WHO defines disabling hearing loss as a pure-tone average ≥ 40 dB HL i.e. a moderate hearing loss according to BSA criteria (British Society of Audiology, 2018).

It is, however, still important to note that trivial hearing loss within a normal range (PTA<25 dB HL) was previously found to associate with cognitive decline (Golub et al., 2019) and depressive symptoms (Golub et al., 2020) among older adults in the regression analysis models.

The hearing threshold of ≥ 30 dB HL was used among various studies as the best cut-point for the population who would benefit from hearing intervention to prevent dementia and cognitive decline (Deal et al., 2017). Therefore, older adults with this level of hearing loss or more may benefit from targeted cognitive screening for early signs of cognitive decline.

1.3.3. Early hearing intervention in older adults in general to prevent cognitive decline

Since the Lancet commissioned on dementia (Livingston et al., 2017) highlighted hearing loss as the modifiable risk factor with the largest populational impact on dementia risk, the focus of treating hearing loss as potentially the highest modifiable cause of dementia has attracted attention.

While there are currently no randomised trials on the effects of treating hearing on cognition, the available observational and pre and post-intervention studies suggest that hearing intervention including hearing aids and cochlear implantation may improve the patient's cognition (Castiglione et al., 2016). Still, the patients who opt for either hearing aids or cochlear implant intervention may be a more selected group of highly motivated, health-conscious older adults than the group who do not pursue such intervention.

The actual effect of hearing intervention on cognition would be best assessed with a randomised controlled trial (RCT) study with long term follow-up. This is the only way to untangle the temporal relationship of hearing loss toward dementia development and effect of other biases. Currently, there are ongoing RCT in the USA and the UK to study this effect (Deal et al., 2017).

However, to assess the role of hearing intervention in improving cognition, an accurate assessment of cognition among hearing aid users and hearing loss population is crucial. For example, the observation that cognitive function seems to improve in some subjects after the hearing intervention may be due to the fact that with the hearing aids, these subjects can understand better the instruction and target signal of the cognitive task measures. If this is the case, maybe the "actual" cognition of the subject was not truly improved after the hearing intervention. On the other hand, the cognition may also improve after the hearing intervention beyond what would be expected from improving hearing alone. Only with an accurate assessment of cognitive function that does not rely on hearing ability would it be possible to untangle this dilemma.

1.3.4. Adapted hearing intervention in the early identified MCI among hearing aid users/hearing loss population.

Various audiological interventions can be offered to the population with MCI and hearing loss. A systematic review suggested that hearing intervention is very important for older adults with hearing loss and mild cognitive impairment (Mamo et al., 2018), as reflected by successful treatment outcomes including the benefit from better communication and improved quality of life. A large retrospective trial in the UK applied structural equation statistical modelling and similarly found that the improvement of cognition among hearing aid users is greater than what would be expected from improvement in social isolation and depression alone (Dawes et al., 2015). This means that hearing aids may also directly improve the cognitive function of the older adults hearing aids users through other means such as improved communication and self-esteem (Dawes et al., 2015).

Hearing intervention successfully improves depression and neuropsychiatric outcomes even with a simple approach such as a personal assistive listening device (i.e. not standard hearing aids), providing that the healthcare providers had a good understanding of the patient's cognitive ability whether he/she can use the hearing equipment and to what extent (Mamo et al., 2017).

Therefore, the importance of identification of these patients with mild cognitive impairment is crucial in order to provide appropriate support and care not only by memory services but also by hearing aid centres. Adjustment of the instructions, manual of care and/or administration of the hearing intervention is needed to better support the needs of this group of patients. Therefore, the identification of MCI patients in hearing aids centre should be given priority to deliver the best suitable care for each individual patient.

1.4. Definition of cognitive impairment

1.4.1. Dementia

According to the International Classification of Disease (ICD) version 10, dementia*(F00-F03)* is " *a syndrome due to disease of the brain, usually of a chronic or progressive nature, in which there is disturbance of multiple higher cortical functions, including memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgement"* (WHO, 2016).

Dementia is the deterioration of the overall function of the brain due to various aetiologies for brain illnesses, resulting in different dementia subtypes. The most common subtype is Alzheimer's type dementia (ICD-10 code F00), i.e. a degeneration of the brain by unknown aetiology with specific characteristic neuropathological and neurochemical features. The detailed diagnostic criteria of Alzheimer's dementia proposed by the National Institute of Neurological and Communicative Diseases and Stroke–Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) include insidious onset and progressive deterioration of memory and other cognitive functions (McKhann et al., 1984).

The second most common type of dementia is vascular dementia (ICD-10 code F01). This is caused by infarction of the brain's vasculature, immediately after stroke onset or due to an accumulated effect after several small stroke incidents (WHO, 2016). Patients can also have mixed type dementia which is the combination of Alzheimer and vascular cause of dementia.

The third common type of dementia is Lewy body dementia. Lewy body dementia (LBD) includes two types of dementia diagnosis, dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD), which resulted from the Lewy bodies deposit in the brain (Peterson et al., 2019). The affected symptoms

and severity differ for person to person with symptoms such as changing in cognition, movement, sleep, and mood along with behaviour (McKeith et al., 2017).

There are over 100 other types of dementia which would fall under the "dementia in other diseases classified elsewhere" (ICD-10 code F02) such as dementia from Pick disease (Frontotemporal dementia), Parkinson disease, Huntington disease etc. For dementia causes that could not be specified, these patients would fall under "unspecified dementia" (ICD-10 code F03).

1.4.2. Mild cognitive impairment (MCI)

The term "mild cognitive impairment" was first coined by Petersen in 1999 (Petersen et al., 1999) in order to describe the transitional stage from normal cognition to dementia. Several other terminologies that were used in the literature previously such as isolated memory impairment etc. are no longer in use.

The accepted diagnostic criteria for MCI was proposed by Peterson and later adapted by ICD WHO. The current ICD version 10 describes MCI under the F06 topic: Other mental disorders due to brain damage and dysfunction and to physical disease and F06.7 category. The description for MCI is *"A disorder characterised by impairment of memory, learning difficulties, and reduced ability to concentrate on a task for more than brief periods. There is often a marked feeling of mental fatigue when mental tasks are attempted, and new learning is found to be subjectively difficult even when objectively successful. None of these symptoms is so severe that a diagnosis of either dementia (F00-F03) or delirium (F05.-) can be made"*(WHO, 2016).

The new ICD version 11 classification (WHO, 2019a) that will become effective in January 2022 and also the current Diagnostic and Statistical Manual of Mental Disorders (DSM–5) standard reference in mental health (American Psychiatric et al., 2017), describes MCI as matching term for mild neurocognitive disorder (code 6D71 under topic 06 Mental, behavioural or neurodevelopmental disorders), which is *"characterised by the subjective experience of a decline from a previous level of cognitive functioning, accompanied by objective evidence of impairment in performance on one or more cognitive domains relative to that expected given the individual's age and general level of intellectual functioning that is not sufficiently severe to significantly interfere with independence in the person's performance of activities of daily living. The cognitive impairment is not entirely attributable to normal aging"* (WHO, 2019b).

The overall description of the disorder is similar to the current ICD version 10. The main key difference between MCI and dementia is that people who suffer from MCI can still perform activities of daily life

(ADL) independently. If the patient's activities of daily life became significantly affected by their cognitive impairment they should be classified as dementia instead of MCI.

Typically, the transition from normal cognition to dementia happens very gradually over several years to decades. Therefore, the MCI stage may be an opportunity window for early diagnosis and intervention. This diagnostic entity of MCI has received a lot of attention during recent years since the intervention in this early stage may potentially change disease prognosis for the patients (Petersen, 2004).

1.4.3. Concepts of cognitive impairment, cognitive capacity and cognitive performance based on the International Classification of Functioning, Disability and Health (ICF)

While the ICD-10 classification is part of WHO family of international classifications that is mainly used for diagnosing diseases, the International Classification of Functioning, Disability and Health (ICF) of WHO is aimed at identifying health and health-related domains (WHO, 2002). There are three major domains described as

- Changes in a person's body functions and structures: This is called a health condition. The problems (deviation or loss) in body functions or structures are categorized as impairments, such as cognitive impairment, hearing impairment. The extent to which the impairment affects the person's activity in performing various tasks and participating in everyday life events depends on the context (environment context and personal context) of the person.
- Level of performance with a health condition: This refers to what a person can do in their current environment, which can be affected by several environmental factors. The current environment can include assistive devices or personal assistance that are already part of their every day lived experience. Although the devices and assistance can not change the impairment in body function, they may eliminate some functioning limitation in their performance.
- Level of capacity with a health condition: This refers to what a person can do in the standardised environment, i.e. a uniform environment controlled for the impact of various environmental factors that can affect a person's functions. For a cognitive assessment, there is thus a requirement to minimise any potential distraction such as background noise, choose the timing of the day to minimise fatigue etc. Any assistance or assistive devices are not allowed, as the WHO phrases this as "naked person" assessment to ensure that the environment adjustment is uniform for all individuals (WHO, 2002).

For individuals with cognitive impairment as well as a change in body function, it is essential to assess both their cognitive performance and their cognitive capacity. The discrepancy between their performance and capacity can determine whether and how environmental factors are interfering with their functions (WHO, 2002). If their current performances are worse than their capacities, this implies that their environments have "barriers" that prevent them from reaching their full abilities. On the other

hand, if their current performances are better than the prediction from cognitive assessment data in the standardised environment (their cognitive capacities), this implies that their current environments have "facilitators" to enhance their cognitive performances. For example, in individuals with hearing impairment as their change in body function, their current hearing performances can be better than their hearing capacities when they have their hearing aids on as facilitators.

Consideration of hearing factors can well demonstrate the barrier/facilitator environmental factors for cognitive function. Cognitive assessment for cognitive capacity would involve uniform environment testing in a quiet room. When assessments are auditory-based, for some hearing-impaired individuals, the quiet environment is more than enough to overcome their hearing problem/reduce listening effort and facilitate them to engage in the cognitive assessment tasks. In this case, their cognitive performances in an everyday environment with background noise as a barrier can be worse than their cognitive capacities tested in a standardised quiet environment (Jafari et al., 2019). However, in everyday life, hearing-impaired individuals may have their hearing aids as assistive devices. Also, they can rely on other context clues, i.e. visual clue and guidance from their personal assistances as facilitators. In this case, their cognitive performance can be better than predicted from their cognitive capacities. A previous study administering cognitive screening test among older adults found that their performance improved when re-tested with hearing amplification assistive devices (MacDonald et al., 2012).

1.5. Currently available cognitive assessment tools

1.5.1. Mini-mental state examination (MMSE)

The MMSE was developed in 1975 to assess cognitive function changes and to detect dementia (Folstein et al., 1975). It is commonly used in clinical and research fields for cognitive screening. The test is based on a 30 point system from six sub-categories which are orientation, registration, attention and calculation, recall, language, copy. An overall score of 26-30 points indicates no cognitive impairment and score below 24 may indicate cognitive impairment (Tombaugh and McIntyre, 1992, Nasreddine et al., 2005). However, the MMSE score is affected by age, education and cultural background. Therefore, the interpretation must be done with caution (Tombaugh and McIntyre, 1992).

Changes in the MMSE score over time need to be carefully interpreted since the decrease in the score needs to be as large as 4 points or more (out of 30 points) to be considered significant due to low test-

retest reliability (Hensel et al., 2007). Still, 3 points or less score decline does not exclude cognitive decline among older adults.

The MMSE also suffers from ceiling effects: a total score >24 does not separate normal cognition from mild cognitive impairment (Diniz et al., 2007). Consequently, the MMSE score is not sensitive to detect MCI, since it was designed to detect dementia and was validated on the dementia population at a time that the concept of MCI was not established (Nasreddine et al., 2005). This means that older adults who pass the MMSE test cutpoint score or have a small decline in the MMSE score over the years can still have MCI. This is not ideal if we want to early identify cognitive impairment for early intervention, as we would want a test that is very sensitive in detecting subtle changes. Therefore, currently, most research projects and clinics that aim to identify cognitive impairment early use other tests than the MMSE (Martinelli et al., 2014, Dong et al., 2010).

1.5.2. Montreal Cognitive Assessment (MoCA)

The MoCA was especially designed to enable early detection of MCI (Nasreddine et al., 2005) after the MCI diagnostic criteria were established. MoCA was validated on an MCI population. MoCA is also based on a 30 point score system similar to MMSE. Compared with MMSE when using the same cutoff score of 26 points, MMSE would have a sensitivity of 18% in detecting MCI versus 90% for the MoCA (Nasreddine et al., 2005).

MoCA consists of 7 components (sub-categories):Executive, Naming, Memory, Attention, Language, Abstract, Orientation. Each sub-category contributes to the total score of 30 points. Memory index score is an additional score that was recently added to the main MoCA scoring system to further explore the memory ability of an individual (Julayanont et al., 2014). The education level of the participants needs to be accounted for when interpreting the MoCA and one point needs to be added for a subject with formal education of 12 years or less (Nasreddine et al., 2005).

The current MoCA version 8 has 3 equivalent options 8.1,8.2 and 8.3 to ensure that repeated testing can be done reliably to prevent practice effects (Costa et al., 2012).

1.6. Montreal Cognitive Assessment (MoCA) for hearing aids users: Why was MoCA chosen in this project?

1.6.1. One of the most sensitive cognitive screening test

Screening for a condition of which early intervention can potentially change the outcome, such as dementia and MCI, requires a sensitive screening tool (Prince et al., 2011). The MoCA is reported to be the most sensitive and reliable cognitive screening tool in early detection of MCI in older adults when compared to other widely used cognitive screening tests such as MMSE, Cambridge cognitive test (CAMCOG) etc. (Martinelli et al., 2014).

This is why MoCA was chosen in this research, to be used as a template for further development of the cognitive screening for older adults with hearing loss.

1.6.2. Less ceiling effect /easier to monitor progress

The MoCA has better discriminant validity than other tests for MCI, and may better characterise cognitive status based on the wide range of performance scores among subjects (Hoops et al., 2009). The MoCA tasks are more challenging so it has a smaller ceiling effect. In a cohort of Parkinson disease older adults with high risk for cognitive decline, nearly 30% of the subjects had the maximum score (30 points) in the MMSE, while only 6.8% of these subjects gave the maximum score on MoCA.

Monitoring disease progression on the MMSE may thus become difficult at the early stages of the decline, if they retain a maximum score at the follow-up visit, despite decreased cognitive ability from baseline.

1.6.3. Short administration time

This cognitive screening tool is to be used in busy clinical or research settings and the effectiveness of the cognitive tool versus the testing duration need to be counterbalanced.

MoCA has good discriminant validity(Nasreddine et al., 2005). Moreover, it can be done within 10 minutes, while other cognitive tools such as Mattis Dementia Rating Scale and the Cambridge Cognitive Assessment (CAMCOG) need more than 30 minutes to complete in normal-hearing adults.

1.6.4. Widely accepted in an outpatient setting

According to guidelines published by Alzheimer's society and endorsed by NHS England, the Dementia Action Alliance, the Royal College of General Practitioners, Royal College of Psychiatrists and the College

of Mental Health Pharmacy, MoCA is suggested to be the first-line cognitive tool to be used in memory clinics and specialist outpatients setting for an initial assessment (Alzheimer's society, 2015).

The test is also recommended for follow up sessions in memory clinics and out-patients setting. Among patients who have already been diagnosed with MCI, a prospective follow up study with repeated MoCA after 6 months can identify disease progression to mild dementia in people with MCI (MMSE score > 25 points) with 94 % sensitivity and 50 % specificity (Alzheimer's society, 2015).

1.7. The traditional Montreal cognitive assessment (MoCA)

The subcategories of the most recent version of MoCA version 8.3 and the details of each task are described below.

1.7.1. Visuospatial/executive-5 points

The following tasks assess executive function and visuospatial ability. They are more challenging than executive tasks in other tests such as MMSE and may be mildly impaired in early MCI patients (Nasreddine et al., 2005) thus making MoCA more sensitive in early detection of MCI.

1.7.1.1. Alternating Trail Making – (1 point)

The subject is given a picture containing 10 small circles with written numbers ranging from one to five and letters ranging from A to E inside and is asked to *"draw a line going from a number to a letter in ascending order"*. The subject gets one point for the correct pattern 1- A- 2- B- 3- C- 4- D- 5- E.

1.7.1.2. Visuoconstructional Skills- (1 point)

The subject is asked to copy a three-dimensional drawing that is shown as accurately as he can. One point is given for a three-dimensional picture with all the lines appropriately placed.

1.7.1.3. Visuoconstructional Skills (Clock)-(3 points)

The subject is asked to draw a clock with the time shown at five past ten. One point is given each for the contour of the clock, the correct 12 numbers placed and the correct hands pointing to the time.

1.7.2. Naming-3 points

The pictures of 3 unfamiliar animals are shown to the subject. The subject is asked to correctly name these to assesses word-finding ability. The task was originally used to evaluate aphasia patients (Spreen and Risser, 2007). Currently, the task is often used to assess the various types of neurological patients including dementia.

1.7.3. Memory/Delayed recall -5 points

The task consists of two learning trials of 5 nouns which would be read verbally to the subject in rate one word per second with 2 registration trials and the subject would be asked to recall the words after 5 minutes.

After the first learning trial of verbally presented 5 target words, the subject is asked to repeat back all the words to the test administrator. No score is given at this stage and the test administrator cannot correct the subject even if he or she said the distorted words or word that sound similar to the target but not entirely correct.

Then the test administrator goes on to read the same 5 target words for the second trial. Again the subject is asked to repeat all target words without any clue or correction from the test administrator and no score is given at this stage. After 5 minutes, the subject will be asked to repeat the 5 target words and will be given one score for each word correctly recalled, exactly as being said by the test administrator. No score is given if he or she mispronounced the target words.

This sub-category of delayed recall was found to be the most impaired among MCI older adults in the original MoCA validation cohort (Nasreddine et al., 2005).

1.7.4. Attention-6 points

Performance in these attention tasks is usually preserved in MCI and becomes impaired in dementia. These tasks can thus distinguish between dementia and MCI but not between MCI status and normal cognition (Nasreddine et al., 2005).

1.7.4.1. Forward digits span (1 point):

The test administrator reads 5 digits in sequence with a rate of one digit per second. The subject is asked to repeat these in the same exact order. One point is given when all digits are repeated correctly in the correct order.

1.7.4.2. Backward digits span (1 point):

The test administrator reads 3 digits in sequence with a rate of one digit per second. The subject is asked to repeat in the backward order. One point is given when all digits are repeated correctly in the correct order.

1.7.4.3. Vigilance (attention to letters) (1 point):

The test administrator reads a sequence of letters with a rate of one letter per second. The subject is asked to tap when he hears the letter A. One point is given when zero to one error was made in the tapping.

1.7.4.4. Serial 7s subtraction (3 points):

The subject is asked to do a mental serial subtraction of 7 from the target number such as 100 or 60 etc. No point is given when no correct subtraction then 1 point for one correct subtraction, 2 points for two to three correct subtractions, and 3 points for four to five correct subtractions.

1.7.5. Language-3 points

These language tasks (sentence repetitions and verbal fluency) demonstrate higher-level language ability and may be impaired at a very early stage of MCI (Nasreddine et al., 2005) thus making the MoCA test more sensitive in detecting MCI than other tests with simpler language components. However, the tasks are not as sensitive in differentiating between MCI and dementia.

1.7.5.1. Sentence repetitions

The subject is asked to repeat two sentences heard after the test administrator. Each exactly repeated sentence is scored one point.

1.7.5.2. Verbal fluency

The subject is asked to give as many words as he can think of that begin with a certain letter in 60 seconds and get one point for 11 words or more.

1.7.6. Abstract-2 points

The subject has to answer what each pair of words has in common, e.g.an orange and a banana (fruit). The subject is given one practice pair and then two test pairs. Each test pair is scored 1 point (total score of 2).

This task evaluates the ability to think abstractly which might be impaired gradually in MCI and more so in dementia (Nasreddine et al., 2005).

1.7.7. Orientation-6 points

The test administrator asks the subject *"Tell me today's date"* and after the subject answers, asks *"Now, tell me the name of this place, and which city it is in."* The orientation task is crucial in any cognitive assessment.

1.7.8. Memory Index Score (MIS)-separate section from MoCA with full score of 15 points

This section was recently added into the MoCA version 8 and helps to identify subjects with MCI who are more likely to develop dementia (Julayanont et al., 2014).

The Memory Index Score (MIS) is a further exploration of the responses in memory/delayed recall sub-category. For MIS, the participants receive 3 scores for recalling each of the target words without any clues. With a total of 5 target words, the full score for MIS is a maximum of 15.

If the participants cannot recall any item in the 5 target words, the test administrator is allowed to give them clues to help with their memories. Firstly, the test administrator gives them categorical clues such as colour, body part etc. for example with this phrase *"I will give you some hints to see if it helps you remember the words, the first word was a body part."* If the participants can answer with the correct target word at this stage, they receive 2 points for each target word. However, if the participants cannot give the correct answer with categorical clues, then multiple choices are given to them, for example with this phrase *"Which of the following words do you think it was, NOSE, FACE, or HAND?"* If they can answer the target word correctly at this stage, they receive 1 point. If the participants cannot answer with the correct target word even after these clues, they receive 0 point for that target word.

This task is used to differentiate between information "encoding" (i.e. memorising the words) and information "retrieval" problems (i.e. target words recognition) (Clément et al., 2010). This Memory index score task is based on the assumption that if the subject has difficulty in retrieving the information from the brain storage but the information has already been stored properly, cues may help to facilitate the retrieval process. On the other hand, if the information has never been stored in the first place, even with cues, the subject would not be able to recall the target words.

1.8. Possible issue of MoCA for older adults with hearing impairment

The sub-categories of MoCA, which may potentially be affected if verbal input were used included (1) Memory (2) Digit span (3) Attention to letters and (4) Sentence repetition (Al-Yawer et al., 2019). These are crucial for the tool's sensitivity in detecting MCI and dementia (Al-Yawer et al., 2019) and cannot be excluded from the total score analysis. The elimination of the auditory dependent tasks reduced the sensitivity of the tool substantially from a passing rate of 71% to 53% in the same cohort (Dupuis et al.,

2015). Therefore, instead of eliminating the items, they should be modified to suit older adults with hearing impairment

1.8.1. Memory (delayed recall)

The sub-categories of MoCA, which are more likely to be reduced among hearing aid users in the traditional verbally administered MoCA, are the registration and delay recall part (Yeok Leng Lim and Loo, 2018). With the verbally administered MoCA, it is not possible to establish whether the reduction of the scores is due to hearing impairment, decreased cognition or both.

The registration part of the Memory sub-category which asks the participant to repeat back the target word may help to identify the problem with the hearing acuity of the target words. My own anecdotal observation was that the target word "RED" was registered as "BREAD" possibly due to lip-reading clues etc. Previous research showed that for hearing loss participants not only was the error in the registration part were higher than the normal hearing group, the hearing loss participants also had more error in the recall part despite considering only the previously correctly registered words (Yeok Leng Lim and Loo, 2018). One possible explanation is that distorted words heard by the hearing-impaired older adults may require more cognitive resources to remember and recall (Sardone et al., 2019).

According to the MoCA administration protocol, the registration part mainly involves asking the participants to tell the test administrator the target word heard. This part does not contribute to the final score of the participants. Despite a study showing that participants with hearing loss may do worse on this registration part; with auditory amplification, the registration score improved from 73% to 93% (Shen et al., 2019). The worse score in this registration part would not be calculated as part of the final MoCA score, therefore would not be reflected in most studies nor participants' record.

After 5 minutes, the subject is asked to report back the target words heard earlier in a word recall part which constitute 5 scores to the final total MoCA score as the delayed recall subcategory. This part is where most hearing-impaired population would lose their score which resulted in their significantly worse MoCA as a whole compared to controls (Yeok Leng Lim and Loo, 2018). The detailed acoustic properties analysis of the target words found that the failure of recalling the words among older adults with hearing impairment was related to these acoustic properties of the misheard words. This correlation was demonstrated since when the word's phonemes were falling out of the participants hearing threshold in any frequency, the participants were more likely to fail to recall that words (Yeok Leng Lim and Loo, 2018).

The delayed recall part could be assessed in more detail by giving additional clues to facilitate the recall process and records in a separate memory index score (MIS) section. However, the MIS was recently added to the MoCA, and this effect has never been studied among the hearing-impaired population. The MIS could be a useful subtest to understand delayed recall in older adults with hearing impairment.

1.8.2. Digits span

A previous study showed that even in quietness, the ability to repeat the target words in a word recognition task was 30% less in older adults with hearing impairment than their normal-hearing age-matched peers. The effect was present even after accounting for age and loudness of the targets (Smith et al., 2012).

Therefore, the evaluation of subject attention on a digits span may not be accurate for older adults with hearing impairment for auditory-based targets.

1.8.3. Attention to letter

For consonant recognition, the hearing impaired subjects' ability is much worse than in normal-hearing peers (Jurgens et al., 2014). When based on the previously discussed word recognition task model by Smith (Smith et al., 2012), if the hearing loss subject would mishear 30% of the target letters (consonant/vowel word), they can easily fail this task which allows only zero to one mistake.

1.8.4. Sentence repetition

To repeat the sentences, the subject needs to be able to register the target sentence first. The difference between word registration and sentence registration is that sentences have other words as a context clue to help the subject guess what the sentence should be about (Spehar et al., 2015).

The ability to fill out this missing gap with the context clue may be especially relevant for older adults with hearing impairment. Further validation of the visually-based sentence repetition is needed to establish appropriate cutpoint score for hearing-impaired older adults.

1.9. Currently available possible alternative of visually based cognitive screening tools

1.9.1. MoCA adapted for the severely hearing-impaired (MOCA-HI)

Lin et al. (2017) have previously examined the performance of cochlear implant candidates on a version of the MoCA adapted for the severely hearing-impaired (MoCA-HI), demonstrating initial utility in the feasibility of using the tool among cochlear implant candidates (Lin et al., 2017). However, cochlear

implant candidates differ from the broader target population of older adults with age-related hearing loss in that they have more severe hearing loss (Dawson et al., 1995). Additionally, they need to be physically fit enough to undergo surgery so tend to be younger (Lin et al., 2012). The more vulnerable population of hearing aid users may thus need different cognitive assessment administration methods than the cochlear implant candidates. Still, the MoCA-HI was not clinically validated against diagnosed cognitive impairment sample.

Moreover, the validation of appropriate use along with suitable referral cutpoint for hearing aid users need to be established for the use of MoCA in this population. We cannot assume a similar cutpoint for this cohort without scientific evidence. The cutpoint of this cohort may differ from the traditional population and cochlear implant users due to their difference in the cognitive profile of hearing aid users (Dawes et al., 2015).

1.9.2. MoCA for people with acquired hearing impairment (MoCA-H)

The research protocol was published in 2019 outlining the development of MoCA for hearing impairment population (Dawes et al., 2019). The traditional hearing-dependent items of language and attention to letters would be re-designed to assess similar cognitive domains. The language task was substituted with constructing sentences from the given visually presented words. Attention to letters task was substituted with reading aloud the numbers that were in the circles as opposed to squares.

The caveat would lie on the application of the test in a real clinical setting. As the use of MoCA-H version, which consists of different tasks than standard MoCA, not only places more burden for the healthcare professionals on the additional training of the tasks and scoring criteria, it is also challenging for healthcare professionals to decide who to use this novel test with. Since many older adults may not be aware of their hearing loss especially the elderly population with memory problems (Gold et al., 1996), it would need to rely solely on the healthcare professional clinical discretionary judgement whether to implement this MoCA-H, since the healthcare professional may not be in the position to perform the hearing test on every individual before making the decision. A retrospective chart review study in the dementia clinic found that an estimate of 31 in 100 diagnosed dementia had undiagnosed hearing loss. The report emphasised the fact that dementia clinicians may not always be able to identify hearing impairment cases and maybe audiological screening of all cases to administer the appropriate cognitive assessment would be beneficial (Jorgensen et al., 2014). Still, there is currently no validated cognitive assessment tool and no established cut-point for this population.

1.9.3. The Repeatable Battery for the Assessment of Neuropsychological Status for Hearing Impaired Individuals (RBANS-H).

The RBANS was primarily developed for the detection of dementia and monitoring of cognitive changes. The RBANS was adapted for use on the hearing impaired (RBANS-H) in order to assess cognitive changes pre and post cochlear implantation (Claes et al., 2016).

There are similar concerns for RBANS-H as for MoCA-HI in that the hearing impairment participants who are cochlear implant candidate population which was used in RBANS-H research differs from older adults with hearing impairment. The tool is currently in the research protocol stage and not yet available for clinical use. Moreover, the test itself is time-consuming and impractical in busy hearing aid fitting sessions.

1.9.4. Visual Cognitive screening test (VCAT)

The visual cognitive screening test (VCAT) (Low et al., 2019) presents all the targets as pictures and may thus be applicable across languages.

However, older adults with MCI and hearing impairment may suffer from language-related memory problems which may not be best picked up by the non-language related task (Yeok Leng Lim and Loo, 2018). Therefore, a visually based modification of MoCA which includes the language component may be a more appropriate option than the current visual cognitive screening test. Moreover, this tool has not been validated in the hearing impairment population which means the cut-point for referral in this population is still unknown.

1.10. The current issues with cognitive assessment among hearing loss older adults

Since currently available screening tools for cognitive impairment require patients to follow orally presented instructions, normal hearing thresholds are implicitly assumed when conducting the test. However, hearing loss is very common among the elderly. In theory, mishearing or misinterpreting the test instructions due to hearing loss may lead to poor test scores. However, previous research showed that hearing loss participants did not improve MoCA score with hearing amplification despite improved hearing in speech tests. The authors acknowledged that other unmeasured confounders such as fatigue and increased listening effort during the test can also contribute to a decreased MoCA score on hearing-

impaired individuals (Saunders et al., 2018b). Therefore, in addition to the direct perceptual effects of hearing loss on test performance, there may be indirect, more “cognitive” effects also at play. These potential confounders could lead to an increased number of false positives of dementia which results in unnecessary further referrals.

On the other hand, false-negative findings are also possible because poor test performance may be interpreted by the clinicians as attributed to the presence of hearing impairment. Timely diagnosis of dementia is critical in promoting positive patients outcomes (Prince et al., 2011), and the development of sensitive, valid, reliable dementia screening tools designed for a hearing-impaired population is of paramount importance. A one potentially useful way of doing this is to adapt commonly used dementia screening tools for visual as opposed to an auditory presentation (Lin et al., 2017).

Currently, there is not any validated cognitive assessment tool for hearing impaired population to be used in a clinical setting which takes into account the hearing loss. Previous research showed that the hearing-impaired population performed worse than their normal-hearing peers with these tools (Yeok Leng Lim and Loo, 2018). This may be evidence that these tools may overstate cognitive impairment when participants are hearing-impaired and therefore not valid for this population.

1.10.1. The need to develop and validate MoCA for hearing aids users.

The previous sections discussed, why the modified Montreal Cognitive Assessment tool needs to be developed, tailored to assess cognition in hearing-impaired older adults, and validated among the population of intended users. The MoCA proposes a threshold of 26 (+1 point for low education </=12 years) to diagnose MCI. However, different cutpoint scores for referral have been suggested for different subpopulation (O'Driscoll and Shaikh, 2017, Davis et al., 2015). For example, the cut point is suggested to be 21/30 for Parkinson’s disease dementia with sensitivity 81 % and specificity 95 % (Alzheimer's society, 2015). Alternatively, the suggestion of different weighting of each sub-category of MoCA for better sensitivity of detecting MCI was also suggested in a specific population such as Parkinson (Fengler et al., 2016).

Therefore, the validation for appropriate cutpoint for this newly developed tool needs to be studied in detail among the intended patients.

Various administration methods were studied by administering cognitive tests for the hearing-impaired population. Several adaptations were proposed to tailor for the hearing-impaired population’s needs.

1.10.2. Auditory based amplified VS unamplified

The single study that attempted to show the effect of hearing amplification found no difference in MoCA score with amplified or non-amplified MoCA administration (Shen et al., 2019). The main reason for these negative results may be due to the fact that nearly half of the patients were in the mild hearing loss range. Since our conversation level is 50-60 dB HL (around 70 dB SPL), the researchers used a speech level of 65 dB SPL for the unaided group, that might be audible by the mild hearing loss participants.

However, the major concern of using MoCA screening is for the disabling hearing loss group who may be at risk of developing dementia (Livingston et al., 2017). Using the unamplified traditional MoCA on this disabling hearing loss group may potentially lead to more false-positives.

1.10.3. Visually based VS Auditory based

Interestingly, despite a non-significant difference in the overall score, the verbally presented MoCA with hearing aids may be less challenging than the visual MoCA (as patients score 1.3 points better with verbal MoCA)(Shen et al., 2019). This was a small study with only 8 participants per arm and needs to be replicated with a larger cohort of participants. However, this result may imply that we may need a different cut-point score for the visually based MoCA than the traditional auditory based MoCA.

This potential difference in the scores may be explained by the fact that auditory based and visually based targets interact differently in our working memory pathway (Baddeley, 2012). The Baddeley model suggested that there are 3 main components for memory; the central executive which is a central system regulating the flow of information to and from the two subsidiary “slave” systems: the phonological loop and the visuo-spatial sketchpad. The phonological loop works with verbal contents when the visuo-spatial sketchpad mainly works with visuo-spatial input (Baddeley, 2012). The two subsidiary systems serve as a working memory circuit.

However, presenting the instruction on the screen may also be processed like lip-reading and sign languages which were processed via the same phonological loop pathway for processing language of auditory instruction, more than the typical visuospatial sketchpad (Rönnberg et al., 2004). Previous research showed that even inner signing (thinking of the signed sentences) also was processed through the phonological loop (McGuire et al., 1997). Therefore, several researchers suggested the language modality free working memory concept where ie. the listening span and reading span are processed similarly in the phonological loop working memory (Daneman and Merikle, 1996). Nevertheless, some

might argue that basic cognitive constructs such as information encoding and retrieval are probably not modality dependent anyway since it is based in the central executive area and those are the critical part for assessing cognitive status.

An accurate validation and cut-point score for the MoCA is required to sensitively identify specific populations at risk of dementia (O'Driscoll and Shaikh, 2017), particularly as changes in MoCA score as small as 1.645 points are considered to be clinically significant changes (Kopecek et al., 2016). Moreover, even though it may not be clear whether the visually presented and traditional auditory presented stimulus were processed via identical cognitive pathways. If the newly developed visual tool is validated among the hearing-impaired cohort, it would be a valid tool to use in this population. This visually-presented tool may have good face validity for clinicians but we need to confirm their diagnostic validity before implementation accurately in clinical setting.

We opted to develop a visual-based version of the MoCA for the hearing impaired populations instead of using the existing MoCA and to validate it on hearing-impaired subjects for the new cut-point. The rationale is because the results of the original auditory-based MoCA can vary in hearing impaired individuals depending on their hearing impairment level and the affected frequencies, with up to 2 out of a total score of 30 difference found in a previous systematic meta-analysis (Utoomprurkporn et al., 2020b).

In addition, the MoCA is a screening tool designed for use by multiple nonspecialist practitioners. Consequently, screening for cognitive impairment with MoCA is usually performed in a general setting such as community clinics, general practitioner(GP) practices, hearing-aid clinics and by health care professionals who are not necessarily trained nor as experienced in cognitive assessments as psychiatrists/psychologists/psychometrists. Due to these factors, implementing MoCA screening among the older population with co-morbidities such as hearing impairment could potentially lead to further variability in the MoCA results.A standardized visually-based MoCA tool would be a valid method to minimize the variability from any potential environmental, test administration and subject characteristics related error.

1.11. Study aims and objectives

The main purpose of this study is to develop the visual-based adapted version of the Montreal Cognitive Assessment (MoCA)(Nasreddine et al., 2005), to assess whether this can accurately distinguish non-

cognitively from cognitively impaired people with hearing loss and to set optimal cut-points for discrimination.

Additionally, to enhance assessment of measure validity we also assessed whether performance on the adapted MoCA is correlated with other non-hearing dependent measures of cognitive function along with central and peripheral auditory processing tests and auditory difficulties reported.

The acceptability of the test usage was determined through thematic analysis of the qualitative interviews.

2. Chapter 2: Material and Methods

2.1. Thesis structure

This research was divided into 3 phases which are presented in chapters 3 to 6. The flowchart for each phase of the study is illustrated in Figure 2. The purpose of each stage along with the participants and setting for each stage are also outlined below.

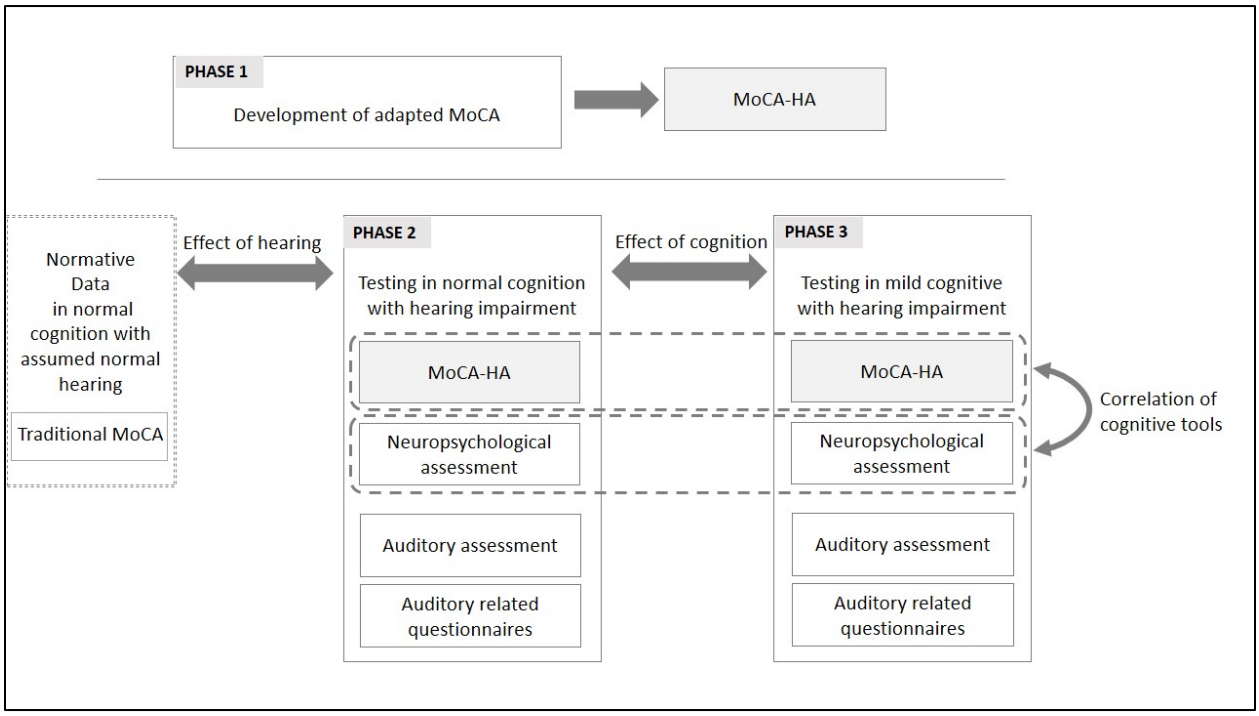

Figure 2 Conceptual framework of the study

Phase 1 was the development process of the adapted Montreal cognitive assessment tool for hearing aids users (MoCA-HA) for older adults with hearing impairment which consisted of feedback from end-users and healthcare providers (chapter3).

Phase 2 was the testing of the MoCA-HA among older adults with hearing impairment who had normal cognition. The data from phase 2 was used to compare with the previously published normative data from the original MoCA validation cohort among the normal cognition with normal hearing population to explore the effect of hearing impairment (chapter4).

Phase 3 was the testing of the MoCA-HA among older adults diagnosed with MCI with hearing impairment. The data from phase 3 was used to compare with the data from phase 2 to explore the effect of cognitive impairment (chapter5).

The data from phase 2 and phase 3 were used to analyse the appropriate cut-point of the MoCA-HA along with the correlation of MoCA-HA with other cognitive tools (chapter 6).

The conclusion and future direction of the study were discussed in chapter 7.

2.2. Ethical approval

The project was approved by the UK National Health Services (NHS) Ethical Committee (IRAS247176) in Appendix A, Appendix B and sponsored by the University College London Joint Research Office (JRO) (ID 18/0306). The study protocol was registered in clinicaltrial.gov (Identifier: NCT03648502.).

2.3. Sample size calculation

This was determined using the EasyROC tool(Goksuluk et al., 2016). The power was calculated for using Receiver Operating Curve (ROC) analysis to address the main aim i.e. to detect whether the adapted MoCA is significantly better than chance at distinguishing participants with cognitive impairment from those without.

Alpha was set at 0.05 and beta at 0.8. The effect size (predicted area under the curve (AUC)) for both tests was set at 0.70 based on the figure for the obtained AUC for the MoCA, which was 0.85 (Roalf et al., 2013). We are using a figure that is lower than that obtained in previous work to ensure a conservative sample size estimate in case the hearing-impaired versions of the tests are less accurate than their non hearing-impaired counterparts. As a result of the calculation, we concluded that we would need 30 hearing-impaired without cognitive impairment and another 30 hearing-impaired with MCI for this validation of the newly developed cognitive screening tool.

2.4. Participants and setting

2.4.1. Patient-public involvement volunteers: Phase 1

In phase 1, we aimed to incorporate the feedback from the clients (hearing aid user older adults) as well as relevant clinicians into the development process. Hearing aid user older adults were invited to take part in the feedback process from the Royal National Throat Nose Ear Hospital hearing aids centre and research registry at University College London Ear Institute.

2.4.2. Normal cognition hearing-impaired (NC-HI) controls: Phase 2

In phase 2, we aimed to explore the use of our newly developed Montreal cognitive assessment among older adult hearing aid users who have normal cognition. These participants would also act as control when a comparison is made with data from the MCI group in Chapter 6.

The hearing-impaired participants with normal cognition group would consist of participants aged 65 or over with hearing impairment but without cognitive impairment. The participants were recruited from flyers distributed in the adult audiology hearing aids clinic at Royal National Throat Nose Ear Hospital (RHTNEH).

Exclusion criteria were uncorrected visual impairment; cognitive and/or physical disability(s) which prevent the performance of the written/drawing elements of the tests, as judged by the researcher, and congenital/childhood-onset hearing loss (<18 years old age) as reported by participants

2.4.3. Mild cognitive impairment hearing-impaired (MCI-HI) group: Phase 3

In phase 3, we aimed to explore the use of the MoCA-HA among older adult hearing aids users with MCI and compare these results with data from the normal cognition (NC-HI) group (Chapter 6).

The hearing-impaired participants with MCI group would consist of participants aged over 65 diagnosed with MCI who are current hearing aid users. All participants were diagnosed with MCI (ICD F06.7) by an NHS memory service doctor and were recruited from memory clinics via clinicians and research registry under Camden and Islington National Health Service (NHS) Foundation trust.

Exclusion criteria were uncorrected visual impairment; cognitive and/or physical disability(s) which prevent the performance of the written/drawing elements of the tests, and congenital/childhood-onset hearing loss (<18 years old age) as reported by participants.

2.5. Informed consent

Identified participants were contacted by the researchers to arrange an initial meeting. All participants will receive information forms (Appendix D, Appendix E, Appendix F)so that they will have a chance to read through information prior to consent.

At the meeting, information sheets were discussed, any questions addressed and written informed consent obtained (Appendix G). Where there were doubts that a person has capacity consent, the researcher (who was trained in assessing capacity) would assess capacity to consent to the research. Where the participant did have the capacity, the researcher would not continue with the interview and the participant would not take part in the research.

2.6. Adapted Montreal Cognitive Assessment (MoCA-HA) for hearing aid users

The MoCA version 8.3 was used as a template for adaptation for hearing aids users. The development process of the tool will be explained in more detail in Chapter 3.

2.7. Auditory assessments

2.7.1. Ambient noise control

Participants were tested in the soundproof room facility at University College London Ear Institute, or for older adults with MCI who could not come to the institute in a quiet room at their home. Memory service who referred the participants for the study would evaluate the appropriateness of the participant's home when they visited the participants on the routine follow up session.

To ensure that the home testing results were reliable, the portable sound level metre was always in place to check for ambient noise before the start of the testing session. The ambient noise was monitored during the session to be below 40 dB SPL as recommended by the British society of audiology (BSA) (British Society of Audiology, 2018)

2.7.1.1. Equipment (sound level metre)

The digital sound level metre model CEL-240 by Casella USA was used to measure the ambient noise when the testing was done at home. The equipment was calibrated annually to ensure accurate measurement.

2.7.1.2. Testing protocol.

The maximum sound pressure should not exceed 40 dB SPL in order for the test to be conducted as per the recommendations from British Society of Audiology (BSA) for conducting audiogram (British Society of Audiology, 2018). However, according to BSA, since we also used noise-excluding earphones (Audiocups) in the audiogram testing session, the tolerance for ambient noise could be greatly improved from this cut point.

2.7.2. Audiogram

The Audiogram measures the subject's hearing threshold, i.e. the quietest sound that the subject can hear at a particular frequency. It is considered a reliable method to measure hearing levels even in memory-impaired patients compared with other self-report hearing difficulties measure (Gold et al., 1996).

2.7.2.1. Equipment (Audiometer)

The portable Audiometre MA41 model from Maico Diagnostics GmbH was used in all participants. The sound was delivered through DD45 headphone and AUDIOCUPS DE LUXE A noise-excluding earcups. All equipment were calibrated together annually.

Previous research has shown that the Audiocup can effectively reduce ambient noise from 13 dB at a lower frequency up to 44 dB at mid to high frequencies, without any enclosure effect. The audiogram obtained was still as accurate as without the Audiocup (Stark and Borton, 1975).

2.7.2.2. Testing protocol

Audiograms were conducted at 250Hz, 500Hz, 1000Hz, 2000Hz, 4000Hz and 8000Hz for both right and left ear according to the British Society of Audiology protocol (British Society of Audiology, 2018).

For analysis purposes, the pure-tone audiogram outcome measure was the average of the thresholds (Pure-tone average: PTA) in 500Hz, 1000Hz, 2000Hz and 4000 Hz of the better hearing ear.

2.7.3. Dichotic digits test

The dichotic digits test was previously developed for the evaluation of central auditory processing among neurological patients (Musiek, 1983). Various different types of central auditory processing difficulties were found in patients with different types of dementia. Specifically, Alzheimer's type

dementia patients usually suffer in communication among noisy background situation (Hardy et al., 2016).

Dichotic speech tests assess listening in a competing background speech and specifically binaural integration for the free recall task. The “Dichotic Digits Test”(DDT) in particular has been proposed as a screening test for central auditory processing pathway abnormalities due to its easy application and short administering time, along with its resistance to peripheral hearing loss (Musiek et al., 1991).

The most commonly used paradigm is the 2 digits pair paradigm, where 2 digits are presented to each ear at the same time and at supra-threshold level to ensure that even the patient with hearing loss can hear this. The difference between the correct response percentage score of the right and the left ear is called “the right-ear advantage”.

The test was proven to be reliable to use among Alzheimer’s dementia patients (Strouse and Hall, 1995). Several retrospective papers have shown that dichotic digits test can be impaired in early cognitive impairment and dementia (Gates et al., 2008, Gates et al., 2010). Prospective cohort studies have shown that the dichotic digits test predict future dementia onset in the population with mild cognitive impairment (Haggstrom et al., 2018).

2.7.3.1. Equipment

The laptop Dell Latitude 7390 and USB mini pcm2704 soundcard was used to install the sound files. The system was connected to the MA41 audiometer and headphone/Audiocups system for delivering of the dichotic digits test sound files though the CD input port for speech testing material.

Dichotic digits test recording was used with permission from Prof. Musiek. The recording consisted of 40 digit-pairs (20 pairs for each ear).

The scores for each ear were recorded in the scoring sheet (Appendix A). The full score for each ear was 40 digits which were then converted to 100 percent.

2.7.3.2. Testing protocol

The headphone/Audiocup system was placed on the participant. The dichotic digits test file was delivered through the laptop. The recording was presented at 50 dB sensation level and comfort level for the participants as suggested in the original paper for DDT (Musiek, 1983). However, the

presentation level can be lower when requested if the participant experienced uncomfortable due to recruitment issue from their hearing loss.

The participant has to follow the random order of written instructions below (right-directed attention, left-directed attention and free recall attention).

- You will hear two numbers in each ear, simultaneously.

  You are required to repeat only the numbers heard in

  The right ear

- You will hear two numbers in each ear, simultaneously.

  You are required to repeat only the numbers heard in

  The left ear

- You will hear two numbers in each ear, simultaneously.

  You are required to repeat all four numbers.

The participant had 6 practices trials with feedback.

2.8. Neuropsychological assessments (non-verbal) for the concurrent validity of MoCA

All included neuropsychological assessments were standard commonly used visually-based tools to avoid confounding factors from the participant's hearing impairment. Visually-based assessments were previously found to accurately and better reflect the hearing impairment population's cognitive abilities when comparing to verbal assessment (Wong et al., 2019). The instructions of the tests were adapted to be presented visually to the participants, which is a common practice for cognitive testings in hearing impairment participants (Pye et al., 2017)

2.8.1. The Rey Osterrieth Complex figure test (ROCFT) copy

The brief, widely used test of visuospatial cognitive abilities involves copying an abstract figure as accurately as possible within a time limit and is well-validated (Shin et al., 2006). The test is validated to be used among the hearing-impairment population (native congenital deaf signers) (Hauser et al., 2006).

2.8.2. The ROCFT Recall

The test involves the recall of the complex figure which has previously been copied as described above (Shin et al., 2006). This test evaluates episodic non-verbal memory and could be a potentially good concurrent validation tool for memory/delayed recall sub-category of MoCA.

Several studies have shown that older adults with hearing loss may have worse episodic memory of target words than normal-hearing peers even after accounting for cognitive status (Yeok Leng Lim and Loo, 2018). However, most studies were done with verbally administered target words. Further study with visually administered target words should be done to ensure this is a real effect among the hearing impaired adults, since the impairment in episodic memory may also be a hallmark for Alzheimer's type dementia (Thompson et al., 2005).

The ROCFT recall is proposed to evaluate the participant's visuospatial memory without tapping into the language/auditory memory of the participant which may be affected by hearing impairment since it measures visuospatial memory. However, a large United Kingdom biobank study suggested that participants with hearing loss may also have visuospatial memory impairment as a separate entity from language/auditory memory (Rönnberg et al., 2014b). The ROCFT may be a good alternative cognitive tool to accurately assess the cognition of older adults with hearing impairment. Further study is needed to understand more about visuospatial memory ability among older adults hearing aid users. Moreover, this tool especially the ROCFT recall can be used to assess the concurrent validity of MoCA-HA memory subcategory.

2.8.3. Corsi-block tapping

The Corsi block tapping is a well-validated test of visual attention and working memory (Kessels et al., 2000). In Corsi-block tapping, similar tasks are done to the MoCA digits span forward and backwards but instead of listening to and repeating the numbers, the test administrator taps the block which has the number on the side and the participant also has to tap the same block in the exact same or in backward order. This test can thus be a concurrent validation tool for MoCA attention sub-category.

The scoring sheet for the Corsi-block tapping is part of the Wechsler Memory Scale-3rd edition (WMS-III) test battery (Lo et al., 2012, Tulsky, 2004, Tulsky et al., 2003). The test administrator tapped the blocks starting with a two-block sequence. Two trials were done for any given length of block sequence. When the participant correctly tapped the same block sequence, they would receive 1 point. Then the block sequence length increased one by one until the participant scored 0 on both trials for that sequence

length or until the maximum of an 8-block sequence was reach. The maximum score for this Corsi-block tapping forward span was 16.

Afterwards, the participant was asked to repeat the block sequence in backward order. The test administrator again started at a two-block sequence and gradually increase in the same manner. The maximum score for this Corsi-block tapping backward span was also 16. The total score for the Corsi block tapping was 32.

2.8.4. Graded naming test (GNT)

The test was developed to identify difficulties with object naming among neurological patients (McKenna and Warrington, 1980). It consists of 30 black and white pictures of objects which have an appropriate amount of familiarity for participants aged over 18. The participant has to report what is the object in the picture. When the participant correctly identifies the object in the picture, a score of one is given.

The re-standardisation of the test was conducted in 1997 on 710 controls aged over 18 to evaluate the task after 20 years (Warrington, 1997). The same task was still a valid measure with very small correlation with age.

This test is used often in accessing the language ability of participants who have Alzheimer's dementia or MCI (Thompson et al., 2005). Moreover, this test only consists of target pictures delivered visually and may be appropriate to implement among hearing-impaired older adults.

To ensure that the participants can potentially give the correct response, certain prompts were allowed. The acceptable prompts according to the protocol were

- Pointing to the salient features of the stimulus;
- Perceptual reorientation when the stimulus is completely misperceived with the phrase “No, it is something else altogether”;
- Semantic reorientation when the response is insufficient or imprecise with the phrase “ What is another name?” or “what else could it be?”.

2.9. Auditory related Questionnaires

2.9.1. The Modified Amsterdam Inventory for Auditory Disability (mAIAD)

The original version of this questionnaire was developed to identify factors that contribute to hearing difficulties in daily life (Kramer et al., 1995). This was validated in 274 adults with various degrees of hearing loss, leading to the development of the modified version with a total of 28 questions (Meijer et al., 2003).

The responses were scored on an ordinal scale ranging from 0 indicating the most difficulty in hearing towards 3 indicating the least difficulty, and as 'almost never' (scored 0), 'occasionally' (scored 1), 'frequently' (scored 2) and 'almost always' (scored 3).

The 28 questions were divided into 5 domains which correlate well with objective hearing measures (Kramer et al., 1996).

- (Speech) Intelligibility in noise (questions 1, 7, 13, 18 and 24)
- (Speech) Intelligibility in quiet (questions 8, 11, 12, 14 and 19)
- Auditory localization (questions 3, 9, 15, 20 and 26)
- Recognition of sound (questions 4, 5, 6, 17, 22, 23, 25 and 28)
- Distinction of sound (questions 2, 10, 16, 21 and 27).

The score of each domain and the total score were calculated by averaging the responses in each domain and all the questionnaire items accordingly (Bamiou et al., 2015).

2.9.2. The Speech, Spatial and Qualities of Hearing Scale (SSQ)

This questionnaire was designed to measure various hearing difficulties mainly in binaural hearing such as hearing in noise, identifying directions of sound and determining the quality of sound. The questionnaire was validated in hearing aid clinics to evaluate difficulty before hearing aids fitting (Gatehouse and Noble, 2004). The response mode is in a visual analogue scale from 0 (can not do at all/ extreme difficulty) to 10 (can do perfectly/no difficulty).

This questionnaire was chosen for this research since cognitively impaired hearing aid users may experience even more hearing problems than cognitively normal hearing aid users (Hardy et al., 2016). Previous research showed that self-reported hearing difficulty is associated with cognitive decline (Maharani et al., 2019). Further study of this hearing difficulty in more detail with the SSQ questionnaire would clarify more about what aspects and domains of difficulty are mostly associated with cognitive

decline. The SSQ has 3 domains which are speech hearing, spatial hearing and sound quality of hearing. The score of each domain and the total score were calculated by averaging the responses in each domain and all the questionnaire items accordingly (Bamiou et al., 2015).

2.9.2.1. Speech hearing (questions 1–14)

The questions ranged from one-one conversation situation, conversation in various difficulty backgrounds to complex situations where divided attention is needed. This Speech hearing domain aims to demonstrate difficulty listening to conversational speech.

2.9.2.2. Spatial hearing (questions 1–17)

The questions ranged from distance and movement discriminations to directional ability. This Spatial hearing domain aims to demonstrate difficulty with sound localization which may be deteriorated due to hearing impairment or additional auditory processing difficulties.

2.9.2.3. Sound quality of hearing (questions 1–19)

The questions ranged from the ease of listening and recognizing different voices/sounds/moods to sound segregation ability. This Sound quality domain aims to demonstrate how well an individual perceived sound.

3. Chapter 3: Development of Montreal cognitive assessment for older adults hearing aid users (MoCA-HA): PHASE 1

In this chapter illustrated in Figure 3, the development process of the MoCA-HA was outlined. The method of gathering information and feedback from various stakeholders of the tool along with the incorporation process of these feedbacks to create MoCA-HA were discussed in detail. At the end of this chapter, the final cognitive screening tool which was the outcome of this phase 1, would be ready to be used in the next phase of the trial. The strength and characteristics of this tool were also discussed in more detail.

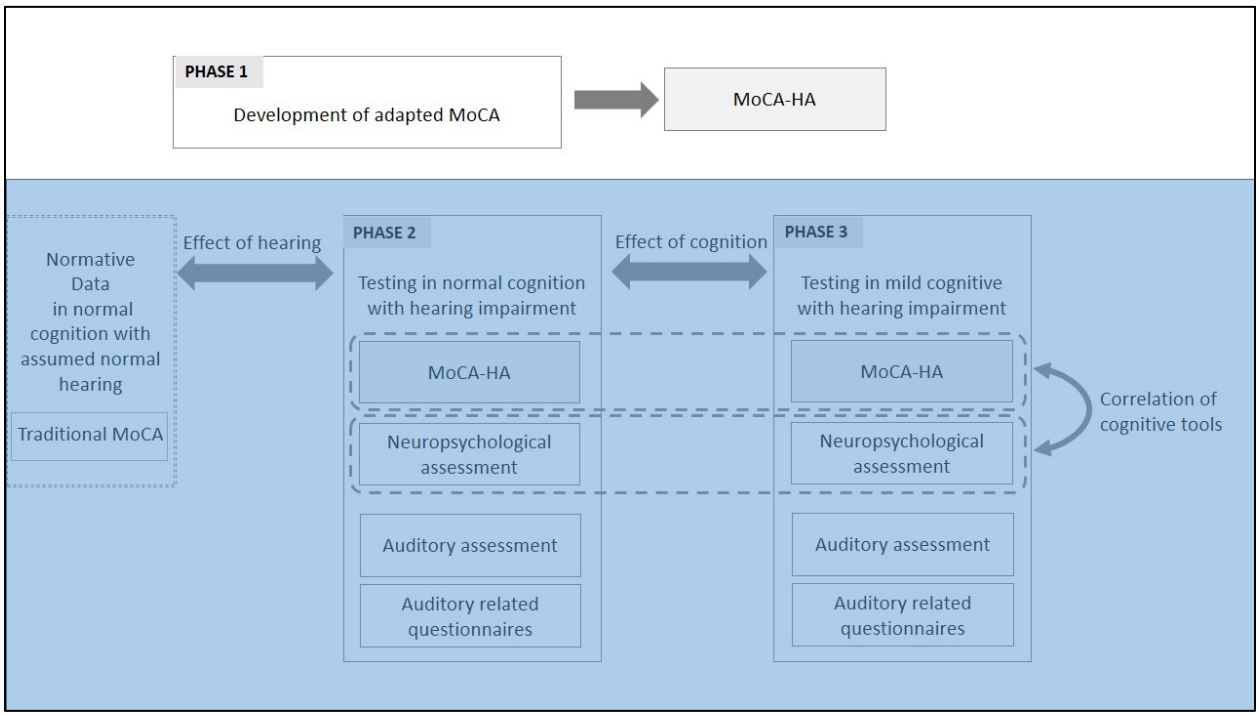

Figure 3 Working framework of Chapter 3 as part of the overall study

3.1. Introduction

When developing new clinical tools, it is useful and recommended to incorporate input from real users. This is the fundamental grounds for "Patient Public Involvement" (PPI). PPI is recommended to be implemented in the earliest stage as possible of research planning. This is to also ensure that the research aims and outcome are what the patients and the public really want (Hoddinott et al., 2018). Currently, it is a recommended practice in the UK for any research conducted in the National Health Services (NHS) to have PPI.

Previously, we thought that healthcare providers had more insight to design and conduct the intended research/intervention for the patients. Research participants were deemed passive recipients of the trial or intervention designed entirely by clinicians. However, we gradually started to realize that the patients and the public can have valuable insights into their conditions and their preferred intervention/method. They can offer their inputs to shape better healthcare that would directly affect them. The paradigm shifted from conducting research to the patients to become "co-designing" the research with the patients (Meyer, 2000).

Especially when designing a tool for people with disabilities, we cannot understand every aspect of their conditions and needs without having members of that population act as their own advocates. Since our work mainly would be implemented among older adults with hearing impairment, not only healthcare professionals that usually work closely with these populations, but the hearing-impaired older adults themselves were also invited to participate in the development process of this tool.

This chapter presented the inputs received from PPI sessions and outlined the recommendation of changes in this newly developed tool and how these were implemented.

3.2. Method

We followed the "action research study" methodology that was originally developed for the education field and has been used in numerous studies in healthcare such as in improving the patient care process (Marshall et al., 2006). The core of action research in healthcare is focused on improving the care by direct input of the patients/participants as the main stakeholder (Bradbury and Lifvergren, 2016) and incorporates several cycles of development before accomplishing the final product (Marshall et al., 2006, Koshy, 2010).

Each cycle consisted of 4 main stages (Observe, Reflect, Plan, Act). The final "Act stage" of the previous cycle would also be observed for information to be used in the next "Observe stage" of the new cycle (Koshy, 2010). The cycle can be repeated several times until the final product is ready.

This method is crucial in developing suitable care, especially for complex patients. Since our cognitive screening tool for hearing aid users aims to be delivered among older adults with hearing loss who may also have other complex medical conditions, action research method was selected in the development process of this tool.

3.2.1. Sample size

We recruited 5 older adults hearing aid users who had previous research experience, particularly with hearing aid research. The purposeful sampling of information-rich active volunteer cases was used (Palinkas et al., 2015, Patton and Patton, 2002), in order to ensure they were vocal and understood about the importance of PPI in shaping the development and design of the tool.

Previous research about usability testing (Faulkner, 2003) indicated that five users could identify 85.5% of usability problems. Therefore, this number is used in several user experience research design studies especially when the research aims to discover problems in the tool (Macefield, 2009).

After all five in-depth interviews were conducted. According to the study field notes, we had reached the data saturation of the identified problems. For the qualitative study, data saturation point means no further significant problems would arise with further interview cases (Saunders et al., 2018a).

3.2.2. Participants

Five volunteer older adults with hearing aids (clients) were invited to be included in the Patient Public Involvement (PPI) process, including an older adult with dual sensory impairments (visual and hearing). The opinions from all related parties were incorporated into the process. As part of PPI process, the feedback from the healthcare providers including psychiatrists, clinical psychologists, audiologists, hearing aid centre manager, otolaryngologists, audiovestibular medicine physicians, general practitioner (users) were also sought after.

3.2.3. Data collection and analysis process

In-depth interviews of each individual participant in a one to one sessions were conducted (Britten, 1995). This method of the interview was selected since it can capture most data expressed freely from the volunteer without any guidance by the researchers. This interview method also caters for a focused area of interest such as opinion about only 1-2 topics.

The opinion of the participants about their experience on the tool was recorded by note-taking for each slide. All opinions were collated. The data analysis was done with inductive analysis procedure which is the thematic analysis approach (Pope et al., 2000, Braun and Clarke, 2006). The issues gradually arose from the data. Subsequently, issues with similar ideas were grouped into different themes for further analysis and understanding. Thematic analysis is the most common type of analysis used in applied

qualitative research such as healthcare (Braun and Clarke, 2014), which focuses more on the application of data rather than on developing new theories. This method may also reduce preconception interference of the data interpretation by researchers when compared to other deductive analysis procedures.

3.2.4. Initial Material for the observation of the feedback sessions

This hearing-impaired MoCA (MoCA-HI) developed by Lin et al. 2017 (Lin et al., 2017) was used in an initial Patient Public Involvement (PPI) process. The PowerPoint slides and the response forms were provided by Lin and the research team.

3.2.5. Action research process

The method involved giving the volunteer the initial material and asking for feedback. The feedbacks were then incorporated into the second stage and the feedbacks were observed again. The cycle of process were

- Plan: The material was prepared to be used with the volunteer.
- Act: The material was being implemented with the volunteer.
- Observe: The feedback was gathered from the volunteers.
- Reflect: The material was then adjusted accordingly and prepared to be presented again to the volunteer in the second cycle of the “Plan”stage

In our research, the cycles were repeated for a total of 4 times, twice for the healthcare professionals and twice for the older adults.

3.3. Development process results

In general, most participants agreed that the project’s aim of creating visually-based cognitive tools wouldhelp to improve the care quality of hearing-impaired older adults. Since all of our participants for our PPI sessions were older adults with hearing aids, they reported that they experienced first-hand what the problems usually were when they tried to communicate with their doctors. Occasionally, they had difficulty to understand their doctors who have foreign accents or soft voices. They reported using all available clues such as facial expressions and lip reading to help communicate with healthcare providers.

Some reported that they always need to use lip reading when trying to communicate with their doctors. Therefore, when we introduced our visually-based cognitive tools to our participants at our PPI sessions,

a few participants said that “they were *quite impressed*” that we can create a more effective way for their doctors to fully assess their cognitive ability despite their hearing problems.

The results from the interview sessions and discussions with relevant stakeholders were incorporated into the final cognitive assessment tool. The principles of “Thematic analysis” were adhered to analyse all the feedback (Braun and Clarke, 2006). They aim to identify and interpret various patterns of meaning or so-called themes within interview data. The feedback can be divided into major themes below.

3.3.1. Feedbacks from professionals: Test administrators

3.3.1.1. Prompt when the slide will be timed

The healthcare professionals who would eventually be a test administrator suggested that they were not certain whether they had to progress the slide by clicking it or that slide has already been timed ie. in the word recalled task. After several iterations, we decided to add a prompt slide before the timed slide which was well accepted by the professionals.

3.3.1.2. Manual for unfamiliar administrators

The option of producing a manual for the test administrators was raised during the development process. This was to remind the professionals about some minor point such as the timed slides etc. However, we tried to make our slide as user-friendly as possible. Therefore, any professionals who are familiar with traditional MoCA administration can comfortably perform this version of MoCA.

Professionals who had experience with traditional MoCA reported no difficulty in utilising the adapted MoCA without further instruction.

3.3.2. Feedbacks from professionals: Response modes: Verbal mode

3.3.2.1. Preferred Verbal response

Both professionals and the older adults preferred verbal response over the written response. They were more familiar with the verbal response and also they felt that it would be less demanding for the cognitively impaired older adults.

3.3.2.2. Uniform response mode:

After an issue with the written response forms, the professionals suggested separating the response modes into verbal and written according to the older adults’ preference. However, all older adults reported that they would prefer a verbal over a written answer.

After discussion with professionals and experts in psychology research, we decided to have a uniform verbal response mode. This is because the different response types may require different cut-point scores and widen the variability.

3.3.2.3. Verbal can include people who might not be good at writing for education or dexterity ie Parkinson's disease

Professionals believed that a verbal response mode would be better for most of their older patients, as fine motor skills may be degraded earlier than verbal skills. Additionally, they did not want literacy to be a barrier to test delivery.

3.3.3. Feedbacks from volunteers: Test material

3.3.3.1. The size of the characters: 48 points is best for visualisation

Our volunteer participant with dual sensory loss (hearing and vision) could still visualize all the instructions with font 48 points with no difficulty. We thus decided to adapt our slides to font 48 according to this participant's feedback and recommendations by the World Blind Union (WBU, 2007).

The font size of 36 points was also presented to the participants since the original MoCA for cochlear implant users used this font size. Most participants, especially our participant with dual sensory issues, could not fully visualise the instructions and target words and preferred font size 48.

3.3.3.2. The contrast of the instructions and backgrounds:

Black and white were selected originally since it is the recommended contrast for material used for those who are visually impaired or colour blind (WBU, 2007). The highest contrast of black and white was reported by our participants to help improve visibility. Good contrast of white letters on black background was preferred by both older adults with hearing loss, the older adult with dual sensory loss and the professionals.

3.3.3.3. Eliminate distraction on the slides

Initially, the picture of the timer's clock was added on the upper right corner of the slides that were timed for the benefit of professionals.

However, several older adults asked for these to be eliminated. They reported that when made aware that the tasks were being timed, they felt anxious and distracted and this impacted on their confidence to perform in the tasks.

It was thus decided to remove the timer's clock pictures and replace them with prompt slides. The wording of the prompt slides were as per the figure below (Figure 4).

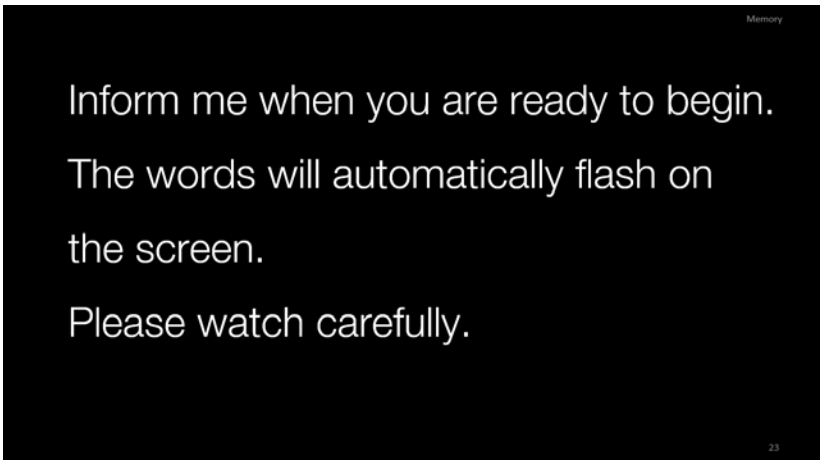

Figure 4 Prompt slide when the following slide has pre-set timed

Therefore all slides were adjusted accordingly then presented again to the participants who were all satisfied with the final product, since it can prompt both the older adults and test administrator without creating further anxiety for the participants. This is also in line with the recommendation by the World Blind Union to minimise all the animation within the slides (WBU, 2007).

3.3.3.4. Opinion about the option for recorded amplified instruction

The volunteers felt that the recorded amplified instructions and target words worsened their performance compared to the original verbally delivered mode. This was because they cannot use lip reading as visual clue. Moreover, they perceived the amplified speakers sound quality as distorted and more difficult to understand. Severe hearing loss participants felt that they would not understand well enough even with their hearing aids and amplified instructions would interfere with their task score.

3.3.3.5. Opinion about the option for written instruction

The volunteer felt that the written instructions and target words were a valid solution for their auditory difficulty. In the past incidences, some of them had encountered healthcare professionals who had

foreign accents. With the hearing loss, unfamiliar accents made it even more difficult for them to understand the healthcare professionals but they did not want to cause any offence so they were trying their best to understand the instructions.

Therefore, they felt that written instructions and target words would overcome this difficulty with ease. They understood that recorded instructions could also overcome this issue; however, as previously discussed, another problem with the distortion can arise. Some volunteers mentioned that literacy might be an issue for some older adults if the instructions and target words were complicated. However, since our instructions and target words were straight forward, the volunteers did not think that literacy would be a barrier for our test among their peer.

3.3.4. Feedbacks from volunteers: Response modes: Written mode

3.3.4.1. Confusing with lots of response forms

The older adults reported that they were not comfortable with several response forms and they felt rather confused. Some suggested that they were comfortable to write, especially older adults with literacy issue. They suggested that maybe written response may not be ideal for them and their peer at a similar age.

3.3.4.2. Can start to write down the response "before" instructed to do so → cannot fully test memory

The original protocol instructed to give the answer sheet to the participant while the task was explained. This was to minimize the disturbance of attention and memory while performing the test. However, a few of our participants wrote down the answer before they were instructed to do so. They were well aware that this behaviour may be viewed as "cheating" the task. Some of them also tried to jot down some clues to help them remember the target words.

3.3.4.3. Can start to write from downward up in backward digit recall tasks

A few participants tried to write the answer of the digit backward recalled from back to front. They reported that this way the task would be much easier. They were not certain that they can perform the task in the standard manner by mentally counting backward and answered with the backward numbers.

3.3.4.4. Can interfere with the recall of words and sentences

A few participants reported that they tend to remember the words much more when they had a chance to write down the word twice before the recalled process. Moreover, they also have additional time to review the words on the answer sheet to add to their memory.

However, a few participants could not complete the sentence repetition task reported to be due to this response mode. They reported that their literacy ability in spelling all the words in the sentences interfere with their working memory to recall all the words.

3.4. The final cognitive assessment tool

The adaptation of the MoCA to suit a population with hearing impairment was previously done for a cochlear implant candidate population in order to assess their underlying cognitive function as surgical candidates and estimate their performances after the surgery (MoCA-HI).

We used the PPI information on the MoCA-HI to adapt the MoCA version 8.3 computer-based tool (that also included the MIS sub-task which did not exist in MoCA-HI), by using only visual input to make it suitable for older adults with all degrees of hearing loss.

The scoring sheet and administration instructions were downloaded from www.mocatest.org. In the final version, the instructions were presented visually on the screen via the Microsoft Powerpoint program. The tool was also adapted according to guidance for the visually impaired population to ensure good visibility for the older adults with possible visual and hearing impairments (WBU, 2007). The durations of each slide visualization in the tasks were set according to the previously published paper by Lin, et al (2017).

The slides were presented to the participants by the administrator. The participants told the administrator when he/she were ready to move on to the next slide. The administrator guided the participants to read the instruction on the screen without further explanation by the administrator. The decision to have the administrator progressing the test to the next slide was suggested by the PPI volunteers, since they judged that some older people may not be comfortable when operating computer screens.

The participants responded to each slide verbally except when they were prompted to draw in the visuospatial/executive sub-test. Their responses for this task were recorded in the original record form (MoCA 8.3). There were some changes from the Lin et al (2017) version in that older volunteers opted to use the original response form. Volunteer PPI participants felt that writing down the word recall response would act as additional practice and help to remember and thus overestimate memory status. The sentences recall task (part of a Language sub-category) was also affected by their writing ability of such compound sentences which took longer than a verbal response.

The final MoCA used was the MoCA version for hearing aids users (MoCA-HA) which incorporated all the changes suggested by the volunteer end-users and the health care professionals. The test was completed within 15 minutes. The example of the visual slides is presented here (Figure 5).

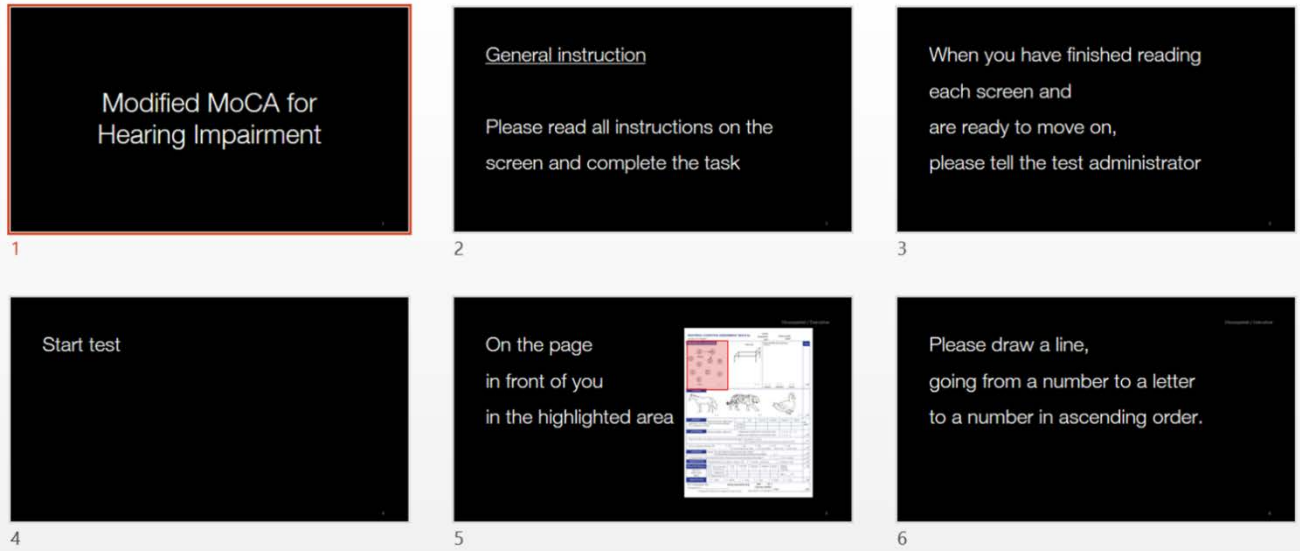

Figure 5 Sample of MoCA-HA cognitive screening tool

3.5. Discussion

3.5.1. Strength of the MoCA-HA

We developed a version of the MoCA tool, modified for older adults with hearing impairment who use hearing aids. It is important to have a MoCA version suitable for this population since previous research has shown that they may be at a higher risk of developing MCI or dementia (Livingston et al., 2017) and interpretation of the results of standard MoCA versions may be confounded by verbal presentation, with key dementia-relevant elements of registration, recall and attention, particularly affected (Al-Yawer et al., 2019).

In order to develop the MOCA-HA, we first adapted Lin et al. (2017) MoCA-HI that was developed for people with cochlear implants, for older adults with age-related hearing loss. Feedback from patients and health professionals informed modification and several changes were made to the measure based on this.

This version was easier to use as judged by the volunteer participants. We propose that this new version which takes into account users' ideas would be of value to everyday practice.

3.5.2. MoCA-HA for hearing aids users compared with MoCA-HI for cochlear implant users

Since cochlear implant candidates with prolonged and severe to profound hearing loss may have poorer speech production pre-operatively (Dawson et al., 1995), a written response for the MoCA may be more appropriate as used by Lin et al (2017). However, for the majority of older adults who attend memory services or general practices, a written response may not be the best option to evaluate their cognition. Reduced performance assessed by written response may be due to impairment in the fine motor skills required for writing rather than on the target cognitive abilities. This added complexity may also cause confusion and stress for older adults according to the feedback from our PPI sessions. A verbal response was much more acceptable in the PPI interviews. Therefore, we decided to use the original scoring sheet of MoCA with the traditional verbal response from the participants.

Another difference among cochlear implant candidates and other older adults with hearing impairment (hearing aids users) are that most of the cochlear implant candidates need to be physically fit enough to undergo surgery and tend to be younger (Lin et al., 2012). In our Patients public involvement (PPI) session, the participants preferred the test administrators to press the button for the next slide and to control the pacing of the task, since they were not comfortable with a computer screen. We implemented these changes in our protocol to enhance the testing experience in our cohort and for potential clinical use in the future.

Previous work on a written version of MoCA for cochlear implant users (Lin et al., 2017) showed significant differences in 2 sub-categories, word recall (better scores in the written version) and sentence repetition (worse scores in the written version). The better performance in word recall in the written version may have resulted from writing the words down twice during the registration phase as this may have resulted in additional practice benefits. During the PPI interview, participants reported that this may have given some additional time to go through the words again on the answer sheet. For the sentence repetition, the worse score may result from the requirement to write down the whole sentence with every single word correctly which would be more difficult and would take longer time in the process than a simple verbal answer.

3.6. Conclusion

With the feedbacks from all involved stakeholders via action research process and detailed thematic analysis, the final cognitive assessment (MoCA-HA) tool for hearing aids users was completed at the end

of phase 1. The tool was ready to be implemented in phase 2 among the wider cohort of older adults hearing aids users.

4. Chapter 4: Characteristics and cognitive/auditory performance of normal cognition older adults with hearing loss population: PHASE 2

This phase aimed to explore the use of the newly developed cognitive screening tool MoCA-HA among older adults with hearing impairment (Figure 6). An additional aim was to examine the performance of this cohort on each element of the MoCA-HA (visuospatial/executive, naming, memory, attention, language, abstract and orientation) by comparing the performance of our participants with normative data of the traditional version of MoCA in order to explore whether the MoCA-HA resulted in similar subscores of cognitive performance in older adults with hearing impairment.

An analysis of the memory sub-category and memory index score was also added to find out if the hearing-impaired participants' memory pathway differs from the normal-hearing population according to these measures.

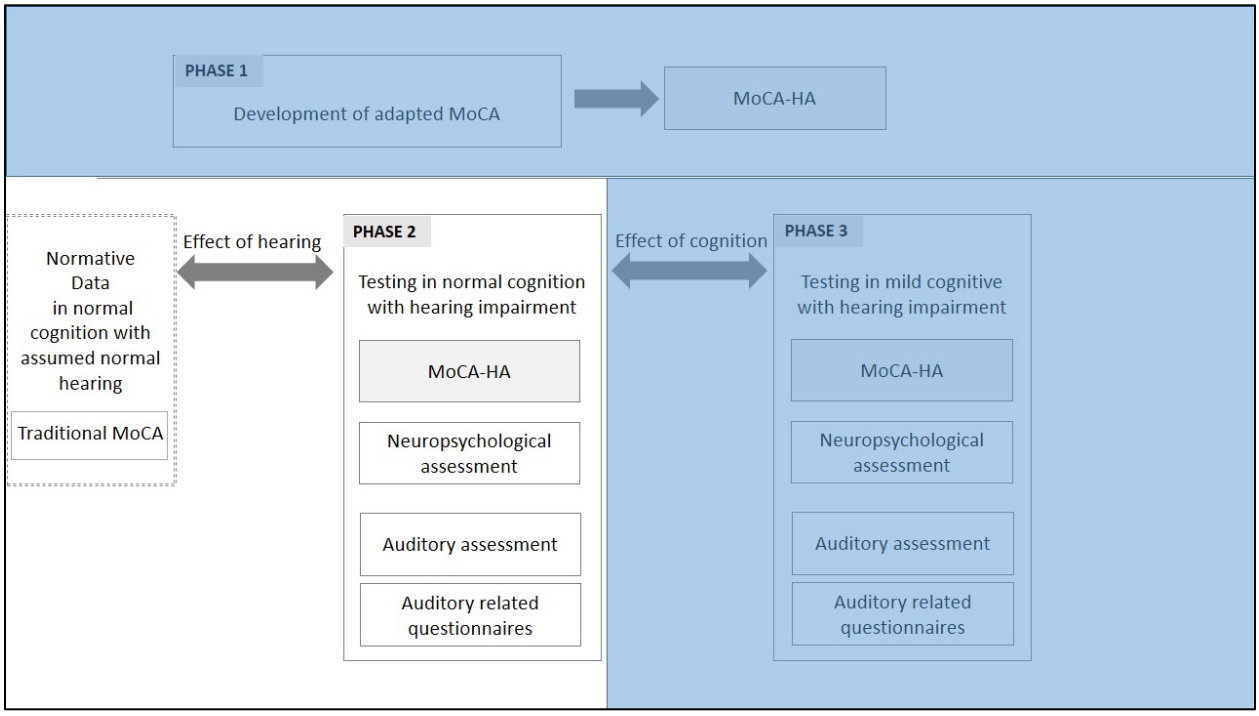

Figure 6 Working framework of Chapter 4 as part of the overall study

4.1. Introduction

MoCA was designed for early screening for mild cognitive impairment. It comprises various elements (sub-categories) which could potentially be impaired in early MCI population. Detailed comparisons of these sub-categories between the normal-hearing normative data and the hearing-impaired cohort may

demonstrate particular cognitive strengths or cognitive weaknesses of individuals with hearing impairment.

Previous research has suggested that the hearing impairment population may potentially have weakness in memory sub-category of MoCA (Yeok Leng Lim and Loo, 2018). However, when assessing with verbally presented traditional MoCA, the hearing impaired population may be disadvantaged since they could not clearly hear the target words, to begin with. Our previously published systematic review about the use of traditional MoCA among the hearing-impaired population (Utoomprurkporn et al., 2020b) identified 2 papers (Yeok Leng Lim and Loo, 2018, Dupuis et al., 2015) which detail the breakdown data for registration and recall part of the MoCA memory sub-category. Dupuis et al (2015) found that the hearing-impaired population were less likely to correctly repeat all 5 words in both registration trial phases. (85% for control vs 60% for hearing-impaired) Overall, people who fail to correctly register all 5 words on both registration trials would be 1.4 times more likely to fail the MoCA (Dupuis et al., 2015). In Yeok Lim et al (2018), the reason underlying this analysis was that they wanted to identify whether the phonological characteristics of the error words in individual participants were consistent with the participant's hearing impairment pattern. These authors reported a difference of the registration percentage for each target word depending on the phonological characteristics. In this current study, we used MoCA-HA which did not rely on hearing ability to assess this cohort. Therefore, the memory subcategory could be accurately assessed to reveal any potential weakness, if any.

Additionally, when analysing the MoCA-HA performance of the hearing impairment cohort, the potential strengths of this cohort such as in visuospatial subcategory may also be uncovered (Rudner et al., 2016a). A visual sensory compensatory mechanism for hearing impairment has been studied extensively among deaf native signer children where visuospatial ability outperformed their peers (Wilson et al., 1997). However, assessing this aspect among older adults with hearing impairment is more complex since other confounders such as age, underlying medical conditions etc can also play a role. Even though, we may not have enough statistical power for sub-category analyses, the analyses may show trends to suggest further study in this field.

The comparison with data from the original MoCA cohort was done mainly for demonstration purposes. The original cohort did not report the hearing status of the included older participants. The analysis in this chapter was done under the assumption that they had normal or nearly normal hearing to complete the verbal MoCA tasks to be included in that study. This may not always be true since 1 in 3 of older adults suffer from hearing impairment (WHO, 2012) and they may not always self-report their hearing

difficulties (Cruickshanks et al., 1998). However, we made this comparison analysis to demonstrate whether the performance of the verbal original MoCA among older adults with sufficient hearing was comparable with the visual MoCA-HA among older adults with hearing impairment.

4.2. Methods

4.2.1. Participants

The inclusion criteria were adults aged ≥65 years with documented hearing impairment (currently wearing hearing aids and/or have an audiogram with a hearing average of ≥30dB HL), and who were not on the cochlear implant waiting list.

The exclusion criteria were uncorrected visual impairment; cognitive and/or physical disability(s) which prevented the performance of the written/drawing elements of the tests, prior diagnosed cognitive impairment and congenital/childhood-onset hearing loss (<18 years old age) as reported by participants.

4.2.2. Participants' recruitment pathway

Hearing aid users were recruited from the hearing aid clinic at Royal National Throat Nose Ear Hospital, London, United Kingdom waiting area. The poster and recruitment flyers were distributed for the interested hearing aid users in the centre. The terminology "dementia", "Alzheimer's" etc were avoided in the recruitment materials by using the term "memory" instead. The recruitment material emphasized that this research would only recruit participants with no memory concern as the control group of the cognitive tool validation scheme. This was to prevent any potential recruitment bias from the participants entering the project with the intention of getting help with suspected memory problems.

The interested participants could get in touch with the researcher via email stated in the flyers or tell the healthcare professionals in the clinic about their interest to be contacted. After the initial contact, the interested participants were asked about any prior history of memory problems. They would be excluded from participation if any history of memory issue was reported.

4.2.3. Materials

4.2.3.1. General Practitioner's Assessment of Cognition (GPCOG)

After the initial contact, the participants would be asked for a convenient time slot to meet for a cognitive screening session to ensure their normal cognition state. To ensure participants in the study

had normal cognition, only those with a General Practitioner's Assessment of Cognition (GPCOG) score of equal 9 or GPCOG score =5-8 with informant score =4-6 were recruited (Brodaty et al., 2004).

The GPCOG was selected as this tool is currently recommended to be used by general medical healthcare practitioners (Alzheimer's society, 2015), and is the only tool available for initial cognitive screening which can be completed without further information from friends nor family members (informants).

Most cognitive screening tests need informant input since older adults with cognitive impairment may not have enough insight to correctly identify their memory issues (Larner, 2005, Larner, 2004). However, with GPCOG, the assessment is divided into 2 parts, the participant and informant. If the participant had a full score in the initial task, no further input from the informant is needed. We decided to use GPCOG as our tool to ensure the good cognitive status of our participants recruited as controls in this study. The informant would also be invited to participate. However, if the participant does not have any friends or family members to be an informant joining them at the session, they can still participate if they had a full score on the GPCOG task. This way participants who attended hearing aid clinics without a caregiver (informant), which in a way indicates more capability, could participate in the trial.

After the initial contact and passing the cognitive screening GPCOG, the participants would be asked for a convenient time slot to meet for the session. All the measures as listed in chapter 2: materials and methods were followed.

4.2.3.2. MoCA-HA

The visually presented computer-based Montreal Cognitive assessment tool (MoCA-HA) from phase 1 which was based on MoCA version 8.3, was used for testing in all 30 recruited normal cognition control participants.

4.2.4. Statistical analysis

The data of the NC-HI cohort was analysed using IBM SPSS statistic software version 25. The comparison of the computed normative data from a previously published cohort for traditional MoCA was done to identify whether there was any difference in the total MoCA score and the sub-categories.

For demonstration purposes, statistical analysis with the Summary independent-samples t-test was done for MoCA and MoCA-HA data, using computed normally distributed data. For nominal data, Chi-squared was used. Correction for multiple comparisons of the 7 sub-categories and the total MoCA-HA

score was done by Bonferroni correction. The corrected alpha by Bonferroni was 0.05/8=0.006, therefore, a statistically significant difference level of the MoCA-HA and traditional MoCA was <0.006.

For memory sub-category, the registration and recall were explored in more detail. The number of participants who could register and recall each target word in each trial was recorded and used to calculate the registration percentage and recall percentage of each target word. The percentages of each target word were compared with Chi-squared to determine any difference registration and recall between the target words. A significant difference of registration/recall percentages implied potential bias from the hearing impairment toward the information encoding process in the MoCA-HA memory sub-categories as previously found in the traditional verbal MoCA (Yeok Leng Lim and Loo, 2018).

The memory index score (MIS) of each target word was also calculated. This was the additional analysis of the recall sub-category. The participants received 3 marks when correctly identifying the target words without any clues, 2 marks when correctly identifying the words with categorical clues and 1 mark when correctly identifying the words with multiple choices clues. MIS scores for each word ranged from 0 to 3 with the total score of the 5 words combined ranging from 0 to 15. The scores for the 5 target words were compared to further explore the difference in the participant's memory retrieval pathway for each target word. The assumptions for parametric statistic analysis (one-way repeated measure ANOVA) were checked. With small values of data for each word (MIS from 0-3 scores), the data did not fulfil the assumptions, therefore, a non-parametric Friedman test was used.

4.3. Results

4.3.1. Baseline characteristics of the participants

A total of 30 hearing aid user participants aged >65 years were recruited into the study to complete the visually presented computer-based MoCA-HA. Their mean age was 75.27 years (SD=5.88, range 65-90 years) with 40% female participants. The mean total years of formal education of the participants was 16.07 years (SD=3.69).

Their pure-tone average of the better hearing ear was 48.67dB (SD=18.05). The duration of their hearing loss ranged between 3-49 years. The comparison of the baseline characteristics with the normative data reported in the original MoCA study by Nasreddine are shown in Table 1

Table 1 Baseline characteristics of the participants compared with original MoCA

Participant Characteristics	Original MoCA (n=90)	Modified MoCA-HA (n=30)	Mean difference	95% Confidence Interval for the difference	P-value
Age	72.8 years (SD = 7.0)	75.3 years (SD=5.9)	2.5	(-5.23,0.35)	0.090
Female Sex	54 (60%)	12 (40%)	N/A	N/A	0.570 (Chi-square)
Years of education	13.3 (SD = 3.4)	16.1 (SD = 3.69)	2.8	(1.24,4.24)	<0.001*
Hearing loss level 4 frequencies average PTA (dB)	N/A	48.67dB (SD=18.05)	N/A	N/A	N/A

*This was statistically significant at p<0.05

4.3.2. Overall MoCA performance and performance in each sub-category

Overall, the total MoCA-HA mean score was 27.27 (SD=2.16) out of 30 and was not significantly different from the score reported in the original verbally presented MoCA 27.14 (SD=2.01) out of 30.

The memory sub-category score tended to be lower on the MOCA-HA than the original MOCA (mean difference = 0.77, 95%CI [0.10, 1.44]) out of 5 scores. However, this difference did not sustain Bonferroni correction for multiple comparisons.

No significant difference was found in other sub-categories such as attention, language and orientation (*Table 2*). All participants scored at ceiling on visuospatial/executive, naming and abstract, therefore no 95% confidence interval or p-value of the mean score difference could be calculated

Table 2 Performance on sub-categories of MoCA

Sub-category of MoCA	Original MoCA** (n=90)	Modified MoCA-HA (n=30)	Mean difference	95% Confidence Interval for	P-value

				The difference	
Visuospatial/ executive	4.69 (SD=0.58)	5.00 (SD=0.00)	0.31	N/A	N/A
Naming	2.85 (SD=0.38)	3.00 (SD=0.0)	0.15	N/A	N/A
Memory	3.74 (SD=1.15)	2.97 (SD=1.69)	0.77	(0.10, 1.44)	0.026*
Attention	5.77 (SD=0.51)	5.80 (SD=0.48)	0.03	(-0.24,0.18)	0.778
Language	2.42 (SD=0.69)	2.40 (SD=0.89)	0.02	(-0.34,0.38)	0.911
Abstract	1.72 (SD=0.51)	2.00 (SD=0.00)	0.28	N/A	N/A
Orientation	5.92 (SD=0.27)	5.97 (SD=0.18)	0.05	(-0.14,0.04)	0.254
TOTAL	27.14 (SD=2.01)	27.27 (SD=2.16)	0.13	(-0.98,0.72)	0.764

*This was not statistically significant after Bonferroni correction (Bonferroni threshold P-value < 0.006)

**This was adopted from previously published work (Lin et al., 2017, Nasreddine et al., 2005).

4.3.3. Memory score breakdown analysis and Memory Index Score (MIS)

The registration percentage for each target word

There was no significant statistical difference between the registration percentage of each target word either in trial 1 (x^2=5.201,df=4,p=0.267) or in trial 2 (x^2=3.041,df=4,p=0.551)

Overall, for all target words, the registration percentage improved in the second trial except for "Leg" which had a 100% registration percentage since trial 1.

Table 3 Registration score for each target words in trial1 and trial2

Target word	**Registration percentage on trial1**	**Registration percentage on trial2**
Leg	100%	100%
Cotton	96.7% (Fail in n=1 case)	100%
School	93.3% (Fail in n=2 cases)	96.7% (Fail in n=1 case)
Tomato	93.3% (Fail in n=2 cases)	96.7% (Fail in n=1 case)
White	86.7% (Fail in n=4 cases)	100%
All 5 words	70.0% (Fail in n=9 cases)	93.3% (Fail in n=2 cases)

70% of the participants (n=11) had correctly identified all 5 words in the first trial. This number increased in the second trial to 93.3% (n=28). When accounting for both trials, 63.3% of the participants (n=19) had registered all 5 words correctly in both trials.

A comparison was made with previously published data of traditional MoCA administration among the hearing loss population (Dupuis et al., 2015) using Chi-square. There was no significant difference in the percentage of participants who had registered all 5 words correctly in both of the trials when using the traditional auditory administered MoCA (60%, n=82 from 136) compared with the MoCA-HA (63.3%, n=19 from 30) (χ^2=0.095, df=1, p=0.758).

Note that in standard practice, the registration scores were not calculated as part of the total MoCA score of the participants. These analyses were done to demonstrate the registration ability among our normal cognition hearing-impaired cohort.

The recall percentage for each target word

After about 5 minutes, the participants were asked to recall the 5 target words. The participants would receive 1 score for each correctly recalled word without any clues (out of total 5 scores). The total score for this recall section was contributed to the final MoCA score. The percentage of recalling the target words were presented according to the number of target words recalled in Figure 7. Twenty-seven percent of the cohort correctly recalled all five target words without any clues. Thirteen percent of the participants did not recall any target word while 87% of the participants recalled at least one word in the trial.

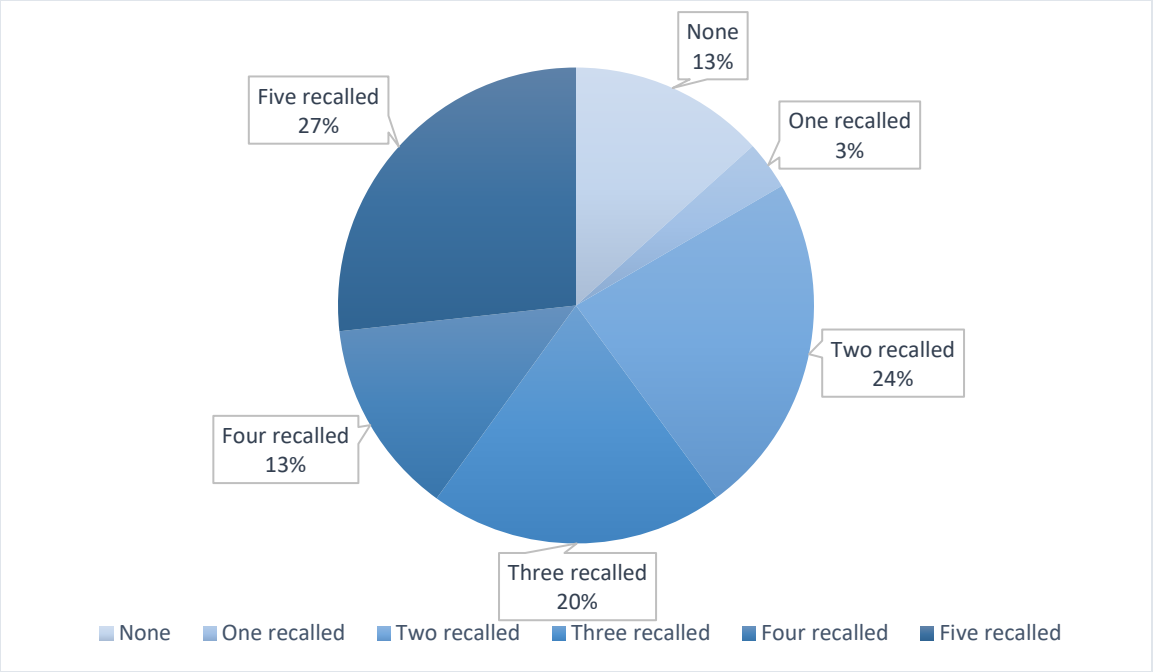

Figure 7 The percentages of recalling the target words were presented according to the number of target words recalled

The recall percentages for each word were also calculated and shown in Figure 8. There was no difference between the recall percentage of each target word (χ^2=5.913,df=4, P=0.206).

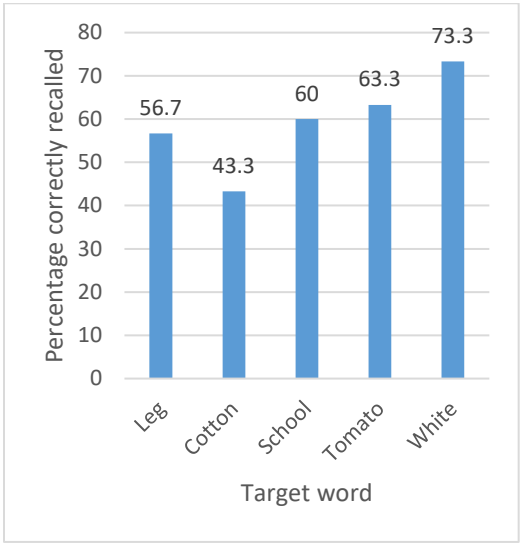

Figure 8 Bar graph demonstrated percentage correctly recalled for each target word

The Memory Index Score (MIS) for each target words

The mean MIS for the cohort was 11.60 (SD=2.98) out of 15. The recall percentage of each target word with no clue (3 scores), categorical clue (2 scores), multiple choice (1 score) and no recall with clues (0 score) are shown in Table 4. There was no significant difference between the mean MIS score of each target word (out of 3) (χ^2=1.907, p=0.753). The mean and 95% confidence interval of the MIS score for each word are shown in Figure 9.

Table 4 Recall percentage for each target words with and without clues

	Leg	Cotton	School	Tomato	White
Spontaneous recall – No clue needed (3)	56.7% (n=17)	43.3% (n=13)	60.0% (n=18)	63.3% (n=19)	73.3% (n=22)
Categorical clue (2)	16.7% (n=5)	40.0% (n=12)	13.3% (n=4)	3.3% (n=1)	3.3% (n=1)
Multiple choice clue (1)	23.3% (n=7)	13.3% (n=4)	26.7% (n=8)	33.3% (n=10)	20.0% (n=6)
No recall with clues (0)	3.3% (n=1)	3.3% (n=1)	0% (n=0)	0% (n=0)	3.3% (n=1)
Total	100% (n=30)	100% (n=30)	100% (n=30)	100% (n=30)	100% (n=30)

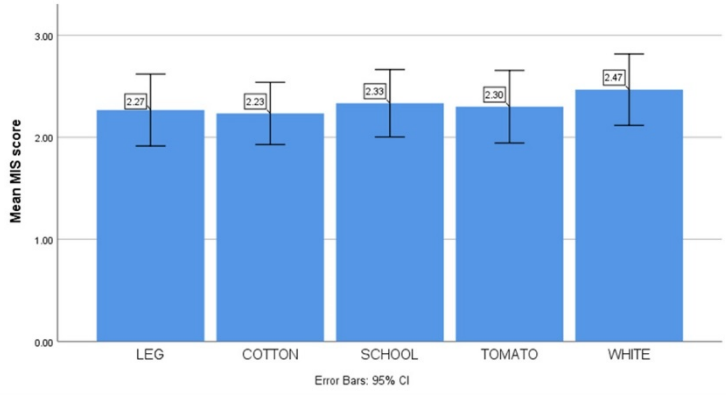

Figure 9 The memory index score (MIS) for each target word.

4.4. Discussion

4.4.1. Overall MoCA cognitive measurement

4.4.1.1. Comparison with previous data of older adults in general (unknown hearing status)

It was found that the modified MoCA-HA was feasible for clinicians and acceptable to participants. It could be administered to all participants and clinicians could obtain valid full scores in all cases. In support of the equivalence of this new tool to the original MOCA, no significant difference was found in the overall score between the MoCA-HA and the original MoCA as reported in the original MoCA validation study (Nasreddine et al., 2005).

There were also no significant differences in MoCA subscores between the MoCA-HA and the original MoCA. There was a difference in memory sub-category scores with the participants tested with the MoCA-HA achieving lower scores than those reported in the original MOCA validation study.

This difference may be due to subtle differences in memory encoding processes when stimuli are delivered visually rather than orally, or true deficits of memory in people with hearing loss, relative to normal hearing age-matched volunteers (Yeok Leng Lim and Loo, 2018). However, it is also possible that this difference may have arisen as a random variation (a false positive) because multiple tests were conducted; this explanation is also suggested by the fact that this potential finding would not have survived the Bonferroni threshold.

4.4.1.2. Comparison with previous data of cochlear implant candidates

Differences were not found in the overall and sub-category scores of the MoCA-HA between the hearing aid users and the controls. This was unlike the previously published work on a written version of MoCA for cochlear implant users, which showed significant differences in 2 sub-categories, word recall (with better scores in the written version) and sentence repetition (with worse scores in the written version). As discussed earlier in chapter 3.5.2, the differences may be a result of written response mode which was not used in the current MoCA-HA.

Overall, the initial results suggest that when using MoCA-HA the hearing aid user scores are comparable to those of the general cognitively healthy population when using the original MoCA. This present work, however, had a relatively small sample size (N=30) with limited power particularly for subcategory analysis of MoCA. This may be particularly pertinent for the recall test, which prior to the Bonferroni correction, did differ between samples, something which may merit further investigation with a larger sample size.

4.4.2. Delay recalled (memory) ability of hearing-impaired older adults

Registration phase

By developing the visually administered MoCA-HA in our cohort, we wanted to overcome the issue of errors in the registration phase of the memory sub-category that could be due to poorer auditory encoding and/or in combination with a true deficit in the encoding brain of the hearing loss participants. This is an important issue to overcome, since this sub-category was found to explain the majority of the difference in MoCA scores of the hearing-impaired population compared with their normal hearing peers (Dupuis et al., 2015). An accurate assessment of the memory sub-category is crucial since it is the first domain that would be impaired when older adults progress to the dementia stage (Julayanont et al., 2014).

However, we found that 63.3% of our hearing loss participants correctly registered all 5 words on both trials on the visually administered MoCA-HA, which was not different from when using the traditional verbally administered MoCA in the previous study (Dupuis et al., 2015). This may indicate that the mode of presentation of the target stimulus did not affect the registration score of the hearing-impaired population. However, in the Dupuis cohort, the hearing-impaired group hearing average (500Hz,1000Hz and 2000Hz) was 33 dBHL (Standard error=1.1) which fell into the mild hearing loss range (25-40 dBHL)

according to the World Health Organization classification (WHO, 2012). In addition, participants in the Dupuis cohort were also allowed to wear their hearing aids, if they owned one, during the MoCA verbal administration that was conducted in a quiet room. Despite, our cohort included participants with all degrees of hearing loss, mainly moderate hearing loss hearing aid users., they were given visually-delivered MoCA-HA to overcome their hearing difficulties. This may explain why there was no difference in the registration score of the two stimulus presentation cohorts in these two separate studies. Nonetheless, the hearing loss population may have registration/encoding problems that are unrelated to the presentation mode of the target stimulus. Their registration scores were around 60% for both visually and verbally-presented stimuli, while the normal hearing peers scored significantly higher at up to 85% (Dupuis et al., 2015).

A visual assessment of verbal memory was previously found to have better validity among the hearing-impaired population than auditorily presented assessment (Wong et al., 2019). However, hearing impairment participants performed worse than their normal-hearing peers on a visually administered 15 words recall task (Dupuis et al., 2015). This would indicate that the mode of information encoding cannot fully explain the decrease in performance of the hearing-impaired older adults and there may be an impairment in the verbal memory encoding pathway among the hearing-impaired population. In our sample of hearing-impaired participants, we did find a tendency of lower score in the memory sub-category when compared to the performance of historical normal hearing controls, although, as discussed earlier, this difference was small and maybe a false positive given that we compared all 7 cognitive sub-categories, in addition to the total score.

Recall phase

No significant difference was found in the recall rates of each word unlike previous research (Yeok Leng Lim and Loo, 2018) with an auditory presented target. In the auditory presented targets, the phonological characteristic of the target words and the hearing loss configuration of the participants can cause the discrepancy in the recall percentage (Yeok Leng Lim and Loo, 2018). These findings indicate that cognitive assessment of the hearing-impaired can be distorted by patient audiological and target word phonological characteristics when using auditory-based targets, and that this bias can be corrected through visual presentation of the same stimuli. Our findings, therefore, suggest that the visually presented MoCA-HA may offer a more accurate reflection of the cognition of the hearing-impaired population, robust to the bias introduced by hearing impairment.

Originally, all five target words were selected to be equally challenging in terms of recall for participants in general. Usually, the word recall ability follows the primacy and recency effect where an individual tends to remember the first (due to more time for mental rehearsal in their head) and the last target words (due to recently hearing the target) accordingly more than the middle one (Glanzer and Cunitz, 1966). Dupuis et al (2015) found that for the hearing-impaired cohort, they tended to have similar recency effect as their normal-hearing peers when they would remember the last few target words gradually better. But the primacy effect of the hearing impaired older adults was down by about 25% compared with their peers (Dupuis et al., 2015). In our cohort of hearing-impaired older adults, even though overall, there was no significant difference in the recall percentage of each target word, a slight trend for participants to have less primacy effect was still present. We did not have the normal-hearing group raw data for comparison, but the original paper of primacy/recency effects among general population showed that the first word should be recalled the most and more than the last word (Glanzer and Cunitz, 1966). Figure 8 demonstrated a lower than expected primacy effect when the first word was recalled better than the middle ones but still less than the last word.

A possible explanation for this phenomenon is that maybe for the hearing-impaired population, the memory of the items presented earlier was not encoded as well as the later presented items or that their memory decays faster with time compared to normal-hearing peers. In Dupuis et al (2015), the authors used verbal target words for the MoCA, therefore the effect of auditory degradation cannot be ruled out (Dupuis et al., 2015). We demonstrated a similar phenomenon in our cohort which may suggest that this encoding/early delay issue among the hearing-impaired population is independent of the presentation modality.

This finding may support the theory of auditory deprivation where hearing impairment causes permanent changes to the brain (Lin et al., 2014, Wassenaar et al., 2019), since the encoding deficit was prominent even when tested via a non-auditory pathway. It was also consistent with imaging studies showing that hearing loss is associated with more marked brain atrophy (Lin et al., 2014) and with white matter break down in the ageing brain (Wassenaar et al., 2019), which potentially leads to cognitive decline.

Memory Index Score: Encoding VS Retrieval pathway

The hearing-impaired older adult's ability to conduct a delayed recall task in MoCA has been studied in previous literature. When the traditional MoCA (verbal) was applied, studies have reported that the

hearing-impaired participants' score was worse than that of the normal-hearing peers particularly in the delayed recall sub-category (Al-Yawer et al., 2019).

Dupuis et al. (2015) investigated whether this memory problem was due to information encoding of the verbally presented stimulus by the hearing-impaired older adults. Even after accounting for only the words correctly identified twice in the registration phase, hearing loss subjects were found to score less than their normal-hearing peers (Dupuis et al., 2015). The authors interpreted this finding as indicative of a problem in information retrieval rather than encoding of the hearing impaired participants. However, the problem may lie on the cognitive demands placed on the hearing-impaired older adults when encoding unclear auditory target words to their memory, as explained by the information degradation hypothesis (Wayne and Johnsrude, 2015). As found in previous research, target words that had acoustic phonemes that coincided with the participants hearing loss frequency tend to be more difficult to recall even after correctly initially registering the words (Yeok Leng Lim and Loo, 2018). Proper assessment of the word retrieval of the hearing impaired participants with visually presented word stimuli, as in our cohort, would be able to explore this area in more detail.

The further assessment of the retrieval process of the target words among the hearing-impaired older adults would be another area that may account for this delayed recall issue among older adults with hearing impairment. We conducted the memory index score (MIS) as part of MoCA-HA to assess the information retrieving pathway of the participants (Julayanont et al., 2014). The clues provided in MIS can facilitate the retrieval process of the information for the participants when the information has already been encoded properly.

We found that among our normal cognition hearing impaired population, the adapted visual version of MIS mean score was 11.60 (SD=2.98). When compared with the standard MIS mean score of 12.2 (SD=2.8) of 2,205 normal cognition older adults (Kaur et al., 2018), the score was not significantly different (P=0.244), (95%CI -1.61,0.41). While it is difficult to interpret a non-significant result as indicating no difference between groups, this could suggest that there may not be a difference in the information retrieval pathway of the delayed recall task of MoCA among the hearing-impaired and normal-hearing older adults.

Previous MoCA research which attempted to assess the retrieval pathway indirectly was done before the development of the Memory Index Score (MIS) in MoCA version 8. Dupuis et al,(2015) addressed the hearing loss effect by only analysing the recalled words that were previously correctly registered words

repeated by the participants. They found that the chronological order of the presented target words played a major role in the recall, as there were more errors in recalling the first target word among hearing-impaired participants compared to controls. This difference gradually decreased to nearly none in the fifth target word. Therefore they concluded that hearing-impaired participants may have a problem in retrieving the information from their memory. However, this was not always the case since they were using verbal MoCA in the trial for the hearing-impaired population. Therefore, a higher cognitive load during encoding of distorted target words, even though previously correctly registered, can also interfere with the result.

This current study preliminarily examined the memory pathway of the hearing-impaired population with visually presented verbal targets. The impairment in memory of the hearing-impaired population if present could thus mainly lie on the encoding pathway of the brain rather than the retrieval pathway. However, the memory sub-category impairment in our cohort did not sustain the Bonferroni correction. Further research with more participants may be able to clarify this in more detail.

If this effect was to be found with a bigger cohort even with visually presented stimuli, it would indicate that degraded auditory input from hearing loss did not only cause perceptually degraded input for the brain to process with more cognitive resources but also caused long-term changes in the brain encoding pathway which would fall under the sensory deprivation theory (Wayne and Johnsrude, 2015). Several previous pieces of research have shown neuroanatomical changes in the brain of hearing loss participants both in the auditory area and other areas (Husain et al., 2011). The duration of hearing loss can also play a major role in the degree of metabolism change of the brain (Han et al., 2019). Future recruitment of participants with long-standing hearing loss (preferably untreated cases) may be useful for better understanding of the hearing loss long-term effect on brain plasticity.

4.4.3. Strengths and limitations

The data set of the original MoCA cohort

Even though this chapter initially demonstrated that the MoCA-HA overall score and sub-category scores were not significantly different to those of the original MoCA when implemented among the normal cognition older adults, this does not mean that the two tools are identical. The unequal and relatively smaller sample size of our cohort, which was not powered for the comparison analysis, may inherently bias results toward the null finding when there was a real effect. Without having access to the original dataset, adjusting for confounders could not be done, which could create more constraints for the small sample size.

Moreover, the original MoCA cohort study was completed in 2005 while our data were collected In 2019. After 15 years, the overall life span, health status and education years of the general population tend to improve, which may result in better overall cognition of the population over the years (Murphy et al., 2019). This should also be taken into account when comparing and interpreting the comparison between the original cohort and this current cohort, since the effect of hearing impairment may not be the only difference between the two cohorts. In addition, as discussed earlier, the original MoCA cohort study did not test for any sensory impairments including the hearing; therefore, we can assume, that cannot be sure that their participants did not have severe hearing impairments that precluded their communications with the test administrators.

Ideally, both the original MoCA and the MoCA-HA should be implemented to the same set of participants to establish their correlation along with comparing the level of correlation by the level of hearing loss. However, in order to establish significant findings, a large cohort of the hearing-impaired population with varying hearing level should be recruited. Our recently published systematic review, which pooled all available data from previous cohorts, indicated that the original MoCA scores was significantly worse among the hearing-impaired population compared to the norm. This lower score was potentially correlated to the degree and frequency of their hearing impairment (Utoomprurkporn et al., 2020b). Consequently, if we were to implement the original MoCA among the NC-HI cohort, their scores would be expected to be lower than from the MoCA-HA due to the mode of delivery disadvantage. Additionally, different aspects of the original MoCA might be expected to be differentially affected (e.g. visuoconstructive elements might be less affected than auditory memory) further complicating interpretation. Therefore, establishing the correlation between the original MoCA and the MoCA-HA, may not be as valid way to indicate criterion validity as establishing the correlation of MoCA-

HA with other validated visually-based cognitive tools as we would demonstrate in Chapter 6. Nevertheless, it should be acknowledged that using historical controls is a limitation of this study since cohorts recruited at different times may differ, as discussed chapter 4.4.3.

The potential weakness and strength of cognitive abilities of the hearing-impaired cohort

The potential weakness of the hearing-impaired cognitive performances in memory sub-category was elaborately analysed in this chapter as this area has always been a focus for the hearing impairment cohort. A visuospatial sub-category of MoCA-HA which could be a potential strength in this cohort as reported in previous research (Rudner et al., 2016a) could not be statistically compared with the original MoCA since we did not have enough variability in the sample data (SD cannot be calculated). This may be due to the brief nature of each sub-category of MoCA-HA which was originally designed for screening purposes, in combination with a small sample size of this current study which was not powered for this sub-analysis. However, even with a tendency to score higher than the normal-hearing cohort, our NC-HI data fail within the mean+/-SD range of the original cohort indicating no significant difference. Further analysis of more detailed visuospatial tasks may reveal this strength, if any. However, it has been demonstrated here that with brief screening tasks as presented in MoCA, no difference was found between the sub-categories.

4.5. Conclusion

The newly developed MoCA-HA was successfully implemented among older adults with hearing impairment (NC-HI) cohort. The overall score along with the sub-category scores of the MoCA-HA were comparable with the original MoCA scores. Further validation of the tool among the hearing impaired older adults with cognitive impairment (MCI-HI) in the next phase 3 of the study would add further understanding of the tool use and implementation in a real clinical setting.

5. Chapter 5: Characteristics and cognitive/auditory performance of MCI older adults with hearing loss population (MCI-HI): PHASE 3

The main aim of this phase 3 study was to explore the feasibility and acceptability of the newly developed cognitive screening tool MoCA-HA among older adults with a diagnosis of MCI and hearing impairment (MCI-HI) as illustrated in Figure 10.

An additional aim was to examine the performance of this cohort on the total score and each sub-category of the MoCA-HA (visuospatial/executive, naming, memory, attention, language, abstract and orientation) in comparison with data from normal cognition controls who also had hearing impairment (NC-HI), obtained in phase 2. This comparison is needed to establish the exact cognitive performance of these MCI-HI older adults on this screening tool when the hearing impairment has been accounted for.

A further aim was to compare the cognitive abilities in terms of neuropsychological performance along with the hearing abilities including hearing level, auditory processing ability and self-reported hearing difficulties of the MCI-HI versus the NC-HI group.

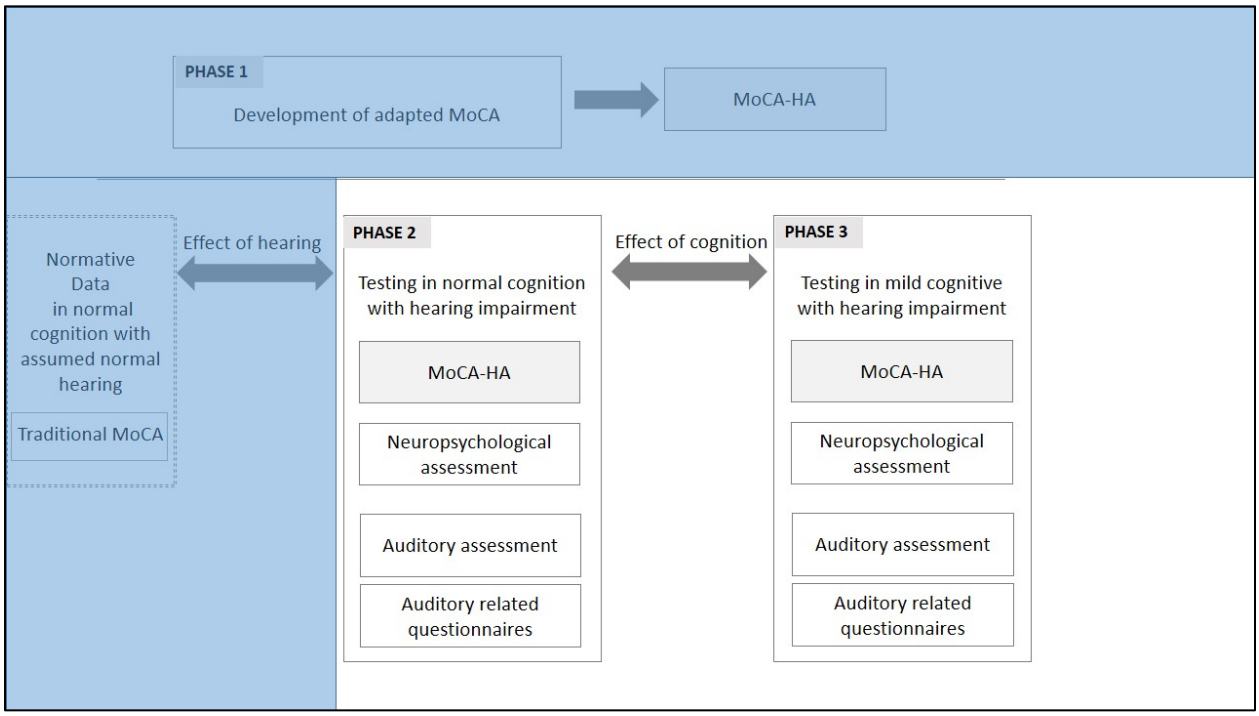

Figure 10 Working framework of Chapter 5 as part of the overall study

5.1. Introduction

The MCI-HI cohort who were the main interest of this study phase 3 had both cognitive and hearing impairments combined. Therefore, by recruiting this population, we could also study the interaction between these two impairments in an individual, which has only been speculated in previous studies.

The potential interactions could be reflected in the MoCA-HA and neuropsychological tasks as well as auditory assessment and auditory-related questionnaires which are described below.

5.1.1. MoCA-HA and neuropsychological tasks

In the traditional MoCA assessment, the MCI cohort did worse than normal cognition controls in all sub-categories except for the attention sub-category. The attention tasks in the traditional auditory MoCA was the only sub-category that showed no significant difference among mild cognitive impairment cohort and normal cognition controls, but the difference was significant when comparing to the dementia group. This indicates that the mild cognitive impairment cohort usually preserves their attention abilities until a later dementia stage (Nasreddine et al., 2005).

Attention is one of the first domains to be affected after the memory domain in the initial stages of Alzheimer's dementia (Perry and Hodges, 1999). This may explain why even in a very early phase of cognitive impairment some individuals may experience problems in participating in activities of daily living. According to the Sohlberg and Mateer Hierarchical Model which was widely accepted for clinical purposes, attention can be divided into 5 hierarchies which start from focused and sustained attention, selective and alternating attention to divided attention (Moore Sohlberg et al., 2000, Sohlberg and Mateer, 1989). Focused and sustained attention ability is mainly used to respond to the stimulus and maintain attention on that one focus task for a period of time. Selective attention involves focusing while ignoring the distraction stimuli when alternating attention allows for shifting the attention between various tasks. Divided attention is focusing on both stimuli or more at the same time.

Divided attention and some selective/alternating attention tasks (ie. disengagement, shifting attention and failure of inhibition of automatic responses) are impaired among early cognitive impairment cohort. However, sustained attention is usually spared in the early stages (Perry and Hodges, 1999).

All attention-related tasks in the traditional MoCA mainly rely on sustained attention where the participants are asked to listen to numbers and remember them, listen for the letter A or do mental 7 subtraction. Therefore, it is not unexpected that these task scores of MCI participants did not differ to those of the controls in the original MoCA cohort.

The attention problems of the hearing-impaired population have been extensively reported in the literature. Still, the majority of studies found difficulties mainly on auditory selective attention including hearing in background noise problems (Shinn-Cunningham and Best, 2008) or divided attention such as the dichotic listening paradigm (Gates et al., 2008). Auditory sustained attention may be difficult to study among the hearing-impaired population due to the listening difficulty confounder factor.

Therefore, it may be a more appropriate domain to study for the normal-hearing population with other underlying conditions (Faught et al., 2016, Gridley et al., 1986).

In MoCA-HA, to overcome this potential listening difficulty confounder, we instead used the visual delivered sustained attention tasks to assess the MCI-HA. This would be an ideal situation to explore the potential interaction effect of hearing impairment toward the MCI cohort's sustained attention abilities which would normally be preserved. Therefore, in addition to the attention sub-category score analysis, each tasks representing attention ability of the MoCA-HA was also explored in detail.

Not only the MoCA-HA, but also all neuropsychological tasks included in this study were validated visually presented tasks. As discussed earlier, this was purposely done to ensure accurate assessment of the hearing impairment cohort. Visual abilities were previously found to be affected by hearing deprivation in many different ways via the multisensory re-organization mechanism of the brain (Bavelier et al., 2006). However, the study of this effect among a MCI cohort has never been conducted before. In this phase 3, we may potentially be able to explore further the interaction of hearing and cognition reflected in the visual abilities of the MCI-HI cohort.

5.1.2. Auditory assessments and auditory-related questionnaires

Both the audiogram and the auditory processing test (dichotic digits test) were included to assess overall hearing abilities of the MCI-HI cohort. Since we targeted to recruit hearing aid users, the hearing level measures from audiograms of the MCI-HI and the NC-HI should be comparable along the line of moderate hearing loss which was when older adults, in general, started to seek for hearing aids (Zhu et al., 2020). However, due to their cognitive ability, the MCI-HI may have different characteristics when adopting hearing intervention which would be interesting to explore in this chapter.

Still, even with comparable hearing thresholds from the audiogram, the auditory processing test representing in dichotic digits test performance may differ for the older adults with cognitive impairment (Utoomprurkporn et al., 2020a). Cognitive impairment can impair the older adults hearing ability especially hearing in background noisy situations which may be reflected in their auditory processing test score (Hardy et al., 2016). In this chapter, the dichotic digits test score was analysed in more detail to explore the effect of mild cognitive impairment toward the MCI-HI performance.

Moreover, the self-reported hearing difficulties via the standard validated questionnaires of the MCI-HI cohort were also explored in this chapter. These questionnaires were used in various other settings to capture the hearing difficulties which could be from audiograms (Gatehouse and Noble, 2004) and

additional difficulties from auditory processing difficulties such as among the stroke cohort (Koohi et al., 2019, Bamiou et al., 2015). As our MCI-HI cohort would have both hearing difficulties, the questionnaires should be valuable tools to aid the clinicians when evaluating their hearing problems. However, the use of these questionnaires among MCI-HI has never been conducted before this cohort. Therefore, in this chapter, their questionnaires' performances would be compared with the NC-HI cohort to explore the effect of cognitive impairment toward the self-reported hearing difficulties.

5.2. Methods

5.2.1. Participants

The inclusion criteria were; diagnosed mild cognitive impairment, age ≥65 years, presence of documented hearing loss as evidenced by currently wearing of hearing aids and/or audiogram with a hearing average of ≥30dB HL and not on a cochlear implant waiting list.

The exclusion criteria were uncorrected visual impairment; cognitive and/or physical disability(s) which prevented the performance of the written/drawing elements of the tests and congenital/childhood-onset hearing loss (<18 years old age) as reported by participants.

5.2.2. Participants' recruitment pathway

Older adults with MCI and hearing loss were recruited from memory clinics at Camden and Islington NHS Foundation Trust, London, United Kingdom. Potential participants were identified in one of two ways. First, healthcare professionals who engaged with the potential cases (known hearing loss from the case files, currently wearing hearing aids or suspected hearing loss during the consultations) at the clinic would ask the patients whether they would like to participate in this research study. If they agreed to be contacted for research, they were asked what method of contact should be best i.e. phone number, email etc.

The second way of identifying the participants was from the NHS research register where patients who had been diagnosed by the memory clinic had given prior consent to be contacted for research. After the initial contact, the interested participants were asked whether, where and when it would be convenient for them to participate.

5.2.3. Materials

5.2.3.1. Auditory & neuropsychological assessment and questionnaires

After the initial contact, the participants would be asked for a convenient time slot to meet for the session. All the measures as listed in chapter 2: materials and methods were followed.

5.2.3.2. MoCA-HA

The visually presented computer-based Montreal Cognitive assessment tool (MoCA-HA) from phase 1 which was based on MoCA version 8.3, was used for testing in all 30 recruited MCI-HI participants.

5.2.4. Statistical analysis

The descriptive analysis of MCI-HI data in phase 3 was done. The data were compared with NC-HI data from phase 2. Statistical analysis with independent-samples t-test was done for the comparisons, having checked assumptions. When the assumptions were not fulfiled, the Man-Whitney-U test was used. The baseline characteristics of the two cohorts were analysed for potential confounders. The comparisons of the MoCA-HA scores were made.

Correction for multiple comparisons of the 7 sub-categories and the total MoCA-HA score was done by Bonferroni correction. The corrected alpha by Bonferroni was 0.05/8 sub-categories =0.006, therefore, a statistically significant difference level of the MoCA-HA and traditional MoCA was <0.006. Similar Bonferroni corrections were done for multiple comparisons in all other cognitive and auditory assessment tools.

Subgroup analysis with matched controls was done as a sensitivity analysis method to account for the differences in the baseline characteristics, if needed. Matched controls analysis was done by repeating the sensitivity analysis after eliminating each unmatched control case until the baseline characteristics of interest were matched.

The comparisons between the subgroup NC-HI cohort and MCI-HI cohort were analysed using non-parametric statistical analysis. Even though the t-test has been well regarded as robust against potential assumption violations (Rasch and Tiku, 1984), the parametric counterpart of Man-Whitney-U test was adopted in this chapter for the subgroup. The reasons were because the subgroup NC-HI cohort had less than 10 participants and unequal size to the MCI-HI cohort by more than 1.5 times which could potentially cause type I error in the analysis even when all assumptions were met (Rasch and Tiku, 1984, Adusah and Brooks, 2011).

5.3. Results

5.3.1. Baseline characteristics of the participants

A total of 30 MCI-HI participants age >/=65 were recruited into the study to complete the visually presented computer-based MoCA-HA. Their mean age was 83.8 years (SD= 6.42, range 74-100 years) with 50% (n=15) female participants. Mean total years of formal education of the participants was 13.27 years (SD= 4.17).

5.3.2. Comparison of baseline characteristics of the NC-HI and MCI-HI

A total of 60 older adults with hearing loss were included in the analysis, 30 NC-HI cases and 30 MCI-HI cases. The NC-HI group has a lower mean age by -8.53 years (95% confidence interval -11.72 to -5.35) with higher education years by 2.80 years (95% confidence interval 0.76 to 4.84 years) than the MCI-HI group as shown in Table 5.

Table 5 Comparison of the characteristic of the MCI-HI in phase 3 with the NC-HI cohort in phase 2 (NC-HI)

Baseline characteristics	**MCI-HI (Phase 3) (N=30)**	**NC-HI (Phase 2) (N=30)**	**Mean difference**	**95% Confidence Interval for the difference**	**P-value**
Age	83.80 (SD=6.42)	75.27 (SD=5.88)	-8.53	(-11.72, -5.35)	<0.001*
Education years	13.27 (SD=4.17)	16.07 (SD=3.69)	2.80	(0.76, 4.84)	0.008*
Better-ear pure-tone average (PTA)	47.75 (SD=14.90)	48.87 (SD=18.05)	1.12	(-7.44, 9.68)	0.793

*This was statistically significant at p<0.05

Due to the discrepancy of the age and the education years of controls and MCI-HI cohorts, the additional subgroup analysis was done to include only the age-matched and education matched controls. As a result, only 9 controls aged over 76 years old were included for the subgroup analysis which demonstrated no significant difference between the age and education years compared with the MCI-HI group (Table 6).

Table 6 Analysis of baseline characteristic in the subgroup of age-matched, education years-matched controls

Baseline characteristics	MCI-HI (Phase 3) (N=30)	NC-HI (Phase 2) (N=9)	Mann-Whitney U	Z score	P-value
Age	83.80 (SD=6.42)	82.11(SD=4.51)	118.50	-0.552	0.593
Education years	13.27(SD=4.17)	15.00(SD=3.16)	93.50	-1.390	0.170

5.3.3. MoCA performance and performance on each task/sub-category

5.3.3.1. Overall MoCA performance

5.3.3.1.1. Compared with all NC-HI cohort

Overall, the total MoCA-HA mean score of MCI-HI participants was 22.03 (SD=3.06). This was significantly different from the NC-HI participants' mean score of 27.27 (SD=2.16) with a mean difference of 5.23 (95%CI 3.86, 6.61). The histogram presenting the range of the total scores of the NC-HI and the MCI-HI group is demonstrated in Figure 11.

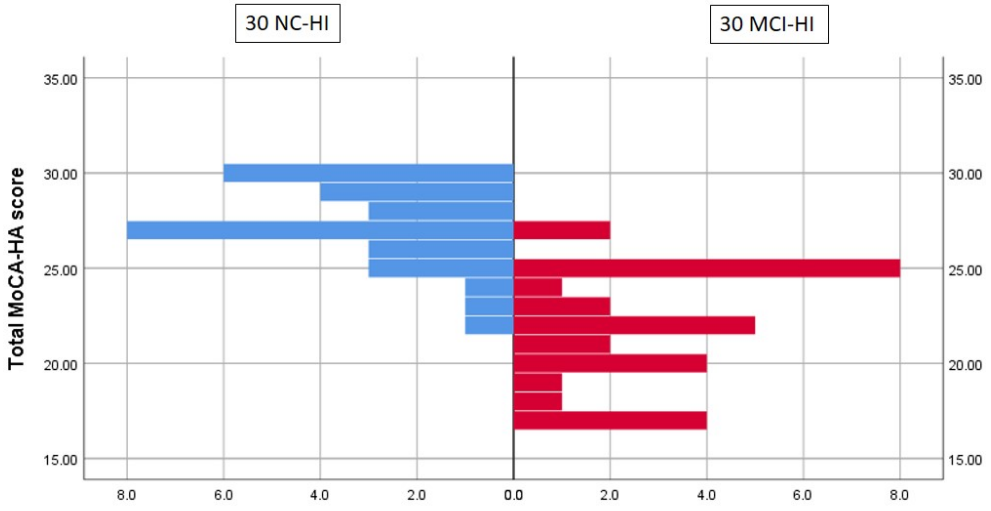

Figure 11 Histogram illustrates the distribution of total MoCA-HA scores for the NC-HI and MCI-HI cohort

5.3.3.1.2. Subgroup analysis with the age and education matched NC-HI

With subgroup analysis, the total MoCA-HA mean scores of the MCI-HI showed a statistically significant difference than the subgroup NC-HI controls (subgroup means 25.89 scores with SD=2.47) (U=43.50, z=-3.087, p=0.001). The range of MoCA-HA total scores for the subgroup NC-HI and MCI-HI cohorts were illustrated in Figure 12.

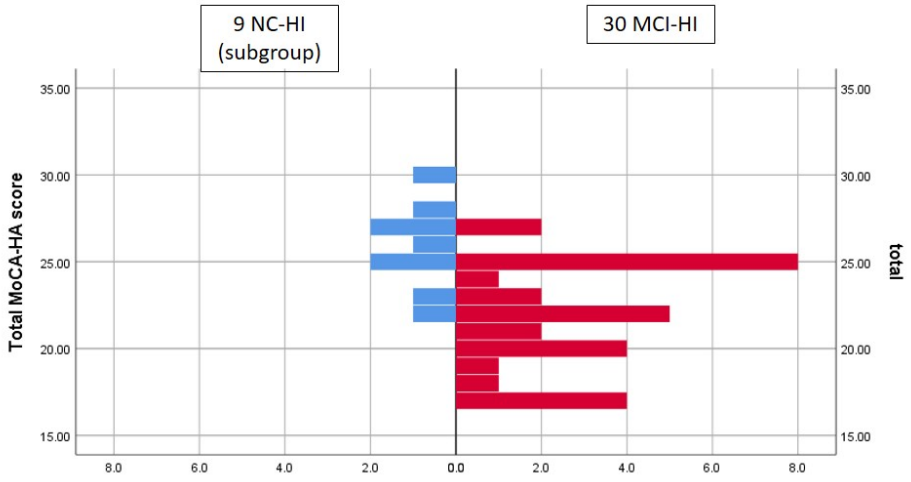

Figure *12* Histogram illustrates the distribution of total MoCA-HA scores for the age and education matched NC-HI and MCI-HI cohort

5.3.3.2. MoCA sub-categories performance analysis

5.3.3.2.1. Comparing with all NC-HI cohort

Significant differences with lower scores were found in all MoCA-HA sub-categories among the MCI-HI group compared with the NC-HI group except for sub-categories naming and abstract (*Table 7*).

Table 7 Performances on sub-categories of MoCA-HA for mild cognitive impairment hearing-impaired participants compared with normal cognition hearing-impaired participants

Sub-category of MoCA-HA	MCI-HI (Phase 3) (N=30)	NC-HI (Phase 2) (N=30)	Mean difference	95% Confidence Interval for	P-value

				the difference	
Visuospatial/executive	3.73 (SD=1.14)	5.00 (SD=0.00)	1.27	(0.84,1.69)	<0.0005*
Naming	2.93 (SD=0.25)	3.00 (SD=0.00)	0.07	(-0.03,0.16)	0.161
Memory	1.06 (SD=1.28)	2.97 (SD=1.69)	1.90	(1.12,2.68)	<0.0005*
Attention	4.97 (SD=1.22)	5.80 (SD=0.48)	0.83	(0.35,1.32)	0.001*
Language	1.57 (SD=1.07)	2.40 (SD=0.89)	0.83	(0.32,1.34)	0.002*
Abstract	1.93 (SD=0.25)	2.00 (SD=0.00)	0.07	(-0.03,0.16)	0.161
Orientation	5.37 (SD=0.93)	5.97 (SD=0.18)	0.60	(0.25,0.95)	0.002*
TOTAL	**22.03 (SD=3.06)**	**27.27 (SD=2.16)**	**5.23**	**(3.86,6.61)**	**<0.0005***

*These were still statistically significant after Bonferroni correction (Bonferroni threshold P-value < 0.006)

5.3.3.2.2. Subgroup analysis with the age and education matched NC-HI

With subgroup analysis, even though all MoCA-HA sub-categories tended to have lower mean scores among MCI-HI than NC-HI participants, only the executive sub-category along with the total MoCA-HA mean scores showed statistically significant difference than controls (p=0.002,p=0.001) as demonstrated inTable 8.

Table 8 Performances on sub-categories of MoCA-HA for mild cognitive impairment hearing-impaired participants compared with age-matched, education year-matched normal cognition hearing-impaired participants.

Sub-category of MoCA-HA	MCI-HI (Phase 3) (N=30)	NC-HI (Phase 2) (N=9) SUBGROUP	Mann-Whitney U	Z score	P-value
Visuospatial/executive	3.73 (SD=1.14)	5.00 (SD=0.00)	49.50	-3.093	0.002*
Naming	2.93 (SD=0.25)	3.00 (SD=0.00)	126.00	-0.785	1.000
Memory	1.07 (SD=1.28)	1.67 (SD=1.80)	113.00	-0.785	0.452
Attention	4.97 (SD=1.22)	5.67 (SD=0.71)	84.00	-1.839	0.070
Language	1.57 (SD=1.07)	2.33 (SD=1.00)	78.00	-1.974	0.049
Abstract	1.93 (SD=0.25)	2.00 (SD=0.00)	126.00	-0.785	1.000
Orientation	5.37 (SD=0.93)	5.89 (SD=0.33)	90.00	-1.775	0.107
TOTAL	**22.03 (SD=3.06)**	**25.89 (SD=2.47)**	**43.50**	**-3.087**	**0.001***

*These were still statistically significant after Bonferroni correction (Bonferroni threshold P-value <0.006)

5.3.3.3. *MoCA attention tasks*

5.3.3.3.1. Compared with all NC-HI cohort

There was no difference in the traditional MoCA attention sub-category (including digit span tasks, attention to letter task and serial 7s subtraction task) between the mild cognitive impairment and normal cognition controls. These tasks were also analyzed for MoCA-HA as illustrated in Table 9.

Table 9 Performances on sub-category attention tasks of MoCA-HA for mild cognitive impairment hearing-impaired (MCI-HI) participants compared with normal cognition hearing-impaired (MCI-HI) participants

Tasks in Sub-category attention of MoCA-HA (Full score)	**MCI-HI (Phase 3) N=30**	**NC-HI (Phase 2) N=30**	**Mean difference**	**95% Confidence Interval for the difference**	**P-value**
Digit spans (2) (forward-backwards)	1.40 (SD=0.81)	1.87 (SD=0.35)	0.47	(0.14,0.79)	0.006*
Attention to letters (1)	1.00 (SD=0.00)	1.00 (SD=0.00)	0	0	NA
Serial 7s subtraction (3)	2.57 (SD=0.73)	2.93 (SD=0.25)	0.37	(0.08,0.65)	0.013*

*These were still statistically significant after Bonferroni correction (Bonferroni threshold P-value < 0.017)

5.3.3.3.2. Subgroup analysis with the age and education matched NC-HI

The sensitivity analysis restricting the NC-HI group to age and education matched groups showed that the sub-category attention along with the attention-related tasks were not statistically significantly different from those of the MCI-HI group (p=0.070).

5.3.3.4. *MoCA verbal fluency task*

The verbal fluency test which is part of the language sub-category of MoCA-HA was also analysed separately since the test can be used as a stand-alone test to assess an individual's language ability and executive function (Mueller et al., 2015).

5.3.3.4.1. Compared with all NC-HI cohort

The mean score of verbal fluency task (part of language sub-category) for the MCI-HI was 15.50 (SD=6.03) which was significantly lower than the NC-HI mean of 18.93 (SD=6.66). The mean difference was 3.43 (95% CI 0.15, 6.72).

5.3.3.4.2. Subgroup analysis with the age and education matched NC-HI

With subgroup analysis, the verbal fluency mean score of the MCI-HI was not statistically significantly different than the subgroup NC-HI controls (subgroup mean= 14.33 scores with SD=6.36) (U=117.50, z=-0.585, p=0.570).

5.3.3.5. Memory index score (MIS)

5.3.3.5.1. Compared with all NC-HI cohort

The Memory Index Score (MIS) means were significantly different between the NC-HI (mean= 11.60, SD= 2.98) and MCI-HI groups (mean= 8.40, SD= 3.31) with a mean difference of 3.2 points (95% confidence interval 1.57 ,4.83) (p<0.001).

5.3.3.5.2. Subgroup analysis with the age and education matched NC-HI

The MIS means were also not significantly different after subgroup analysis of the age-matched, education years matched controls (NC-HI cohort subgroup mean =9.00 with SD=3.28)(U=123.50, z=-0.386, p=0.710)

5.3.4. Neuropsychological assessments

5.3.4.1. Corsi-block tapping

5.3.4.1.1. Compared with all NC-HI cohort

The MCI-HI cohort showed a trend towards lower mean scores for the forward digit span, the backward digit span and the total digit span of Corsi-block tapping when compared with the NC-HI cohort. However, the mean differences were not statistically significantly different as shown in Table 10.

Table 10 Corsi-block tapping scores for mild cognitive impairment hearing-impaired participants (MCI-HI) compared with normal cognition hearing-impaired participants (NC-HI).

	MCI-HI (Phase 3) (N=30)	**NC-HI (Phase 2) (N=30)**	**Mean difference**	**95% confidence interval of the difference**	**P value**
Forward digit span	7.97 (SD=1.75)	8.77 (SD=1.76)	0.80	(-0.11, 1.71)	0.082
Backward digit span	5.90 (SD=1.54)	6.57 (SD=2.08)	0.67	(-0.28, 1.61)	0.163

Total digit span	13.87 (SD=2.79)	15.33 (SD=3.24)	1.47	(-0.10, 3.03)	0.065

5.3.4.1.2. Subgroup analysis with the age and education matched NC-HI

The subgroup analysis with age and education matched controls yielded similar results of no significant differences between the two cohorts as shown in Table 11.

Table 11 Corsi-block tapping scores for mild cognitive impairment hearing-impaired participants (MCI-HI) compared with age-matched, education year-matched normal cognition hearing-impaired participants (NC-HI).

	MCI-HI (Phase 3) (N=30)	**NC-HI (Phase 2) (N=9) SUBGROUP**	**Mann-Whitney U**	**Z score**	**P-value**
Forward digit span	7.97 (SD=1.75)	8.11 (SD=1.36)	125.50	-0.323	0.760
Backward digit span	5.90 (SD=1.54)	6.00 (SD=2.24)	133.00	-0.069	0.954
Total digit span	13.87 (SD=2.79)	14.11 (SD=3.10)	119.50	-0.381	0.715

5.3.4.2. ROCFT and ROCFT recall

5.3.4.2.1. Compared with all NC-HI cohort

The MCI-HI cohort had the ROCFT copy, the ROCFT immediate recall and the ROCFT 30 minute recall mean scores statistically significantly lower than the NC-HI cohort as demonstrated in Table 12 ($p=0.005$, $p<0.001$,$p<0.001$). One participant in the MCI-HI cohort refused to complete the task due to physical movement restriction for drawing.

The mean scores were compared by independent t-test which is robust against potential assumption violations. ROCFT copy showed a slight ceiling effect for the NC-HI cohort which resulted in the skewed data, therefore, non-parametric statistic (Mann-Whitney U test) was also conducted for the mean comparison to ensure accuracy of the analysis. Similarly, the data showed significant difference scores between the two cohorts ($U=167.50$, $z=-4.275$, $p<0.0005$).

Table 12 ROCFT copy and recall mean scores for mild cognitive impairment hearing-impaired participants (MCI-HI) compared with normal cognition hearing-impaired participants (NC-HI).

	MCI-HI (Phase 3) N=29	**NC-HI (Phase 2) N=30**	**Mean difference**	**95% confidence interval**	**P value**

				of the difference	
ROCFT Copy	31.01 (SD=7.29)	35.33 (SD=1.32)	4.32	(1.51, 7.13)	0.004*
ROCFT immediate recall	12.22 (SD=5.90)	20.85 (SD=4.29)	8.63	(5.94, 11.31)	<0.0005*
ROCFT 30 minutes recall	11.91 (SD=5.78)	19.63 (SD=5.20)	7.72	(4.85, 10.58)	<0.0005*

*Statistically significant difference at p<0.05 and after Bonferroni correction (Bonferroni threshold P-value < 0.017)

5.3.4.2.2. Subgroup analysis with the age and education matched NC-HI

The subgroup analysis with age and education matched controls yielded similar results of statistically significant differences between the two cohorts as demonstrated in Table 13.

Table 13 ROCFT copy and recall mean scores for mild cognitive impairment hearing-impaired participants (MCI-HI) compared with age-matched, education year-match normal cognition hearing-impaired participants (NC-HI).

	MCI-HI (Phase 3) N=29	**NC-HI (Phase 2) N=9 SUBGROUP**	**Mann-Whitney U**	**Z score**	**P-value**
ROCFT Copy	31.01 (SD=7.29)	35.67 (SD=0.71)	39.500	-3.197	.001*
ROCFT immediate recall	12.22 (SD=5.90)	19.89 (SD=5.10)	44.500	-2.956	.002*
ROCFT 30 minutes recall	11.91 (SD=5.78)	18.94 (SD=5.24)	45.000	-2.938	.002*

*Statistically significant difference at p<0.05 and after Bonferroni correction (Bonferroni threshold P-value < 0.017)

5.3.4.3. Graded naming test

5.3.4.3.1. Compared with all NC-HI cohort

The MCI-HI cohort had a graded naming test mean score of 15.10 (SD=6.54) which was lower compared with the NC-HI cohort mean score of 23.13 (SD=2.56). The mean difference was 8.03 (95%CI 5.39, 10.67) which was statistically significantly different (p<0.001).

After prompting with standardized cues ie. pointing, perceptual or semantic reorientation to ensure that the participants can potentially give the correct response, the MCI-HI cohort had a mean score of 15.97 (SD=7.20) which was lower compared with the NC-HI cohort mean score of 25.07 (SD=2.68). The mean

difference was 9.10 (95%CI 6.21,11.99) which was statistically significantly different (p<0.001) as demonstrated in Table 14.

Table 14 Graded naming test mean scores for mild cognitive impairment hearing-impaired participants (MCI-HI) compared with normal cognition hearing-impaired participants (NC-HI).

	MCI-HI (Phase 3) N=30	**NC-HI (Phase 2) N=30**	**Mean difference**	**95% confidence interval of the difference**	**P value**
Graded naming test	15.37 (SD=6.58)	23.13 (SD=2.56)	7.78	(5.15, 10.38)	<0.0005*
Graded naming test with prompt	15.60 (SD=7.61)	25.07 (SD=2.68)	9.53	(6.55, 12.51)	<0.0005*

*Statistically significant difference at p<0.05

5.3.4.3.2. Subgroup analysis with the age and education matched NC-HI

The subgroup analysis with age and education matched controls yielded similar results of statistically significant differences between the two cohorts as demonstrated in Table 15.

Table 15 Graded naming test mean scores for mild cognitive impairment hearing-impaired participants (MCI-HI) compared with age-match, education year-matched normal cognition hearing-impaired participants (NC-HI).

	MCI-HI (Phase 3) N=30	**NC-HI (Phase 2) N=9 SUBGROUP**	**Mann-Whitney U**	**Z score**	**P-value**
Graded naming test	15.37 (SD=6.58)	22.67 (SD=2.24)	36.00	-3.317	.000*
Graded naming test with prompt	15.60 (SD=7.61)	24.11 (SD=2.42)	36.00	-3.312	.000*

*Statistically significant difference at p<0.05

5.3.5. Auditory assessment

5.3.5.1. Audiogram

The duration of their hearing loss ranged between 1-61 years (the participant with 61 years of hearing impairment had the impairment onset age over 20). In the MCI-HI cohort, pure-tone average of the 4 frequencies of the better hearing ear was 47.75dB (SD=14.90). When compared with the NC-HI controls means of 48.87 (SD=18.05), there was no significant difference between two cohorts with a mean difference of 1.12 dB HL (95% confidence interval-7.44,9.69).

5.3.5.2. Dichotic digits test

5.3.5.2.1. Directed-attention paradigm

For the MCI-HI cohort, the percentage of correct dichotic digit scores for the directed-attention and free-recall attention paradigm on both ears tended to be lower than the normal cognition NC-HI controls.

The directed-attention paradigm showed a slight ceiling effect especially for the NC-HI cohort which resulted in the skewed data, therefore, non-parametric statistic (Mann-Whitney U test) was conducted for the mean comparison to ensure accuracy of the analysis as demonstrated in Table 16. The descriptive data displayed the median and the inter-quatile range (IQR) for the cohorts. The right and left directed-attention dichotic digit scores were significantly lower for the MCI-HI cohort. However, there was no significant difference in the right- left ear difference scores between the two cohorts.

Table 16 The percentage correct of Dichotic digit scores in the directed-attention paradigm for mild cognitive impairment hearing-impaired participants (MCI-HI) compared with normal cognition hearing-impaired participants (NC-HI).

Dichotic digit test paradigm		**MCI-HI (Phase 3)**	**NC-HI (Phase 2)**	**Mann-Whitney U test**	**Z score**	**P value**
Directed-attention	Right	87.50 (IQR=28.75)	97.50 (IQR=8.75)	215.00	-3.236	0.001**
	Left	82.50 (IQR=48.75)	95.00 (IQR=23.75)	256.00	-2.418	0.015*
	Total	77.50 (IQR=36.88)	95.00 (IQR=15.63)	221.00	-2.959	0.003**
	Rt-Lt Ear difference	0.00 (IQR=32.50)	2.50 (IQR=13.75)	385.00	-0.336	0.742

*Statistically significant difference at p<0.05

** Statistically significant difference after Bonferroni correction (Bonferroni threshold P-value < 0.0125)

5.3.5.2.2. Free-recall paradigm

The percentage correct of Dichotic digit score in free-recall attention paradigm data were compared by the independent t-test. Only the left DDT free-recall attention paradigm was statistically significantly different than controls after the Bonferroni correction with a mean difference of 23.44 as demonstrated in Table 17.

The difference between the right and the left ear DDT free-recall attention paradigm, i.e. the" right ear advantage" in dichotic listening was also calculated.

The right free-recall DDT among the MCI-HI was significantly different than the left by 24.91 (95%CI 10.66, 39.17) (p=0.001). However, among the NC-HI cohort, there was no significant difference between the right and the left ear DDT free-recall attention mean scores with a mean difference of 4.70 (95%CI -3.63,13.03) (p=0.256).

The right ear advantage was significantly larger among the MCI-HI cohort than the NC-HI cohort by 20.21. This larger right ear advantage was mainly due to the lower left ear DDT score among MCI-HI participants.

Table 17 The percentage correct of Dichotic digit scores in the free-recall paradigm for mild cognitive impairment hearing-impaired participants (MCI-HI) compared with normal cognition hearing-impaired participants (NC-HI).

Dichotic digit test paradigm		**MCI-HI (Phase 3)**	**NC-HI (Phase 2)**	**Mean difference**	**95% confidence interval of the difference**	**P value**
Free-recall attention	Right	80.60 (SD=19.72)	83.65 (SD=20.00)	3.05	(-7.70, 13.80)	0.572
	Left	55.69 (SD=33.00)	79.13 (SD=21.26)	23.44	(8.55, 38.34)	0.003**
	Total	68.15 (SD=19.69)	80.65 (SD=18.08)	12.50	(2.12, 22.89)	0.019*
	Rt-Lt Ear difference	24.91 (SD=37.47)	4.70 (SD=20.19)	-20.21	(-36.42, -4.00)	0.016*

*Statistically significant difference at p<0.05

** Statistically significant difference after Bonferroni correction (Bonferroni threshold P-value < 0.0125)

5.3.6. Auditory related questionnaires

5.3.6.1. The Modified Amsterdam Inventory for Auditory Disability (mAIAD)

All 5 domains of the mAIAD were calculated as shown in Table 18 ranging from 0 (almost never/extreme difficulty) to 3 (almost always/no difficulty).The MCI-HI cohort tended to have slightly higher mean

scores in almost all domains including the total mAIAD score than the NC-HI controls. However, these differences were not statistically significant.

Table 18 mAIAD score for mild cognitive impairment hearing-impaired participants (MCI-HI) compared with normal cognition hearing-impaired participants (NC-HI).

mAIAD domain	mAIAD questions	MCI-HI (Phase 3)	NC-HI (Phase 2)	Mean difference	95% confidence interval of the difference	P value
Speech Intelligibility in noise	1, 7, 13, 18, 24	1.80 (SD=0.75	1.68 (SD=0.81)	-0.12	(-0.53, 0.28)	0.544
Speech Intelligibility in quiet	8, 11, 12 , 14, 19	2.17 (SD=0.64)	2.07 (SD=0.72)	-0.10	(-0.45, 0.25)	0.584
Auditory localization	3, 9, 15, 20, 26	2.03 (SD=0.73	1.89 (SD=0.93)	-0.14	(-0.57, 0.30)	0.527
Recognition of sound	4, 5, 6, 17, 22, 23, 25 and 28	2.40 (SD=0.51)	2.42 (SD=0.63)	0.02	(-0.27, 0.32)	0.874
Distinction of sound	2 , 10, 16, 21, 27	2.22 (SD=0.62)	2.18 (SD=0.56)	-0.04	(-0.35, 0.26)	0.787
Total	**1-28**	**2.16 (SD=0.53)**	**2.09 (SD=0.65)**	-0.06	(-0.37, 0.24)	0.676

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5.3.6.2. The Speech, Spatial and Qualities of Hearing Scale (SSQ)

None of the 30 MCI-HI participants could complete all items in the SSQ questionnaire. Therefore, a comparison of the scores between the two cohorts of MCI-HI and NC-HI was done using the overall average score. The average score was calculated by using the total score in all answered questions divided by the number of questions answered. Most situations listed in the questionnaire were not applicable to the participants.

Out of all 60 participants in the whole cohort of hearing aid users, only 28 participants could answer the SSQ sound quality question 15, which was “If you turn one hearing aid off, and do not adjust the other, does everything sound unnaturally quiet?”.

Only 37 out of 60 participants could answer the SSQ sound quality question 16, which was “When you are the driver in a car can you easily hear what someone is saying who is sitting alongside you?”. Only

47out of 60 participants could answer the SSQ sound quality question 2, which was “When you hear more than one sound at a time, do you have the impression that it seems like a single jumbled sound?”.

On average for the available data, the scores out of 10 (0= can not do at all to 10= can do perfectly) for each participant in the MCI-HI and NC-HI cohorts were presented in Table 19. No significant differences were found between the MCI-HI and NC-HI scores in any domain including the total SSQ.

Table 19 SSQ scores on average for each domain for MCI-HI and NC-HI cohort

SSQ domain	MCI-HI (Phase 3)	NC-HI (Phase 2)	Mean difference	95% confidence interval of the difference	P value
Speech domain	4.77 (SD=2.06)	4.73 (SD=2.12)	-0.03	(-1.11, 1.05)	0.950
Spatial domain	5.59 (SD=2.48)	5.27 (SD=2.35)	-0.32	(-1.57,0.93)	0.614
Sound quality domain	6.95 (SD=1.68)	6.87 (SD=1.73)	-0.27	(-1.15, 0.61)	0.547
Total	**5.81 (SD=1.87)**	**5.64 (SD=1.78)**	**-0.02**	**(-1.11,0.78)**	**0.723**

For comparison, when evaluating only the overall average answers, the older adults without hearing impairment normative data had an average score of 7.7 (SD=1.2) out of 10 (Banh et al., 2012), whereas older adults with hearing loss mean age 71 years (SD=8.1) in the original SSQ cohort (n=153) had an average SSQ score of 5.5 (SD=1.9) (Gatehouse and Noble, 2004). Both of our cohorts had similar hearing levels to the normative data cohort. For the NC-HI cohort, the score difference to the norms was no significant difference, while the MCI-HI scored slightly more indicating less perceived hearing difficulties but this was also not statistically significant (Table 20).

Table 20 SSQ scores of MCI-HI and NC-HI cohort compared with normative data (Gatehouse and Noble, 2004).

	Normative for older adults	Mild cognitive impairment With Hearing impairment (Phase 3)	Normal cognition With Hearing impairment (Phase 2)

The average score overall SSQ items (SD)	5.5 (SD=1.9)	5.81 (SD=1.87)	5.64 (SD=1.78)
The difference from the norms (95% confidence interval)		-0.31 (-1.05, 0.43)	-0.14 (-0.88, 0.60)
P value of the difference		P=0.414	P=0.710

5.4. Discussion

5.4.1. Baseline characteristic and subgroup analysis

Overall, we found that the hearing level of the MCI-HI and NC-HI were similar which allowed a comparison of their cognitive ability controlling for hearing level. However, the MCI-HI cohort tended to be older with fewer education years than the NC-HI cohort. Therefore, the need for the subgroup analysis of age-matched, education years-matched arose.

We opted to recruit participants aged 65 or older, as this is cut-point onset age for most dementia cases, with the term young-onset dementia used when dementia occurs at an age younger than 65 (Kuruppu and Matthews, 2013).

Most papers for older adults with and without mild cognitive impairment had a mean recruitment age around 75 years old (Nasreddine et al., 2005, Julayanont et al., 2014), similar to our normal cognition hearing aid users cohort. However, our mild cognitive impairment hearing loss cohort had a higher mean age of 83.8 years than the controls as demonstrated in Figure 13.

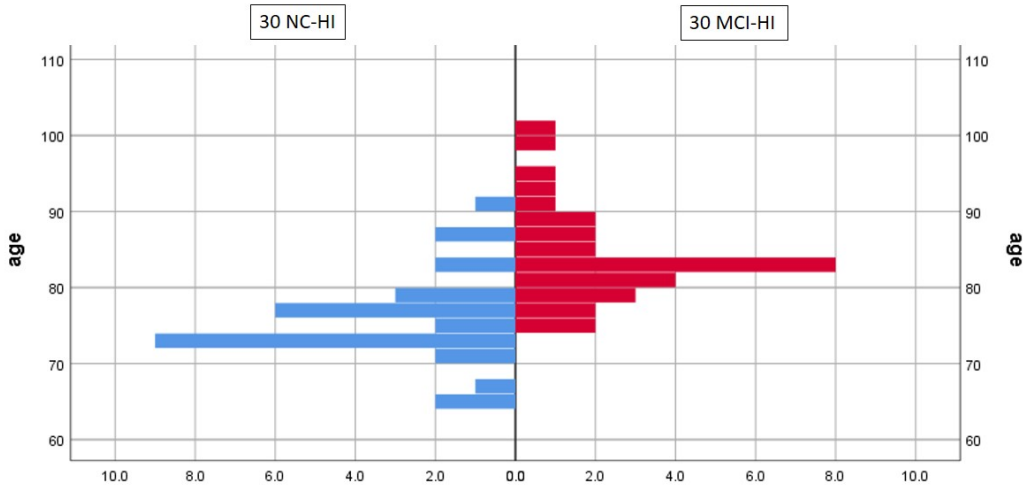


Figure 13 Histogram comparing the age of control and MCI participants

Intuitively, one might argue that it was expected that the MCI cohort would have a higher mean age than a normal cognition group. However, that was not the case when compared to previously published papers of MCI as mentioned earlier. This over 8 years of difference between the two groups may be due to the fact that we only targeted MCI individuals who wore hearing aids. Previous research showed that despite an unusually high prevalence of hearing loss among patients in a memory clinic, the participants who had poorer cognition were more likely to have their hearing problem under detected (Gold et al., 1996). This may delay the patients in seeking medical intervention such as hearing testing and hearing aid fitting.

In our cohort of hearing aid users, the participants with MCI and with hearing aids tended to be older than their peer normal cognition group. This finding may indicate that cognitive screening is needed among hearing-impaired older adults but in addition that hearing screening may also need to be implemented for patients with mild cognitive impairment. This is particularly important since these patients under-report their hearing problems (Gold et al., 1996). The Lancet commission on dementia suggested that hearing loss may be the highest modifiable risk factor for developing dementia (Livingston et al., 2017). Therefore, this early hearing screening and timely intervention may be beneficial in preventing the progression to dementia in this MCI population. Further research is needed to understand more about the effect of hearing intervention toward cognition.

5.4.2. Overall MoCA-HA cognitive measurement

Overall, we found significantly lower MoCA-HA total score and mean scores of all sub-categories, with the exception of naming and abstraction sub-categories, in the MCI-HI compared to the NC-HI cohort. The reasons that no differences were found in these two sub-categories may be due to the low sample size, since we found only 2 cases with abnormal scores in naming and only one case with an abnormal score abstract in our cohort.

When we repeated the analysis only for the age and education-matched cohort, the sub-category executive was still significantly lower for MCI-HI than NC-HI participants. This is consistent with the original MoCA study where executive tasks were found to distinguish well between the normal cognition cohort and the mild cognitive impairment cohort (Nasreddine et al., 2005).

5.4.2.1. Attentional problems among MCI-HI participants

We found that MCI hearing-impaired participants in this cohort scored less well than controls in the sustained attention-related tasks presented on the MoCA-HA. This effect was not found in the traditional MoCA among MCI participants with unreported hearing status (Nasreddine et al., 2005). The effect can be due to the administration mode of the MoCA (visual vs auditory) or the difference in the cognitive characteristic of MCI participants with and without hearing impairment. However, it is not clear why the serial 7s subtraction task performance should differ whether instructions are auditorily or visually delivered. Our findings of poorer performance in MCIs with hearing impairment may indicate that they have sustained attention problems whereas MCIs, in general, do not have these.

In MoCA-HA, all the tasks are visually based therefore visual attention is required for adequate performance. Visual attention among the hearing-impaired population was previously found to differ from their normal-hearing peers (Sladen et al., 2005). The participants needed to respond to a visual stimulus appearing on the screen and make a decision when comparing with the reference fixed target. This task mainly used sustained attention and selective attention abilities. The hearing-impaired cohort was found to be more cautious in responding to the visual target (slower reaction times with fewer errors) and better in detecting a signal at wider angles than their normal-hearing peers. The study was conducted in congenitally deaf participants who may not always exhibit the same cognitive characteristic as age-related hearing loss older adults who develop hearing loss later in life. However,

our research may suggest a potential issue of visual attention among MCI with age-related hearing loss cohort.

These differences in attention-related tasks were in the same direction but became not statistically significant when the analysis was repeated for the age and education years matched controls. However, this may be due to the insufficient sample size since only 9 controls were included in the analysis. Even after the modification in the MoCA-HA, all tasks are still measuring sustained attention where the participants are asked to focus their attention on the screen and look for the appearing numbers or letters, which are a similar attention aspect as the traditional MoCA. Further research with a larger cohort may be needed to establish the visual sustained attention abilities among the MCI hearing impairment cohort.

5.4.2.2. Verbal fluency task among MCI-HI participants

MoCA-HA uses a verbal phonemic fluency test that is unaffected by age decline (Elgamal et al., 2011) that asks the participant to list words beginning with a certain letter in 1 minute.

The MCI-HI had significantly lower verbal phonemic fluency score than the NC-HI, as expected in view of their cognitive impairment (Mueller et al., 2015), although no significant difference was found when compared with control samples of age and education years matched. However, this may due to the limited sample size (only 9 controls were included). Further research with a larger cohort may be needed among the MCI hearing impairment cohort to explore the verbal fluency ability. In addition, for comparison, the score of NC-HI was compared with the published normative data mean score of 19.08 (SD=6.59)(Wysokiński et al., 2010), which showed no significant difference (p=0.922). This is a particularly interesting finding for hearing-impaired older adults since it might suggest that despite communication difficulties, hearing impairment does not affect their ability and speed to retrieve words from their mental lexicon (Shao et al., 2014).

5.4.2.3. Memory index score

As expected, the memory index scores of the MoCA-HA among the MCI-HI were lower than the NC-HI, which reflected their impaired information retrieval pathways from mild cognitive impairment. Previously published data found that the memory index score section alone could distinguish the MCI cohort from normal cognition controls (Kaur et al., 2018). However, the implementation of the whole MoCA test was found to be better in capturing MCI cases than the index score alone (Goldstein et al., 2018).

The memory index score lower than 7/15 points was proposed to increase the risk of converting to dementia among MCI older adults, with the mean score for MCI non-converter to dementia = 8.45 (SD=0.44) and MCI converter to dementia mean score = 6.72 (SD=0.28) (Julayanont et al., 2014).

Our MCI-HI cohort had the memory index score of 8.40 (SD= 3.31) which was comparable with the published mean of the MCI older adults in general (mean=7.25, SD=0.87) (p=0.068) and the MCI non-converter to dementia (p= 0.935). However, the scores of our MCI-HI cohort were significantly better than the MCI converter to dementia cohort with a mean difference of 1.68 (95% confidence interval = 0.49, 2.87) (p=0.009). This effect should be explored further in larger cohorts of MCI hearing aid users since the potential effect of hearing intervention as protective factors for dementia were also previously proposed (Utoomprurkporn et al., 2020b).

5.4.3. Neuropsychological assessment

5.4.3.1. Corsi-block tapping

Even though the MCI-HI tended to score lower than controls in the Corsi-block tapping of digit forward/digit backward and total tasks, these differences were not statistically significantly different. Still, the MoCA-HA attention tasks which also test similar domains demonstrated differences between the two groups.

We opted to use purely visually delivered stimuli to avoid the effect of hearing impairment when assessing the MCI-HI. The Corsi-block tapping test is widely used as a visual analogue of the digits span test, which is partly represented in MoCA-HA. However, we found no significant difference of the Corsi block tapping-digit span which should be presented since the MoCA-HA digit span was significantly different.

A possible alternative explanation may rely on the preserved visuospatial ability among the MCI population. Visuospatial ability is usually maintained in an early stage of cognitive impairment when the memory and attention were already impaired (Perry and Hodges, 1999). Several MCI-HI participants in our cohort reported that they found it was much easier to perform the tasks when they opted to remember the visuospatial pattern of the tapped block instead of remembering the numbers as told. In the MCI cohort, while the memory has already been impaired, visuospatial ability can still potentially be preserved (Iachini et al., 2009, Martins-Rodrigues et al., 2019), therefore, there is a possibility that the visuospatial ability may facilitate their ability to perform the task.

The visuospatial ability of the hearing-impaired population was studied extensively since this population was believed to have a better visuospatial ability as a compensatory mechanism for their hearing loss. This is true for a profoundly deaf population who may rely on sign language and lip-reading for which visual vigilance is needed (Rudner et al., 2016a). The Corsi-block tapping span score was found to be better in the hearing-impaired signers (Wilson et al., 1997), while the ones who were not exposed to sign language performed similarly to their peers (Parasnis et al., 1996). However, for the hearing impaired population in general, there is still some controversy. Their visuospatial memory was found to be worse than their normal-hearing peers (Rönnberg et al., 2014a, Rudner et al., 2016a), which may be a result of hearing impairment towards the global memory of older adults. More than half of our NC-HI reported that since they struggled in communication within background noise, therefore, in addition to a hearing aid, they also attended lip-reading classes locally or attended the classes offered at our recruited hospital. This may potentially positively affect their visuospatial ability as found in the profoundly deaf population. Previous research in children has shown that even for a normal-hearing cohort learning sign language for at least 1 year could also improve Corsi-block tapping performance comparing with their peers (Capirci et al., 1998).

Since both of our cohorts of NC-HI and MCI-HI had a similar hearing impairment level, the comparison of their visuospatial memories' scores could only explore the effect of their difference cognition but may not the effect of hearing impairment. Therefore, the normative data for normal cognition older adults with no known hearing impairment are shown here for comparison. The digits span normative data for older adults age 70-79 is 9.19 (Standard error=0.15) for digits-forward and 5.71 (Standard error=0.14) for digits-backward when there are verbal responses (Wilde et al., 2004), whereas the normal cognition with hearing impairment in our cohort scored slightly worse than that for the digits-forward 8.77 (Standard error=0.32) but slightly better for the digits-backward 6.57 (Standard error=0.38) when responding on the Corsi-block. The better score in digit-backward may be due to the added benefit of a visuospatial clue which was found to be more prominent in the digit-backward task (Wilde et al., 2004).

Although we found the tendency that the MCI-HI did worse than the NC-HI cohort in the Corsi-block tapping digit span task, we were underpowered to explore this effect in more detail since it may have a relatively small effect given what we know about the impact of mild cognitive impairment toward their visuospatial abilities (Perrochon et al., 2014). Further research with a larger cohort may be needed to demonstrate these characteristics of a mild cognitive impairment with hearing impairment cohort.

5.4.3.2. ROCFT copy and ROCFT recall

The ability to copy the complex pattern such as the ROCFT reflected the participants executive functions especially planning and organizing (Shin et al., 2003, Shorr et al., 1992) and visuospatial skills. The executive function of the MCI-HI was significantly lower than the NC-HI as demonstrated in the MoCA-HA executive sub-category. Their ROCFT copy scores also showed similar patterns.

Although memory impairment is the first function affected in the most MCI diagnosis, their executive functions are also commonly impaired (Traykov et al., 2007). Still, the impairment in executive function usually is mild since, by definition of MCI, their activities of daily life should not be affected by the impairment (Petersen, 2004). Therefore, as expected, we found a relatively smaller mean difference score in the ROCFT copy task than with ROCFT recall tasks, which reflect the memory domain among MCI-HI. The ROCFT recall tasks were significantly worse among MCI-HI compared with the NC-HI group in both immediate recall and delay recall tasks.

These differences may have been present due to the better performance of NC-HI than normal when performing these tasks. When compared with their age-matched normative data without hearing loss (Chiulli et al., 1995), the NC-HI performed significantly better in ROCFT copy ($p<0.001$), immediate recall ($p<0.001$) and delay recall ($p=0.001$), while the MCI-HI performed similarly to the norms ($p=0.426$, $p=0.611$, $p=0.697$ respectively) as demonstrated in Table 21. It is noted that the normative data study was conducted in 1995, therefore the general health and education levels of our participants may not be similar with those from the study.

Table 21 ROCFT scores comparison with normative data

	Mild cognitive impairment With Hearing impairment (Phase 3)	**Normative for older adults age 80-91 years**	**Normal cognition With Hearing impairment (Phase 2)**	**Normative for older adults age 70-79 years**
ROCFT Copy	31.01 (SD=7.42)	29.8 (SD=4.6)	35.33 (SD=1.32).	31.7 (SD=3.6)
ROCFT immediate recall	12.16 (SD=5.99)	12.9 (SD=6.4)	20.85 (SD=4.29)	15.5 (SD=6.6)

ROCFT 30 minutes recall	11.86 (SD=5.87)	12.4 (SD=6.0)	19.63 (SD=5.20)	15.4 (SD=6.4)

Previous research showed that the MCI population performed worse than their normal cognition controls in ROCFT copy, immediate and delay recall tasks (Kasai et al., 2006). For the MCI-HI in our cohort, the differences were significant only when compared with the normal cognition and hearing impairment population but not when compared with the normal cognition population in general. This possibly implies that hearing impairment contributes to better performance in ROCFT among older adult hearing aid users which gradually declines to be comparable with their normal-hearing peers when MCI occurred. As discussed earlier, the improvement of visuospatial ability among our NC-HI cohort may be a result of lip-reading ability of these individuals. Previous data in the deaf signer cohort also found slightly non-statistically better ROCFT recall score than their normal-hearing peers. Therefore, interpretation of ROCFT along with other visuospatial tasks should be done carefully in the hearing impairment population since normal scores do not always mean no cognitive impairment was presented.

5.4.3.3. Graded naming test

We found significantly different graded naming test scores among the MCI-HI and the NC-HI which indicate difficulties in word retrieval for the MCI-HI cohort (Warrington, 1997). Moreover, the MCI-HI cohort did not gain improvement of the graded naming test score after the recommended prompt which emphasised the word retrieval problem among this population. This was in agreement with the lower memory index score of MoCA-HA among MCI-HI which also reflected a significant word retrieval issue compared with NC-HI. Information encoding and retrieval pathways (used in the naming tasks) among the MCI population were widely studied in many aspects since a memory problem is the main hallmark of MCI. Recent neuroimaging studies confirmed the problem in the word retrieval pathway among the MCI population compared with controls (Wang et al., 2016, Weigard et al., 2020).

Interestingly, the mean graded naming test score of NC-HI was in the 90 percentile of the United Kingdom normative data (Warrington, 1997). This again, as discussed in Chapter 4.4.2 regarding the MIS score of NC-HI, demonstrated that hearing impairment per se did not cause word retrieval difficulty. The problem found among the MCI-HI cohort where the graded naming test mean score was in the 10 percentile range should be a result of their cognitive impairment, not the hearing impairment.

5.4.4. Auditory assessment

5.4.4.1. Audiogram

The better ear pure-tone averages of the MCI-HI and the NC-HI were approximately 50 dB HL i.e. a moderate hearing loss (British Society of Audiology, 2018). This was expected since we aimed to recruit hearing aid users. Most older adults who seek medical advice and intervention usually have moderate hearing loss (Zhu et al., 2020) even though previous research studies showed that even milder hearing loss would also benefit from hearing intervention with a hearing aid (Ferguson et al., 2017).

Both the normal cognition and mild cognitive impairment cohorts had similar hearing levels. This makes further comparisons of the two cohorts in the auditory processing dichotic test and the auditory-related questionnaires more straight-forward.

5.4.4.2. Dichotic digits score

The reason dichotic digits test was chosen for this cohort was because it is not only simple and reliable to use among MCI (Strouse and Hall, 2009) but it can also be a good screening test for the auditory processing pathway as a whole (Musiek et al., 1991). Auditory processing tests especially the dichotic digits test were found to explain up to 20% variance in MoCA cognitive performance score (Gosselin et al., 2019). We found that among MCI-HI participants with a lower MoCA-HA cognitive performance score, their dichotic digit score was also lower. The left DDT free-recall score was significantly lower for the MCI-HI cohort compared with controls which also contribute to the larger DDT ear difference among this group.

The larger DDT ear difference among the cognitive impairment cohort was previously demonstrated in our recent meta-analysis (Utoomprurkporn et al., 2020a). The dementia population had an ear difference of 24.38 while there was no significant ear difference among normal cognition controls. The result was similar to this current cohort where we found an ear difference of 24.91 among MCI participants.

Previous research suggested that a low total DDT score can be a predictor for future dementia (Gates et al., 2011). The dichotic auditory testing paradigm has gained a lot of attention in recent years since it was believed to probe into the divided attention problem which can be found early in cognitive impairment patients (Perry and Hodges, 1999). We also found that among MCI-HI participants, the total DDT score was lower than normal cognition controls. In detail, the reason for the lower DDT total score was mainly from a lower left ear DDT score among the MCI-HI cohort. Our MCI-HI participants can

perform the DDT without difficulty since the instructions were simple and straight forward. Moreover, the fact that they can report the digits presented to the right ear showed that their cognitive ability was not a barrier for executing DDT tasks and also that divided attention deficit cannot solely explain the lower DDT performance. Therefore, this selective lower performance on the left ear suggested that abnormal auditory processing was present among this MCI population.

Abnormal processing of speech stimuli from the left ear which resulted in a lower left ear DDT free-recall score may be a result of corpus callosum changes. Corpus callosum plays a role mainly in processing speech from the left ear. When the speech is presented to the right ear, it can be transmitted directly via a cross pathway to be processed in the primary auditory cortex on the left hemisphere. However, when the speech is coming from the left ear, it is first transmitted to the right hemisphere, and then via the corpus callosum to be processed in the left. A neuroimaging study found that corpus callosum white matter changes and/or atrophy were associated with early neurodegenerative changes in dementia (Hampel et al., 1998).

5.4.5. Auditory related questionnaires

The two questionnaires are commonly used tools for accessing hearing difficulty among hearing aid users and also the auditory processing difficulty cohort (Bamiou et al., 2015). We have already established via an auditory processing assessment test that the MCI-HI cohort had worse Dichotic digits scores than controls but the self-reported questionnaires seem to fail in capturing this, unlike in previously published research among non-MCI cohort (Bamiou et al., 2015).

We found several problems when implementing the questionnaires among our older adult cohort which mainly involved the validity of the answers. These two questionnaires are very commonly used in hearing aid clinics. However, the implementation and interpretation of these questionnaires among individuals with suspected cognitive impairment should be done carefully, since they may not always accurately report their hearing difficulties.

5.4.5.1. The modified Amsterdam inventory for auditory disability (mAIAD)

For the MCI-HI cohort, only 19/30 participants completed all the 28 questions of the questionnaire while 26/30 participants of the NC-HI cohort completed all the questions. The question that participants refused to answer the most was question 4 which was “Can you hear cars passing by?”. One participant from the NC-HI control refused to answer this question compared with 4 participants from MCI-HI. The

question may seem relatively simple for most people. However, for MCI participants, it involved several cognitive components. From the interview, while completing the questionnaires, MCI-HI participants tried to remember the last time they were outside of their houses when they could hear the cars. Several of them could not remember the last time they were out. A few of them said they did not go out any more for safety reasons such as they could not remember the way or they got confused with the traffic sounds. Most of them speculated the answer on the principle that if they were outside, they think they would hear the car passing by which may not always be accurate.

The significant discrepancies between the cognitive impairment patients' reported hearing disabilities versus their actual abilities reflected in objective testing and report by their carers have been demonstrated in previous research (Gold et al., 1996). The study was conducted in a memory clinic among a probable Alzheimer's dementia cohort where they found a significantly higher prevalence of hearing impairment than in a general older adult population. However, there was much less reported hearing disability reflected in the hearing handicap questionnaire among the patients. The finding was somewhat similar to our cohort where even though not significantly different the MCI-HI tended to report fewer difficulties in all domains.

Gold et al. (1996) also asked the patients' carers for their input about the patients' hearing handicap in order to distinguish whether the patients did not have the problem or simply did not report the problem due to their cognitive impairment. As expected, there was a significant discrepancy between the carers' reports and the patients' reports, that was attributed to the patients not providing an accurate report of their disabilities (Gold et al., 1996). This emphasizes the importance of hearing screening or modified questionnaires for carers and relatives in the memory clinic because we cannot solely rely on the self-reported hearing problems of these patients.

5.4.5.2. The speech, spatial and qualities of hearing scale (SSQ)

In SSQ, the questions involve more complex components and hypothetical situations than the mAIAD. Most questions require two or three steps of abstract imagination and memory of the situations such as "(1)If you turn one hearing aid off, (2)and do not adjust the other, (3) does everything sound unnaturally quiet?" or "(1)When you are the driver in a car (2)can you easily hear what someone is saying (3)who is sitting alongside you?". Our normal cognition hearing-impaired older adults were able to complete the questionnaires, as demonstrated in previous studies (Zhang et al., 2015). However, the MCI-HI group left several questions without an answer. This may be because mild cognitive impairment older adults may find it difficult to think about abstract and hypothetical situations (Sudo et al., 2010).

Not only is the memory problem the hallmark of MCI (Petersen et al., 1999), Sudo et al. (2010) also found that the abstract thinking impairment was the only parameter found to discriminate between MCI and controls (Sudo et al., 2010). Although unlike the memory sub-category, we did not find a significant difference in the abstract sub-category of MoCA-HA among these two cohorts which may be due to small sample size. Still, this subtle difference may be the reason for the inability to complete the SSQ questionnaires among MCI.

When compared with the normative data, the MCI-HI also tended to report fewer hearing difficulties even with similar pure-tone average hearing thresholds and additional auditory processing difficulties. Again, this may make the reliability of the hearing questionnaires for MCI-HI cohort questionable in that they tended to underestimate their hearing problems (Gold et al., 1996). It also indicates the importance of specially designed hearing questionnaires for the MCI population which take into account the cognitive ability of the individual. This is to ensure an accurate and practical interpretation of the hearing problems among these MCI hearing aid wearers.

5.4.6. Strengths and limitations

The current study was the first study of its kind to explore the interaction of hearing and cognition in the cohort with both mild cognitive impairment and hearing impairment. Therefore, the effect of the interaction which has only been speculated in previous research could be directly explored in a real participant cohort. However, recruitment and testing among this cohort had also posed some challenges. Even though we carefully selected the cognitive and hearing assessment tools taking into account their difficulties, some of the tools such as the self-reported hearing questionnaires could not be fulfilled. However, this also revealed that maybe alternative questionnaires tailored for this population are needed.

The biggest limitation of the comparison made in this chapter was the small number of age and education-matched controls. The analyses which were significantly different among the MCI-HI and NC-HI, did not show significant differences in the subgroup analysis of the matched controls which may be due to the issue of statistical power. A larger cohort of age and education-matched controls may be able to reveal significant differences in these analyses.

5.5. Conclusion

The newly developed MoCA-HA was successfully implemented among older adults with mild cognitive impairment and hearing impairment (MCI-HI) cohort. The overall score along with the sub-category scores of the MoCA-HA were analysed compared with the performance of the NC-HI. The comparison of the MCI-HI and NC-HI performances in the cognitive assessment tools revealed the unique characteristic of hearing and cognitive impairment interaction in their information retrieval pathways, executive functions and visuospatial abilities. While, the auditory assessment tools revealed their auditory processing difficulties independent of their audiograms, these may not always be captured by the standard self-reported hearing questionnaires unlike in other cohorts.

6. Chapter 6: Validation of a cognitive screening tool to identify hearing loss in older adults with cognitive impairment

This chapter aims to use all the available combined data from phase 2 and phase 3. The primary aim is to identify the appropriate cut-off score for the MoCA-HA that could screen and distinguish MCI-HI from the NC-HI cohort. An additional aim is to assess the correlation of the MoCA-HA with other neuropsychological assessment tools along with the audiogram (auditory assessment). As a result, the quality of our newly developed cognitive assessment tool (MoCA-HA) would be established based on all the available data.

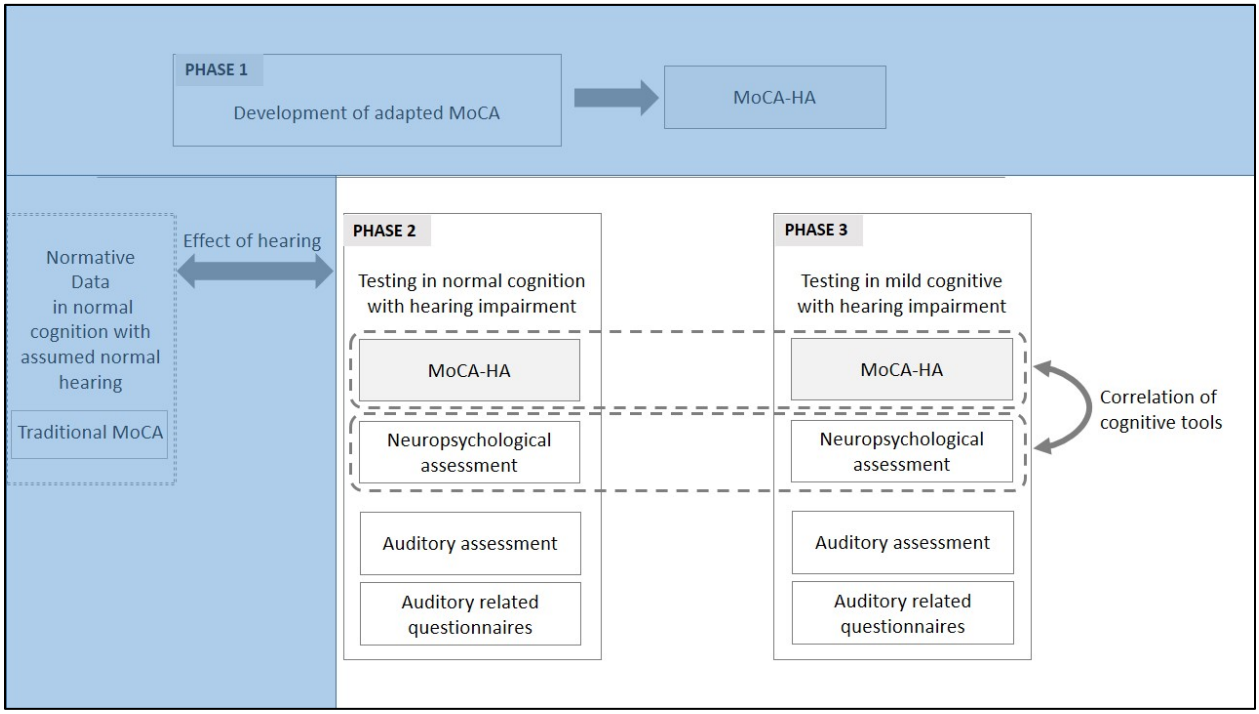


Figure 14 Working framework of Chapter 6 as part of the overall study

6.1. Introduction

6.1.1. Principle for early detection of conditions

A screening test attempts to separate individuals who may have the disease from others who may not. The test is intended to be used among a cohort where the condition might be suspected to identify the affected person early (Wilson et al., 1968).

The World Health Organization (WHO) recommends 10 key points to evaluate whether the intended condition is suitable for screening (Wilson et al., 1968). These are discussed in the context of cognitive screening of older adults with hearing loss.

6.1.1.1. The condition sought should be an important health problem.

Mild cognitive impairment is considered to be an important health problem since it can have numerous consequences for the individual and the community. On the individual level, MCI can affect an individual's decision making (Boyle et al., 2012), cause psychological distress and depression (Halahakoon et al., 2019) and reduce their overall quality of life (Barrios et al., 2013). On the community level, cognitive impairment can lead to high psychological, physical and financial distress for the family and carers of that individual. Previous research showed that the family members of individuals with MCI often reported worse quality of life for the patients than the patient themselves (Barrios et al., 2013).

Moreover, the risk of future incident cognitive impairment is higher in older adults with hearing loss (Livingston et al., 2017). This potentially higher prevalence of MCI among the hearing loss population also makes it an important health problem in this group.

6.1.1.2. There should be an accepted treatment for patients with recognised disease.

At present, no treatment nor intervention has proven to improve cognition in people with MCI or reduce their risk of dementia. Various treatments have been studied for patients with MCI. Even though at the moment no medication has demonstrated clinical utility in MCI, in clinical practice anti-dementia medications such as Acetylcholinesterase inhibitors (AChEIs) (i.e., donepezil), and memantine have been used in MCI. However, studies supporting these medications were mostly done among mild to moderate dementia patients. For the MCI cohort, these medications did not show benefit toward overall global cognitive improvement nor the rate of conversion to dementia, but are associated with increased frequency of side effects (Patnode et al., 2020).

Among the suggested widely accepted non-pharmacological interventions that may potentially reduce cognitive decline are exercise (aerobic and mental) and increased social engagement (Langa and Levine, 2014).

Cognitive training or mental exercise was found to be beneficial among MCI cohort but not for the dementia groups (Hill et al., 2017). Interestingly, the dementia group only minimally benefits from more stimulating and engaging training than the MCI cohort (Hill et al., 2017). This may indicate that cognitive intervention among MCI is not only much more effective but also simpler to conduct than among

dementia group. Similar results were found across several meta-analyses (Hill et al., 2017). This lack of benefit among the dementia group may suggest that early intervention in the MCI stage before the cognitive function excessively deteriorates should be promoted. Still, the WHO recommendation is that despite the low-quality of evidence, cognitive stimulation has adequate evidence to show a benefit for older adults with all forms of cognitive impairment (MCI and dementia) (WHO, 2017). In addition to mental exercise, physical exercise should also be offered for MCI patients since the combination of mental and physical exercise can significantly increase the overall cognitive function and activities of daily living for the MCI (Karssemeijer et al., 2017).

Increased social engagement may also be beneficial for the MCI population. A regression model with retrospective data found that MCI had a 34.3% chance of reverting back to the normal cognition stage at 4 years instead of progressing to the dementia stage (Shimada et al., 2019) when they participated in more socially engaged activities such as travelling, reading a newspaper, attending classes or community meeting and engaging in fieldwork. However, retrospective data could not establish the causality of these social activities toward the improvement of dementia. Therefore, a prospective randomized control trial would be needed for the purpose.

A hearing intervention can also help to stimulate people with MCI social engagement with others through more effective communication. Previous retrospective research showed that a hearing intervention was associated with a delay in the onset of dementia diagnosis, depression and anxiety among older adults with hearing loss (Mahmoudi et al., 2019). For a MCI with hearing impairment, in particular, there is ongoing prospective research by our team at UCL to reduce cognitive decline through a hearing intervention.

Therefore, when we identify MCI patients earlier among the hearing loss population, interventions could be implemented earlier which may potentially slow down the progression to dementia in these patients.

6.1.1.3. Facilities for diagnosis and treatment should be available.

After the screening to detect potentially mild cognitive impairment patients, the onward referral for further confirmation of the diagnosis and treatment of this condition should be offered for all patients.

Several models of such facilities are offered around the world. The main focus is that every suspected MCI case from the screening test should have a comprehensive history taking and physical examination (Langa and Levine, 2014). This can be done by skilled primary care physicians to rule out other conditions that can cause a reversible mild cognitive impairment condition such as depression, multiple

medication effects, abnormal thyroid hormone or vitamin deficiencies (Langa and Levine, 2014). However, onward referral for specialist doctor input may also be useful in many cases.

In the UK, the onward referral can go through the patients' general practitioners to the memory services which are widely available. The service is mainly run by the geriatric psychiatrist consultant doctors who not only can confirm the diagnosis of MCI but can also conduct further needed investigations and treatments for the patients. This could be done in a community memory clinic level which is ideal to maximize the penetration of the facilities in the population.

6.1.1.4. There should be a recognizable latent or early symptomatic stage.

The early cognitive impairment phase is well recognized. As discussed earlier, this mild cognitive impairment stage can precede the dementia diagnosis stage for many years (Petersen, 2004). Some literature even calls this stage "symptomatic pre-dementia stage" (Langa and Levine, 2014).

The annual progression rate from MCI to the mild dementia stage was estimated to be 22% per year (Davis et al., 2018). Interestingly, even though MCI diagnosis increases the chance of developing future dementia, not every case would progress. Therefore several research works have been conducted in this stage to explore potential interventions to prevent the progression.

6.1.1.5. There should be a suitable test or examination.

The original document by WHO defines the "suitable test" as a well-validated tool with appropriate sensitivity to detect the disease and specificity to identify people who do not have the disease. This highlights the need to validate the MoCA-HA tool on the hearing impaired population of older adults.

Moreover, for older adults in general, a mild cognitive impairment stage can be identified with existing objective clinical assessments of cognition (Langa and Levine, 2014, Alzheimer's society, 2015). Therefore, detecting the cognitive impairment at the early symptomatic stage before the patient has a dementia diagnosis is not only practical but should be promoted.

6.1.1.6. The test should be acceptable to the population.

This was emphasized in the Phase 1 of the project which was the Patient-Public Involvement (PPI) phase. It focused on the feedback of the tool and making appropriate adjustment for this novel tool to be acceptable to the intended implemented population as much as possible.

Moreover, our MoCA-HA is a very brief and non-invasive cognitive assessment tool. This makes the tool gain easier acceptance among the population and healthcare professionals. As most screening tests, the

more convenient the screening process, the more acceptance the screening test would gain from the population.

In addition to the simple screening test process, the health education of the population is also playing an important role in the social acceptance of the test. Cognitive impairment and dementia are common conditions that are familiar within our society. The consequences of the diseases are also apparent. Therefore, a simple cognitive screening tool for early identification of the conditions is gaining acceptance among the community easily.

6.1.1.7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.

The disease progression of cognitive impairment has been studied extensively. The natural history of the dementia stage for an individual according to the US modelling data is as follows. For an older adult age 65 years with an average lifespan of 81.6 years, the predicted age for MCI onset would be 74 years old and dementia at age 77.1 years (Davis et al., 2018).

The incidence of having newly diagnosed MCI for the normal population age 65 years or above is estimated to be around 4-10 % annually (Davis et al., 2018). Of these MCI cases, 22% would progress to the mild dementia stage annually. Dementia is divided into 3 stages according to Clinical Dementia Rating (CDR) into a mild, moderate and severe stage (Morris, 1993). The classification is based on six domains which are memory, orientation, judgement and problem solving, community affairs, home and hobbies, personal care. The memory domain gains the most weight in the classification. The mild dementia stage is diagnosed when an individual memory problem starts to affect daily life activities. The moderate dementia stage is considered when the memory problem is more severe with newly learned material rapidly vanished. Severe dementia stage is considered when only a fragment of the patient's memory remains.

6.1.1.8. There should be an agreed policy on whom to treat as patients.

The original WHO report mainly focuses on the threshold of identifying the affected patient according to the treatment available. For example, when encountering borderline cases, clinicians need to be mindful that we are only offering treatment for diagnosed patients and using agreed policy to determine that case.

The diagnosis criteria for who to treat as patients in MCI and dementia conditions are described explicitly in the International Classification of Disease (ICD) version 10 and 11 as discussed in Chapter 1. Their treatment options were discussed in topic 6.1.1.2

Therefore the agreed policy on whom to be diagnosed as a mild cognitive impairment and dementia patient is very well established without any controversy. However, in some uncertain cases, clinical judgment may still be needed to facilitate the diagnosis.

6.1.1.9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.

Cognitive screening can lead to an early onward referral for the patient to receive appropriate treatment before other healthcare-related consequences progress. The cost-effectiveness of implementing cognitive screening in primary care versus the unassisted clinical judgement has been previously studied in the UK setting (Tong et al., 2017). Using cognitive screening was found to improve the patients quality of life by up to 3.48 quality-adjusted life years (QALYs) per 1,000 patients and to reduce the overall cost of healthcare, social care and informal care of the individual significantly which are worth up to £196,251 per 1,000 patients (Tong et al., 2017).

Our MoCA-HA should be a valuable tool to help guide primary care physicians in a similar way to reduce the burden of medical care as a whole.

6.1.1.10. Case-finding should be a continuing process and not a "once and for all" project.

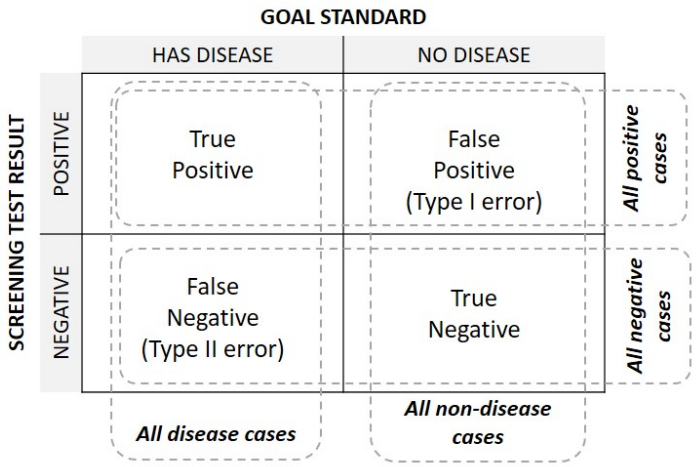
The case-finding should be done continuously with re-testing throughout their life span. As mentioned earlier, older adults with hearing loss post a higher risk of developing future dementia. The risk increases when they get older. This means that our 65 year old hearing-impaired patient who passes the screening test today, may deteriorate and later fail the re-screening test next year.

Moreover, even though a cognitive screening test has a high sensitivity in detecting potential cases but it is not 100%, there can still be undetected cases. These high-risk cases would be identified in a sequential screening test.

6.1.2. Sensitivity and Specificity of the test

An ideal test should be able to correctly identify affected cases when also correctly sparing non-affected cases. However, that may not always be the situation for every test. All possible outcomes of the screening test are illustrated in Table 22.

Table 22 All possible outcomes for the screening test adapted from (Wilson et al., 1968)



Sensitivity is the term used to determine the proportion of true-positive correctly identified among all disease (affected) cases. To simplify, sensitivity is the rate where the diseased person is correctly identified as having the disease. Therefore, the higher the sensitivity, the higher the chance that the test captures the true-disease cases in the population.

Specificity is the term used to determine the proportion of true-negative correctly identified among all non-disease (non-affected) cases. To simplify, specificity is the rate where the non-disease person is correctly identified as not having the disease. The higher the specificity, the higher the chance that the test captures the true non-disease cases in the population.

False-positive is when the non-disease person is incorrectly identified as having the positive test result which indicates that they may have the disease. This error condition is not ideal since it can create further unnecessary investigations for the person. For cognitive screening tests, high false-positive can also create suffering for the individual (Boustani et al., 2011) and unnecessary onward referral before they later discovered that they do not have cognitive impairment.

False-negative is when the diseased person is incorrectly identified as having the negative test result which indicates that they may not have the disease. For cognitive screening tests, a false-negative may lead to a missed opportunity for early treatment of the disease.

6.1.3. Screening tool versus diagnostic cognitive assessment tool

Some assessment tools can be considered both as screening and diagnostic tools. However, there are several differences between the two as outlined below in Table 23. As a result, some adjustment may be needed if we want to implement a diagnostic tool as a screening tool and vice versa.

Table 23 Comparison between screening and diagnostic tool

	Screening tool	**Diagnostic tool**
Purpose	To identify as many potential cases in the community. The accuracy of the test may not be the main concern since the onward referral is needed for the definite diagnosis.	To establish the presence or absence of the disease to facilitate decision making in the diagnosis and treatment. Therefore, the accuracy and precision of the tool is the main focus.
Target population	To be implemented at the community level or at a large asymptomatic population level to identify potential cases early.	To be implemented among a small group of symptomatic or asymptomatic suspected patients who had a positive screening test to confirm the final diagnosis.
Positive results meaning and threshold	To indicate that an individual may have the disease and warrant onward referral. Therefore, the test should not miss any potential disease cases. The high sensitivity of the tool is the main priority.	To indicate that an individual has a confirmed diagnosis for the treatment. Therefore, the test should not include any potential non-disease cases. The high specificity of the tool is the main priority.
Implementation Cost	The cost should be small to use in a larger population. This usually means brief/not time-consuming, non-invasive and less training for the staffs.	The higher cost can be justified to outweigh the risk of inaccurate diagnosis. Therefore, if necessary, some diagnostic tool can be more time-consuming, more invasive and require more training for the staffs.

6.1.4. Test validation principles

Test validity is the degree to which the evidence supports the appropriate interpretation of the test score (Messick, 1995). In order to interpret the test score accurately, the test has to be

validated/implemented among the intended target group of participants in a context similar to that intended to measure.

Therefore, the MoCA-HA was used among the hearing-impaired older adults both with and without a diagnosis of cognitive impairment to assess the test validity.

In this chapter, the data from hearing aid users with normal cognition versus those with MCI are compared. The differences in the task's performance along with an appropriate cut- point score for the tasks will be identified. The appropriate cut off point score for the newly developed MoCA-HA will be established.

Test validity encompasses three separate entities that require separate validations: *content validity*, how the content of the test is measuring the intended subject; *construct validity*, how each sub-test contributes to the overall test scoring; and *criterion validity*, how the test performance scores distinguish the cohort compared with other tests such as the gold standard. The current view is that we can conduct a unified experiment instead of a separate one to explore all possible entities (Messick, 1995).

Since, the existing tool was used with the same tasks/sub-categories with a changed mode of delivery, the content and the construct validity of the original MoCA paper should still apply. The discrepancy between the visual presentation and the auditory presentation of the tasks has already been discussed in Chapter 4. In this chapter 6, we mainly conducted a criterion validation of our novel MoCA-HA. Criterion validation is divided into concurrent validation and predictive validation. The key difference between the two subtypes is the timing of the test. Concurrent validity refers to when the two tests were conducted at the same time while predictive validity refers to when the other outcome test was done at a later stage than the first test. For patients with mild cognitive impairment, predictive validity would be whether the test can predict progression into the dementia stage which is difficult to conduct since the progression of MCI patients is usually varied (Petersen, 2004) with a previous study showing that more than half of MCI patients took longer than 3 years to develop dementia (Tschanz et al., 2006). Therefore we mainly focused on the concurrent validity subtype of the criterion validity in this project.

With concurrent validity, we want to explore whether the MoCA-HA can differentiate older adults with hearing loss with mild cognitive impairment from those with normal cognition when compared with other cognitive assessments conducted at the same time. We rely on the ICD-10 gold standard diagnostic criteria of mild cognitive impairment as described in Chapter 1, implemented by clinicians

with experience in diagnosis of MCI and dementia from NHS memory services. Moreover, we also assessed concurrent validity with other validated neuropsychological tools which rely solely on visual input, rather than auditory input. This is to ensure the validity of the MoCA-HA cognitive assessment tool against other visually delivered tools.

6.2. Methods

6.2.1. Participants

The MoCA-HA data from normal cognition-hearing aid users in phase 2 and mild cognitive impairment-hearing aid users phase 3 were used to determine the validity of this novel tool.

6.2.2. Statistical analysis: Diagnostic performance

The Receiver Operating Characteristic [ROC] curve is often used to evaluate the overall effectiveness of a newly developed binary outcome diagnostic tool. The ROC curve is plotted between false-positive rates (1-specificity) of the test on the x-axis against the true-positive rates (sensitivity) value of the test on the y-axis in various thresholds environments.

The Area-under-curve (AUC) of the plot determines the diagnostic property of this tool where a higher value (ranging from 0-1) indicates a better diagnostic value of the tool (Bradley, 1997). When the AUC is 1.00, the diagnostic tool can correctly identify the disease and non-disease with a sensitivity of 100% and specificity of 100%. When the AUC is 0.5, the diagnostic tool has a 50% chance of correctly identifying the affected individual, i.e. a chance level for binary outcome indicating no diagnostic ability of the tool. Therefore, when interpreting AUC, the value between 0.7 to 0.8 is considered acceptable, 0.8 to 0.9 is considered excellent and more than 0.9 is considered outstanding (Mandrekar, 2010). The AUC can also be used to compare which diagnostic tool has better diagnostic property (Bradley, 1997). A formal hypothesis test of H_0 is that AUC $= 0.5$ versus H_1 of an AUC not equal to 0.5. The diagnostic test would have a significant diagnostic value when a p-value is < 0.05 or the 95% confidence interval of the AUC is not including 0.5 (Mandrekar, 2010).

After identifying that the tool has a good diagnostic value, the next step would be to determine the best cut-point score for MoCA-HA referral. There are currently two widely accepted methods to determine the appropriate cut-point score for any given dichotomous diagnostic tool.

The first method is intuitive visualization of the ROC for the point that has the most proximity to (0,1). This method does not need additional calculation and is being widely adopted by many clinicians. The most appropriate screening cut-point would be determined from the graph. The co-ordinate that has

the highest sensitivity (on the y-axis) and specificity (least value on the y-axis of 1-specificity) would be used to identify the cut-point threshold.

The second method is the Youden index (*J*) which was introduced in 1950 (Youden, 1950). In this method, the cut-point that had the highest value from the Youden index formula of (sensitivity+specificity)-1 would be determined as the most appropriate cut-point (Greiner et al., 2000). Previous research showed that when a direct comparison of the two criteria was done, the Youden index was found to provide a superior accurate classification of the cohort than direct visualization of ROC (Perkins and Schisterman, 2006). However, relying on this Youden index means we give equal weight to the sensitivity and specificity which may not always be the optimal case for the screening tool from the point of view of clinical utility. As mention earlier, a good screening tool should give priority to high sensitivity.

Moreover, the appropriate cut-point should not solely rely on the statistical method described above but should also consider other factors such as the burden of false-positive or false-negative on further unnecessary investigations, psychological consequences of the intended screening population etc. However, there has not been a direct study assessing these burdens for cognitive screening toward older adults. Previous systematic review data suggested that for a cognitive screening tool, sensitivity and specificity of around 80% or more would be considered promising to implement in an older adult cohort (Lin et al., 2013b).

This decision needs to be made carefully since for any given cut-point the higher the sensitivity, the lower the specificity would be ie. the higher chance of having a false-positive test result. In general, for any screening test, we would like to have a test that has higher sensitivity in order to not miss any potentially affected cases. As mentioned earlier, this allows for some possible false-positive cases which would later be identified in the diagnostic testing stage. Therefore, for a diagnostic test, we would prefer the test with high specificity to correctly identify the affected individual without any error.

6.2.3. Statistical analysis: Correlation with other neuropsychological tests

The data were analysed to fulfil assumptions of Pearson correlation including normality. When the data fulfilled the assumption, the Pearson correlation statistical test was used to determine the correlation of MoCA-HA with other previously validated neuropsychological tests to establish the concurrent validity of this novel tool. The effect size of the Pearson correlation is represented by its correlation value which ranges from -1 to 1. The negative number indicates an opposite direction of the correlation ie when A

increases, B decreases. The positive number indicates the same direction of the correlation ie. when A increases, B increases. In the Pearson correlation, a zero number indicates no correlation. Therefore, when we interpret the strength of the correlation, we should consider only the absolute number (ignoring the minus) and a correlation that is closer to zero indicates a weaker correlation.

In behavioural science, a Pearson correlation coefficient ranging from 0.1 to 0.3 (or -0.1 to -0.3) is considered a weak correlation. A correlation ranging from 0.3-0.5 (or -0.3 to -0.5) is considered a moderate correlation. A correlation of more than 0.5 (or less than -0.5) is considered a strong correlation (Cohen, 1988).

To determine whether the correlation is statistically significant from zero, the α level of significance was set at 0.05. The p values < 0.05 were considered statistically significant, indicated with an asterisk (*) and value <0.01 were considered highly statistically significant, indicated with two asterisks (**).

When the data did not fulfil assumptions for the Pearson correlation analysis, the Spearman rank correlation was used as a non-parametric statistical analysis counterpart. For all the neuropsychological assessments in the below analyses, ROCFT copy was the only variable that did not have a normal distribution due to a slight ceiling effect especially among NC-HI participants, therefore, the Spearman rank correlation was used for the analysis.

6.3. Results

6.3.1. ROC analysis

The ROC analysis was done for all 30 NC-HI controls and 30 MCI-HI cases. The ROC graph plot of the sensitivity against the 1- specificity of the MoCA-HA is illustrated below in Figure 15.

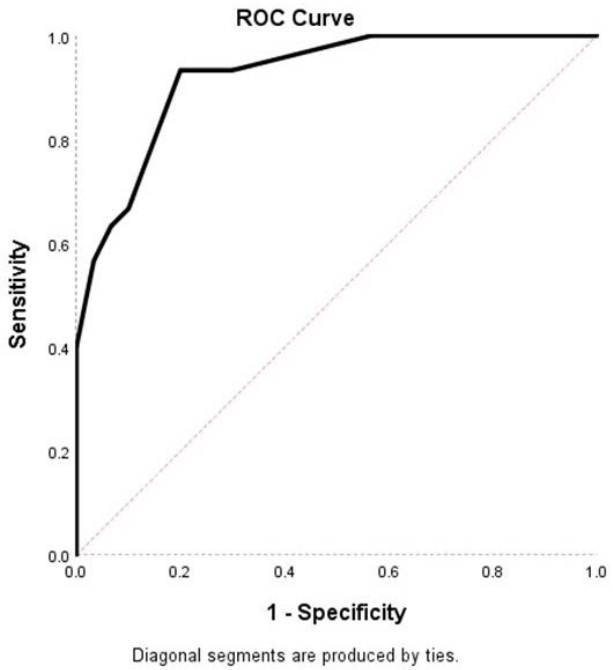


Figure 15 ROC analysis of MoCA-HA

The area under the curve (AUC) of the ROC was also calculated to identify the diagnostic property of the MoCA-HA. The area under curve was 0.922 with the standard error of 0.033 (95% confidence interval 0.858 to 0.987). Not only did the range not include 0.5 which showed a statistical significance ($p<0.001$), but the AUC was also more than 0.9 which indicated an outstanding diagnostic property.

The analysis of the coordinates of the ROC curve to determine the most appropriate cut-point via the Youden index was also demonstrated in Table 24. From the analysis, the coordinate which yielded the largest value of the Youden index of 0.733 should be the most appropriate cut-point. The cut-point was identified to be 25.5 (highlighted in grey) which resulted in the sensitivity of 93.3% and the specificity of 80%. Since the MoCA-HA in practice does not have a half score, the overall score below 26 may be adopted for clinical implementation.

Table 24 Coordinates of ROC curve

Positive if Less Than or Equal To[a]	Sensitivity	1 - Specificity	Youden index
16.000	.000	.000	.000
17.500	.133	.000	0.133
18.500	.167	.000	0.167
19.500	.200	.000	0.200
20.500	.333	.000	0.333
21.500	.400	.000	0.400
22.500	.567	.033	0.534
23.500	.633	.067	0.566
24.500	.667	.100	0.567
25.500	.933	.200	0.733
26.500	.933	.300	0.633
27.500	1.000	.567	0.433
28.500	1.000	.667	0.333
29.500	1.000	.800	0.200
31.000	1.000	1.000	.000

a.The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

6.3.2. Subgroup analysis of the ROC for age-matched and education years matched controls.

The ROC analysis was done for the age-matched, education years matched 9 controls (as described in Chapter 5.3.2) and all 30 MCI cases. The ROC graph plot of the sensitivity against the 1- specificity of the MoCA-HA is illustrated below in Figure 16 ROC curve of the age-matched, education matched controls.

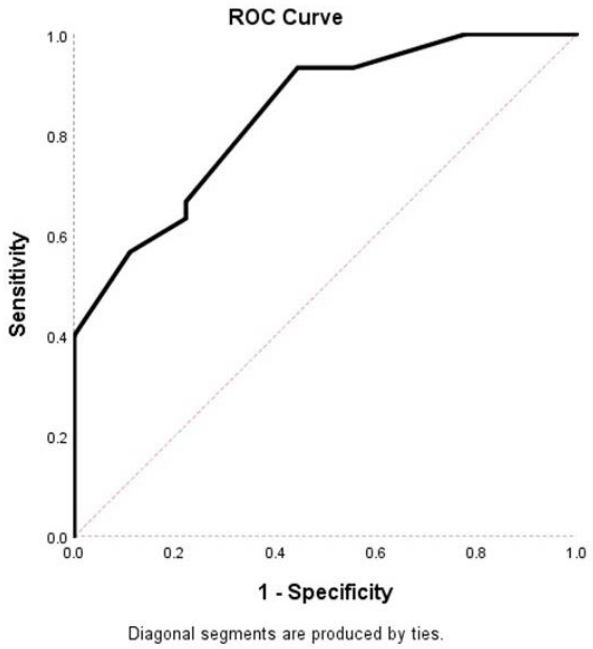


Figure 16 ROC curve of the age-matched, education matched controls

The area under the curve (AUC) of the ROC subgroup analysis was also calculated. The area under curve was 0.839 with the standard error of 0.072 (95% confidence interval 0.698 to 0.980). The range did not include 0.5 therefore the analysis was statistically significant (p=0.002).

The analysis of the coordinates of the ROC curve to determine the most appropriate cut-point via the Youden index for the age-matched, education years matched controls was also demonstrated in Table 25. From the analysis, the coordinate which yielded the largest value of the Youden index of 0.489 should be the most appropriate cut-point. The cut-point was identified to be 25.5 (highlighted in grey) which resulted in the sensitivity of 93.3% and the specificity of 55.6%.

Table 25 Coordinates of subgroup analysis of the ROC curve

Positive if Less Than or Equal To[a]	Sensitivity	1 - Specificity	Youden index
16.000	.000	.000	0.000
17.500	.133	.000	0.133
18.500	.167	.000	0.167
19.500	.200	.000	0.200
20.500	.333	.000	0.333
21.500	.400	.000	0.400
22.500	.567	.111	0.456
23.500	.633	.222	0.411
24.500	.667	.222	0.444
25.500	.933	.444	0.489
26.500	.933	.556	0.378
27.500	1.000	.778	0.222
29.000	1.000	.889	0.111
31.000	1.000	1.000	0.000
16.000	.000	.000	0.000

a.The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

6.3.3. Correlation between the MoCA-HA and other neuropsychological tests

6.3.3.1. ROCFT copy and recall

Since ROCFT required the participants to draw the pattern which reflected their visuospatial and executive ability, the detailed analysis of ROCFT and each task of the MoCA-HA sub-category executive/visuospatial was done as illustrated in Table 26.

There were significant correlations of ROCFT copy and recall with all the tasks and the total MoCA-HA executive sub-category score. Strong correlations (r>0.5) were found between the ROCFT immediate recall and the MoCA-HA copy bed task. Moderate correlations were found between the ROCFT copy/recall and MoCA-HA trail task along with the ROCFT 30 mins recall and all the tasks.

Table 26 Correlation between ROCFT copy/recall with each MoCA-HA executive subcategory task

		MoCA-HA Trail	MoCA-HA Copy bed	MoCA-HA Draw clock	MoCA-HA Executive Total
ROCFT Copy	Spearman rank correlation	.480**	.271*	.294*	.469**
	Sig. (2-tailed)	.000	.038	.024	.000
ROCFT Immediate recall	Pearson Correlation	.384**	.527**	.279*	.484**
	Sig. (2-tailed)	.003	.000	.032	.000
ROCFT Recall 30 mins	Pearson Correlation	.386**	.477**	.306*	.482**
	Sig. (2-tailed)	.003	.000	.018	.000

Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).*

In addition to the correlation with the MoCA-HA executive subcategory, the ROCFT copy and recall were also moderately to strongly correlated with the MoCA-HA attention, language subcategory and total MoCA-HA score as illustrated in Table 27.

Moreover, the ROCFT immediate recall and 30 minutes recall, were also strongly correlated with the MoCA-HA recall subcategory (r=.615 and r=.634) while the ROCFT copy had a weak correlation (r=0.298).

Table 27 Correlation between ROCFT copy/recall and MoCA-HA subcategory

		MoCA-HA Executive	MoCA-HA Naming	MoCA-HA Recall	MoCA-HA Attention	MoCA-HA Language	MoCA-HA Abstract	MoCA-HA Orient	MoCA-HA total
ROCFT Copy	Spearman rank Correlation	.469**	.064	.281*	.473**	.484**	.020	.259*	.502**
	Sig. (2-tailed)	.000	.631	.031	.000	.000	.879	.047	.000
ROCFT Immediate recall	Pearson Correlation	.484**	.158	.609**	.350**	.416**	.102	.339**	.681**
	Sig. (2-tailed)	.000	.232	.000	.007	.001	.443	.009	.000
ROCFT Recall 30 mins	Pearson Correlation	.482**	.094	.628**	.355**	.496**	.031	.291*	.701**
	Sig. (2-tailed)	.000	.478	.000	.006	.000	.817	.025	.000

Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).*

6.3.3.2. Corsi block tapping: Digit Span test

The correlation between the overall MoCA-HA score with the digit span tests (forward and backward) was examined. The digit spans test is considered to test the participant's attention, thus the correlations between the digit span test and each attention task of MoCA-HA were also performed.

We found no significant correlation between the digit span forward, backward and total score with each attention task, however, a statistically significant moderate correlation was found for all digits span tests with the total MoCA-HA score.

A moderate correlation was also found with the language sub-category score. In addition, weak correlations were found between the total Digits span score with MoCA-HA executive, attention and recall sub-category score. The Pearson correlation analysis of the correlation with each MoCA-HA sub-category is illustrated below in Table 28.

Table 28 Pearson correlation between Digit span test and MoCA-HA sub-categories

		MoCA-HA Executive	MoCA-HA Name	MoCA-HA Recall	MoCA-HA Attention	MoCA-HA Language	MoCA-HA Abstract	MoCA-HA Orient	MoCA-HA Total
Digit Span Forward	Pearson correlation	.240	-.014	.239	.222	.360**	-.066	.070	.321*
	Sig (2 tails)	.064	.916	.065	.089	.005	.614	.598	.012
Digit Span Backward	Pearson correlation	.268*	.024	.243	.270*	.261*	.074	.185	.345**
	Sig (2 tails)	.039	.857	.062	.037	.044	.572	.157	.007
Digit Span Total	Pearson correlation	.299*	.006	.283*	.289*	.364**	.006	.151	.392**
	Sig (2 tails)	.020	.963	.028	.025	.004	.963	.251	.002

Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).*

6.3.3.3. Graded naming test

The graded naming test had a strong correlation with MoCA-HA total score (r=786 and r=.782 with prompt). It also showed moderate to strong correlations with most MoCA-subcategories except MoCA-HA naming and abstract subcategories as illustrated in Table 29.

The score for the graded naming test after the participants received some prompts was also analysed. All the responses from the graded naming test with prompts showed slightly less correlation with MoCA-HA sub-categories and total score.

Table 29 Pearson correlation between Graded naming test and MoCA-HA sub-categories

		MoCA-HA Executive	MoCA-HA Naming	MoCA-HA Recall	MoCA-HA Attention	MoCA-HA Language	MoCA-HA Abstract	MoCA-HA Orient	MoCA-HA total
GNT	Pearson Correlation	.683**	.245	.585**	.391**	.414**	-.022	.486**	.773**
	Sig. (2-tailed)	.000	.059	.000	.002	.001	.866	.000	.000
GNT with Prompt	Pearson Correlation	.634**	.237	.607**	.398**	.379**	-.003	.459**	.743**

	Sig. (2-tailed)	.000	.069	.000	.002	.003	.980	.000	.000

Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).*

6.3.4. Correlation between the MoCA-HA and hearing level

The Pearson correlation was analysed for the MoCA-HA score against the participants' hearing level. There was no significant correlation between the MoCA-HA score and better ear 4 frequencies pure-tone average among the total participants as depicted in Figure 17 (r=-0.196, p=0.133). Within the NC-HI cohort and MCI-HI cohort, there were also no significant correlations between the MoCA-HA score and the pure-tone average (r=-0.347, p=0.06 and r=-0.305, p=0.101 respectively)

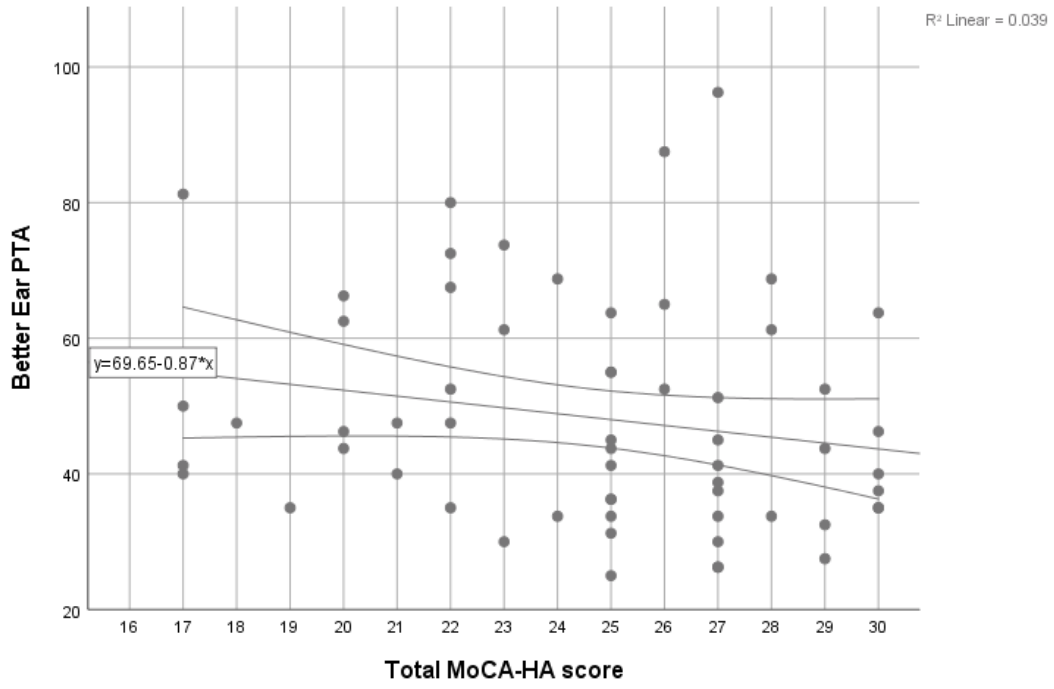


Figure 17 Scatter plot of MoCA-HA total score against the better ear pure-tone average of the participants.

6.4. Discussion

6.4.1. Diagnostic property and the subgroup analysis for age-matched control

The MoCA-HA showed an outstanding diagnostic property when implemented among adults aged 65 and older who have hearing aids with AUC of >0.9. When considering only the age-matched control cohort of mean age over 80 years old, the AUC diagnostic property of the tool is still 0.839, which is considered to be excellent (AUC 0.8-0.9).

It was decided to perform the subgroup analysis of the age-matched older controls. This also resulted in matched education years since the older controls cohort tended to have lower education years. The same was also noted in previous research (Flynn, 1987, Murphy et al., 2019). The subgroup analysis helps us gain insight into the diagnostic property of the MoCA-HA in detecting MCI for each individual case from their peer cohort. We found an excellent diagnostic property with AUC > 0.8 after the subgroup analysis. This indicates that the sample size is sufficient for this analysis.

6.4.2. Cut-point referral threshold

Different cut-points may be needed for different populations and purposes. As discussed earlier, even for the same cognitive assessment tool, appropriate cut-points for diagnostic and screening may also differ (Tombaugh and McIntyre, 1992).

According to our data analysis, the most appropriate cut-point for diagnosis of mild cognitive impairment would be 25.5 (i.e. a score of <26 would be diagnostic of mild cognitive impairment). If we use this cut-point, the sensitivity of detecting MCI among hearing aid users aged 65 or above would be 93.3% with a specificity of 80%.

The same optimal cut-point of 25.5 was identified in the age-matched cohort. Even though the specificity decreased to 55.6% when considering the detection of MCI among the older age-matched cohort, the test still maintained the same high sensitivity. With a sensitivity of over 90% similar to the traditional MoCA, our MoCA-HA is an excellent screening tool for detecting MCI among older adults with hearing loss.

There is an on-going debate whether MoCA was designed to be a screening tool for mild cognitive impairment, rather than a diagnostic tool (Nasreddine et al., 2005). A Cochrane systematic review and meta-analysis of MoCA concluded that there is not enough evidence to recommend using traditional MoCA in various clinical settings as a diagnostic tool for dementia. Due to its low specificity of <60% and high sensitivity of >90% when using 25/26 as the cut-point in the meta-analysis, the tool may be more

suitable to use as a screening test (Davis et al., 2015). This is consistent with our analysis that a cut-point of 25/26 provides a good screening threshold for MCI with >90% sensitivity, despite low specificity in older age/education-matched controls.

Despite the tendency to have a subtle lower MoCA memory sub-category score among the hearing-impaired cohort compared with the normal-hearing peers. For the total MoCA-HA score, the same cut-point score of 25/26 is still applicable. The superior visuospatial ability for the hearing-impaired population as discussed in Chapter 5.4 may play a role in offsetting the impaired memory ability in the total MoCA-HA score. Further research may be needed to clarify the effect of visuospatial ability toward MoCA-HA in this population. Nonetheless, for clinical application, the cut-point of 25/26 which is also used in the traditional MoCA, is proven in this current work to also be applicable for the MoCA-HA.

6.4.3. Strong correlation with other neuropsychological tools

Most neuropsychological tests usually rely on hearing the instruction and the stimulus. Therefore, when the patient has hearing loss, an accurate assessment can be challenging. We have selected widely used and well-validated neuropsychological tests that depend only on visual stimulus for accurate assessment of our cohort of older adults with hearing loss. Moreover, the correlation of these validated tools with the novel MoCA-HA would also demonstrate good validity of the tool.

The MoCA-HA scores showed a strong positive correlation with all visually-based neuropsychological tools in this project that included ROCFT copy/recall, Corsi-block tapping and the Graded naming test. These findings indicate excellent concurrent validity of MoCA-HA against other visually-administered tools.

6.4.3.1. ROCFT copy and recall

The ROCFT copy and recall had good correlation with MoCA-HA visuospatial executive and attention as expected. In order to draw the complex figure, executive function, visuospatial function and attention would be recruited. We also found good correlations with the MoCA-HA language subcategory. The MoCA-HA language subcategory score consists of 2 points for sentence repetitions and 1 point for verbal fluency. Sentence repetitions were found to assess not only the language ability but also attention and concentration (Meyers et al., 2000). Verbal fluency similarly also assesses the executive and working memory (Nasreddine et al., 2005). Since the ROCFT taps into both executive and attention ability, its correlation with the MoCA-HA language subcategory as shown in our cohort would be anticipated.

As expected, the immediate recall and the 30 minute recall of ROCFT were strongly correlated with the memory/Delayed recall sub-category of the MoCA-HA ($r=.615$ with $p<.0001$ and $r=.634$ with $p<.0001$ respectively). Even stronger correlations were found with the total MoCA-HA score ($r=.668$ with $p<.0001$ and $r=.700$ with $p<.0001$ respectively). As discussed earlier, the memory sub-category should be emphasized when evaluating the cognitive function of older adults with hearing loss. Perhaps, the visuospatial memory ability to recall the ROCFT complex figure which took over 30 minutes to wait and 5 minutes to draw could easily to some extent be replaced with the brief MoCA-HA recall/memory subcategory score in this context. Therefore, the MoCA-HA tool showed excellent correlations and concurrent validity with other visually-based memory assessment tools, and should thus be suitable to use among this group of population.

6.4.3.2. Corsi-block tapping: Digit Span test

The Corsi-block tapping digit span test involved asking the participant to remember the block tapped by the examiner and tapped the same block which utilized executive function, visuospatial memory and attention. We found that Corsi-block tapping task had a good correlation with the MoCA-HA executive/visuospatial, recall/memory, attention and language subcategories.

The lack of correlation between the digit span from Corsi-block tapping test and the MoCA-HA digit span tasks may be due to the limited sample data point. The digit span task (forward/backwards) on MoCA-HA has a score of 0 when the participant fails to correctly identify all numbers and 1 when they correctly identify all numbers. On the other hand, the digit span of the Corsi-block tapping has a score ranging from 0 to 16. Only 5 participants failed the MoCA-HA digit span forward (score=0). These participants scored 5,6,7,8,10 out of 16 in the digit span forward on the Corsi-block tapping.

6.4.3.3. Graded naming test

Even though the graded naming test is widely used to assess the language function of an individual, it was developed to be highly correlated with the overall intellectual function (McKenna and Warrington, 1980). Therefore, the moderate to strong correlations which were found between the graded naming test with almost all the MoCA-HA subcategories were expected. However, we did not find a significant correlation between the graded naming test and the MoCA-HA naming, abstract subcategories, possibly due to insufficient power of the study.

Since only 2 participants in our cohort of 60 participants had MoCA-HA subcategory naming less than the full score of 3, there were not enough data to draw a correlation between the MoCA-HA subcategory naming and the graded naming test. Three cases had a score of 2 out of 3 in the MoCA-HA attention subcategory with scores of 4, 18,28 out of 30 in the prompted graded naming test. A similar situation was seen for the MoCA-HA abstract subcategory where only one participant in the whole cohort scored 1 out of the 2 full scores. There were not enough data points to establish a correlation of the MoCA-HA abstract with any other neuropsychological test including the graded naming test.

The reason why we observed more correlations of the graded naming test without prompt and the MoCA-HA sub-categories and total score compared with the graded naming test with prompt, is maybe due to the design of MoCA-HA where a prompt is not allowed.

6.4.4. No correlation with hearing level

This study found no correlation between MoCA-HA score and hearing level which means that the participants hearing loss was not interfering with the MoCA-HA performance. Therefore MoCA-HA can give an accurate reflection of the hearing-impaired population cognitive performance.

Our recent meta-analysis found a correlation between traditional MoCA with hearing sensitivity in that hearing-impaired participants performed 1.66 points worse than controls in MoCA (Utoomprurkporn et al., 2020b). The meta-analysis was done among papers using traditional MoCA, not the MoCA specially designed for the hearing-impaired population.

Taking together the findings presented in this chapter with our meta-analysis, the evidence indicates that participants with hearing impairment can be disadvantaged from using traditional auditory administered MoCA, but that we are able to provide accurate cognitive testing, unbiased by hearing impairment, when using the MOCA-HA as a screening test in this population.

Several papers found no difference in the participant performances between the visual and auditory modality presentations of MoCA among some hearing-impaired populations such as competent older adult postlingual cochlear implant users (Parada et al., 2020) and mild hearing-impaired older adults (Shen et al., 2019). Nevertheless, older adults with moderate or more severe hearing-impaired hearing aid users as in our cohort do not always perform well with auditory administered MoCA even with amplification (Saunders et al., 2018b). This population represents about one in three of older adults over age 65 (WHO, 2018). Therefore visually administered MoCA such as MoCA-HA which is specially

designed for hearing aid users should be implemented to accurately reflect their cognitive performances.

6.4.5. Strengths and limitations

The MoCA-HA had an excellent diagnostic property even after the subgroup analysis of matched controls. Moreover, the same optimal cut-point of 25.5 was identified in both analyses with sensitivity > 90%.

High sensitivity indicated that the MoCA-HA could be an excellent screening tool. Despite, the specificity decreased to 55.6% with the older age-matched controls analysis, this is still within an expected range from a previous meta-analysis (Davis et al., 2015). With this specificity resulted in potential false-positive cases, counselling of the test result meaning beforehand along with established referral pathway for further assessment are important for the MoCA-HA test implementation.

Age-adjusted normative data for the MoCA has been proposed in various population-based studies (Borland et al., 2017, Rossetti et al., 2011). The normal cognition older cohort was previously suggested to have lower mean MoCA score which is similar to what our data showed. If participants scored 25 (<26 cut-point) in the MoCA at age 65, they would have failed the screening test; but when they are aged over 80, the same fail score may demonstrate normal cognition, which resulted in false-positive cases ie lower the specificity. However, the proposed for age-adjusted lower MoCA cut-point in an older cohort was not widely accepted since it can introduce underestimation of vascular and neurodegenerative effect toward cognition (Nasreddine et al., 2012). Our data agree with Nasreddine et al. by maintaining the same cut-point of <26 to yield equally high sensitivity across all age groups for MoCA-HA tool.

6.5. Conclusion

The MoCA-HA has an outstanding diagnostic property with AUC > 0.9 for the diagnosis of MCI in older adults (aged 65 or older) who are hearing aid users. The tool also has strong correlations with other validated visually-based cognitive assessments and not interfered by the hearing ability of the participants.

The cut-point of the MoCA-HA for onward referral for further cognitive evaluation is recommended to be 25/26. This cut-point yields sensitivity of 93.3% similar to the traditional MoCA. However, due to relatively moderate specificity among aged-matched controls, as with other screening tests and the traditional MoCA, an onward referral is needed to confirm the final diagnosis.

The newly developed MoCA-HA is a valid cognitive screening tool to be used among older adults with hearing loss age of 65 or older. Early identification of potentially mild cognitive impairment condition among the hearing loss older adults can help with early onward referral for further diagnosis and intervention.

7. Summary and overall discussion

The main aim of this thesis was to develop and validate a tailored cognitive screening tool for older adult hearing aid users which was successfully done. In addition to the main aim, the relationships between cognition and hearing in cognitively healthy older adults with hearing impairment and the older adult with both mild cognitive impairment and hearing impairment were also studied.

The summary and considerations of these characteristics along with potential further research areas are described below.

7.1. MoCA-HA development and application: PHASE 1

Previous visual adaptations of the MoCA were mainly focusing on assessing the eligibility and predictability of who will do well in post-operative recovery outcomes among the cochlear implant candidates. Therefore, the specific characteristics of the broader population of older adult hearing aid users, who may be more vulnerable to cognitive impairment, were not necessarily considered.

We started by conducting several Patient Public Involvement (PPI) sessions, which recruited hearing aid user volunteers in order to obtain feedback. This helped to uncover several problems with the previously attempted visual adaptation versions of the MoCA. For example, these older adult hearing aid users were not comfortable to press from one computer slide to another by themselves or writing the answers down on multiple answer sheets.

We used this feedback to refine the MoCA-HA to be ready for implementation among the hearing aid users with and without cognitive impairment. In our study, all participants including the ones with cognitive impairment and hearing impairment could complete the MoCA-HA without any issue, which reflected the good understanding of this population in the development process of the tool.

7.2. Considerations for older adults with hearing impairment in general: reflected from NC-HI cohort (PHASE 2)

7.2.1. Information encoding and retrieval

Hearing impairment may potentially cause a problem in memory, which was present even when testing with the visually presented targets of MoCA-HA in the memory sub-category when compared with normative data. Still, this effect was not large enough to cause a statistically significant difference with normal hearing controls after Bonferroni correction.

Recalling the target words as presented in the memory sub-category is thought to rely on two main pathways, information encoding (storage) and information retrieval. While we did not specifically assess the encoding pathway in the current study, using visually presented targets should overcome the encoding difficulties that may be related to auditory impairment. We still found a slightly lower memory sub-category score, however, the normal MIS score suggested the presence of a preserved information retrieval pathway in the NC-HI group. This indicated that the information encoding pathway may be impaired among older adults with hearing impairment even when they are tested via non-auditory stimuli. More importantly, this may further indicate that the encoding ability of the brain, in general, suffers from a permanent negative effect of hearing impairment as previously described by the sensory deprivation theory (Husain et al., 2011).

The encoding problem was previously found among the hearing-impaired population with MoCA, however, the effect could not be demonstrated as clearly with traditional auditory presented MoCA when an encoding problem can also stem from mishearing the target words or increasing listening effort (Dupuis et al., 2015, Yeok Leng Lim and Loo, 2018).

The retrieval pathway of the hearing-impaired population was explored with various tests in this current study including a detailed analysis of word fluency task, memory sub-category, the memory index score (MIS) of MoCA-HA and the graded naming test. All data showed a comparable performance among the NC-HI and normative data indicating the unaffected information retrieval pathway among older adult hearing aid users.

7.2.2. Visuospatial ability

As discussed earlier, previous studies of the visuospatial ability of the hearing impaired population have shown conflicting results with better (Rudner et al., 2016a) to worse(Rönnberg et al., 2014b) performance in the hearing impaired than their normal-hearing peers. This may arise from different testing paradigms of visual abilities in each study. For example, selective attention tasks in a peripheral visual field were found to be better in the hearing-impaired population (Bavelier et al., 2006).

However, what seems to be a consistent trend is that individuals who needed to potentially utilise lip-reading and sign language ie. the early onset or the profound hearing impairment population may have better visuospatial abilities than their normal-hearing peers (Rudner et al., 2016b, Bavelier et al., 2006, Rudner et al., 2016a). Evidence of cross-modal plasticity among the hearing impairment population was shown in neuroimaging studies and early adoption of sign language could enhance this process (Simon

et al., 2020). Even though we specifically excluded these populations with childhood early-onset hearing impairment and only targeted hearing-impaired older adults hearing aid users who are not from cochlear implant waiting lists to avoid this potential confounder, we still found better visuospatial ability among our NC-HI cohort.

Currently, there are several local support groups for hearing aid users which provide various kinds of supports including the manipulation of the hearing devices, psychological support and lip-reading and facial cue interpretation lessons. Several participants in our NC-HI cohort were also active participants in these other supporting activities. Therefore, not surprisingly, their visuospatial abilities were found to be better than the normative data in the Corsi-block tapping digit backward, ROCFT copy and recall.

7.3. Considerations for older adults with mild cognitive impairment with hearing impairment population: reflected from MCI-HI cohort (PHASE3)

7.3.1. Information encoding and retrieval

The overall memory of the MCI-HI cohort was significantly worse than the NC-HI as demonstrated in the memory sub-category of MoCA-HA score. As discussed earlier, hearing impairment can contribute to the decrease in encoding ability of these MCI-HI similarly to the effect found among NC-HI, if not more.

For the information retrieval pathway, in this current cohort, a problem was not found among the hearing-impaired population in general, but it was prominent among the ones with mild cognitive impairment. We demonstrated their impairments in the verbal fluency task of MoCA-HA test, in which we asked them to list as many words as they could that begin with a certain letter. The problem in the retrieval pathway was also revealed in the lower memory index score (MIS) of MoCA-HA and the lower graded naming test score among the MCI-HI comparing with NC-HI.

A problem in the information retrieval pathway is not unique to the MCI-HI since it has been widely reported among the MCI population in general. For example, the word fluency test is considered to be the most commonly reported language performance impairment among the MCI population, which showed the problem in word retrieval in this population (Demetriou and Holtzer, 2017).

The problem in both information encoding and retrieval pathways due to the combined hearing and cognitive impairment can cause the MCI-HI population to perform worse in all visually based cognitive

assessment tools in this study and potentially causing the difficulty experienced in the self-reported hearing-related questionnaires.

7.3.2. Visuospatial ability

Even though the MCI-HI cohort had significant less visuospatial ability than the NC-HI, their abilities were still comparable to the normative data, as demonstrated in the Corsi-block tapping and ROCFT test results. As discussed earlier, this showed a positive effect of hearing impairment toward the visuospatial ability among hearing aid users. However, it may make it difficult for an interpretation of the MCI-HI overall cognitive function by means of visuospatial tasks, that are intended to eliminate the confounding effect of their hearing impairment.

On the other hand, a preserved visuospatial ability among the MCI-HI cohort may help them in real-life situations such as lip-reading in conversations in noisy environments or navigating in busy streets when they cannot fully rely on their hearing for spatial and environmental sounds. These skills should be utilized and targeted in rehabilitation programmes for these patients.

7.3.3. Self-evaluation of hearing problems

The problem with memory and information retrieval among the MCI-HI population could potentially affect their self-reported hearing difficulties in various situations as reflected in the questionnaire responses. These questionnaires are commonly used in hearing aid centres to evaluate hearing difficulties among the patients.

The SSQ and mAIAD have previously identified self-reported hearing difficulties in individuals with abnormal auditory processing tests, and show strong to moderate correlation with a low left dichotic digit score (Bamiou et al., 2015). The MCI-HI had significantly lower left dichotic digit scores than the NC-HI but did not show significantly different self-reported scores in the questionnaires. This implies that these questionnaires fail to capture the hearing problems in the MCI-HI population.

We have demonstrated reliability problems of these questionnaires among the MCI-HI which could be a “hidden” population in any hearing aid centre. Therefore, the cognitive status of the client should always be taken into account when interpreting the self-reported hearing questionnaires. Moreover, cognitive screening of clients in the hearing aid centre may be beneficial to uncover the hidden mild cognitive impairment cases who may unknowingly need additional support with their hearing intervention care plan.

7.4. Limitations and weaknesses

7.4.1. Age difference in the controls (NC-HI) and the MCI-HI group

When considering the whole sample of participants recruited to our study, participants in the MCI-HI were older than the NC-HI. We addressed this issue by a sensitivity analysis matching the NC-HI to the MCI-HI. This sensitivity analysis yielded good and consistent results due to the excellent discrimination ability of the MoCA-HA tool. However, this may uncover a problem among MCI-HI in delaying hearing treatment which should be explored further.

We found that not only was the mean age of MCI-HA hearing aid users higher by over 8 years, but they also failed to report hearing difficulties in commonly used hearing-related questionnaires. This may delay their seeking for help behaviours which leads to the delay of the treatment.

Targeting to recruit the NC-HI cohort with a higher mean age may be a possible solution if this effect was anticipated when designing the study. However, recruiting older adult hearing aid users of mean age over 80 who have normal cognition may be challenging. Moreover, specifically targeting only older adults for the NC-HI cohort may lead to a control cohort that is not truly representative of the population in hearing aid centres, which may in turn interfere with the applicability of this tool in a real-life situation.

7.4.2. The limited sample size for hearing-related questionnaire problems

We calculated the sample size for our primary aim of validating MoCA-HA. Therefore, the sample size may be underpowered to detect differences in the hearing-related questionnaires. Moreover, we did not expect that the commonly used questionnaires among hearing aid users and auditory processing difficulties population would not be applicable for the specific group of hearing aid users who have mild cognitive impairment.

In order to identify the problem in more detail along with the insight of the MCI-HI population for appropriate modification of the questionnaires, a qualitative focus group interview type of study design may be more appropriate than our current quantitative study design. After the development of the adapted questionnaires, they would need to be validated in a quantitative study of a larger hearing aid users cohort than this current study.

7.5. The role of MoCA-HA in clinical and research settings

7.5.1. Screening for cognitive impairment in hearing-aid clinics

The MoCA-HA can be used for screening of potential cognitive impairment cases among hearing-aid users in clinical settings. The session is brief and can be incorporated in their annual hearing clinic visits for hearing-aid adjustment or their annual visits with the general practitioners (GPs). The MoCA-HA requires only minimal training and can be implemented by health care professionals (HCPs) such as audiologists, health visitors, nurses and GPs.

We have validated the MoCA-HA in this research to establish the referral cut-point of <26 to require onward referral. The sensitivity of detecting mild cognitive impairment with the MoCA-HA is over 90%, which is considerable for a screening tool. However, the interpretation of what the screening result means should be clearly communicated to the HCPs and the patients. Even though the specificity is 80% in the hearing-aid users aged over 65 in general, the specificity decreases significantly for hearing-aid users aged over 80 years. This means there are potential older cases, who may not be found to fulfil criteria of mild cognitive impairment diagnosis later after onward referral .

Further research is needed to evaluate the impact of onward referral of these false-positive cases. Their emotional and psychological distress, along with their family members, should be thoroughly investigated. The cost-effectiveness analysis should be done to identify the most appropriate screening and referral model which suit different clinical settings. A feasibility study of MoCA-HA use in various clinical settings could unveil further element which may affect clinical judgement for onward referral of the patients.

7.5.2. Evaluate improvement in cognitive ability after hearing-aid uses

The MoCA-HA can be used to evaluate the impact of hearing-aids in the improvement of cognitive performance by comparing the pre/post hearing-aid use. As discussed earlier in Chapter 1.4.3, the role of assistive devices such as hearing-aids is important as a facilitator to improve a person's performance.

For the hearing impaired population, the impairment is reflected in the decreased hearing capacities, which can limit their activities and participation in daily life. Wearing hearing-aids can help to reduce limitation in their task performance, even though the devices do not treat their hearing impairments per se, in that they still have the same level of hearing impairments and capacities (WHO, 2002). As a result, their hearing performance can be improved with the hearing-aids.

When testing their cognitive performances without hearing-aids through auditory tasks such as remembering the instruction/target words heard etc., these subjects may seem to perform worse, despite perfectly "normal" cognitive capacities due to hearing loss acting as a barrier. In this case, the improvements in their cognitive performances after wearing hearing-aids are solely mediated through the improved hearing performance. In this case, there is now no need for further treatment or rehabilitation for their cognitive function. However, the way to ensure "normal" cognitive capacity among the hearing-impaired population needs to be done in a way that hearing function cannot interfere with their results. The use of MoCA-HA, which is the non-auditory-based cognitive screening tool, can play a role in this regard.

If the cognitive capacities tested non-auditorily with MoCA-HA also reflect the decrease in their capacities from cognitive impairment, we now know that in addition to the hearing rehabilitation via assistive devices, we need to also offer cognitive stimulation and rehabilitation for the patients (Faucounau et al., 2010). Therefore, using the MoCA-HA to access the patients' cognitive capacity accurately is crucial in customising the patients' treatment plan.

Moreover, among these patients with combined hearing and cognitive impairment, the MoCA-HA can be used in the follow up after hearing-aid fitting sessions to determine whether their cognitive capacities have improved via the stimulation programmes, which also include auditory stimulation. MoCA-HA assessment at this stage can help to determine whether to continue the additional support on their cognitive stimulation.

7.6. Future directions for further research

7.6.1. The application of MoCA-HA in various populations

7.6.1.1. Normal hearing population

In chapter 4, we demonstrated that the performance of the NC-HI in MoCA-HA was not significantly different from the original MoCA performance of the older adult cohort in general (with presumably no known hearing impairment). This implied that no difference was found in the visually administered MoCA-HA and traditional auditory administered MoCA. It also suggested that the MoCA-HA could be implemented among the normal-hearing population. However, we did not specifically test this hypothesis.

By adding the normal hearing older adult population, we would ensure validity among older adults with all hearing abilities. The healthcare professionals can use MoCA-HA in all older adults without establishing their hearing impairment status beforehand. This would make the application of MoCA-HA in settings such as memory clinics, primary care clinics and GP practices simpler.

7.6.1.2. Dementia with hearing impairment population

The main aim of the MoCA-HA is to early identify hearing aid users who are at risk of mild cognitive impairment. Therefore in the current validation study, we opted to recruit the MCI-HI cohort and established the referral cut-point for them.

Implementing the MoCA-HA on the population with both dementia and hearing impairment would provide us with a referral cut-point in screening for potential dementia cases in the hearing aid centres. Further referral should be prioritized among these patients with lower MoCA-HA scores for a thorough assessment for timely dementia treatment if appropriate. Moreover, it would help in the follow-up process of the known MCI hearing aid users when a prompt referral is needed once they start to develop early dementia.

7.6.2. Modified hearing questionnaires for MCI population with hearing loss

7.6.2.1. Simple for the MCI cognition

MCI may result in impaired language performance (comprehension and expression) very early on in their disease progressions (McCullough et al., 2019) and also a problem in the word retrieval pathway as previously discussed. Therefore, when considering questionnaire implementation in this MCI population, their language and retrieval abilities should be taken into consideration.

The MCI-HI cohort recruited in this study was from community-dwelling samples. They may still actively engage in their community even though some reported that they stopped participating in some activities such as going to the church or their building meeting a long time ago due to their hearing problems. Therefore, they may not always recall or be able to describe the last time they were in these challenging situations as listed in the mAIAD and SSQ questionnaires.

A focus group interview of the MCI hearing aid users to determine the list of situations they commonly encountered may help to overcome the retrieval problem. Moreover, the questionnaires should use simple language for easy understanding among the cognitively challenged population since the ability to understand the concept described in the situation may also be impaired in this population (McCullough et al., 2019).

7.6.2.2. *Modified for relative to observe and answer*

Another alternative way to uncover the hearing problems of the MCI population is through informants. An individual with MCI may not be aware of their own problems so most cognitive screening questionnaires usually rely on input from their relatives as well as the patients (Brodaty et al., 2004, Abd Razak et al., 2019, McGovern et al., 2016). Previous research found that the informants may be more accurate in identifying cognitive impairment than the patients themselves in some populations such as in a low education cohort (Chio et al., 2018, Narasimhalu et al., 2008).

In the hearing field, using informant reported hearing issues is not commonly done in adults, since we believe that the reported difficulties should be directly from the one who experiences them. However, the informant observed questionnaires are commonly used in the paediatric hearing aid user population. Examples are the LittlEARS Auditory Questionnaire (Tsiakpini et al., 2004) for children from 0-2 years and the Parents' Evaluation of Aural/Oral Performance of Children (PEACH) with normative data from 0-5 years (Ching and Hill, 2007) which are used when the language may be a barrier for children in communicating hearing problems with the hearing aid (Bagatto et al., 2011).

As discussed earlier, language ability may be impaired among the MCI so the use of checklists of observed difficulties in various situations, similar to the lists that we usually give to the parents and teachers of the hearing-impaired hearing aid user children, may be used as an adaptation template. However, the situations need to be relevant and applicable to the older adult population.

Some sample situations already exist in the SSQ, mAIAD questionnaires that could be used for the informant such as “Do you hear the doorbell?” or “Can you tell which direction the car is coming from?”. In these cases, sometimes the MCI-HI may not be aware that they did not hear the doorbell or the car/bus coming toward them but the relatives should be able to report these issues.

7.7. Conclusion

We have developed and validated the Montreal cognitive assessment tool for hearing aid users (MoCA-HA). The development phase was done with feedback from clinical professionals and older adult hearing aid users. The tool has excellent discrimination property and also good correlations with other existing cognitive measures. MoCA-HA is suitable to be used in a hearing aid centre for early screening for potential mild cognitive impairment and research purposes. The appropriate cut-point for an onward cognitive assessment referral is 25/26, which yields a similarly high sensitivity (93.3%) to the traditional MoCA.

Older adults with combined cognitive impairment and hearing impairment can experience problems with memory and information retrieval which may affect their self-awareness of hearing problems. They may not report hearing difficulties when asked, despite having auditory processing difficulties demonstrated in dichotic digit test. This population may still have preserved visuospatial ability which could potentially add benefit for an auditory rehabilitation programme through facial cues and lip-reading.

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Appendix

Appendix A: Research Ethics Committee (REC) approval letter

NHS
Health Research Authority

London - Surrey Borders Research Ethics Committee
Research Ethics Committee (REC) London Centre
Ground Floor
Skipton House
80 London Road
London
SE1 6LH

Telephone: 0207 972 2568
Fax:

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

13 September 2018

Professor Doris Bamiou
UCL ear institute
332 Grays Inn Rd, Kings Cross, London
WC1X 8EE

Dear Professor Bamiou

Study title:	**Validation of the "Montreal Cognitive Assessment (MoCA) and Addenbrooke's Cognitive Examination III (ACE-III) " as cognitive screening tools for the hearing impaired.**
REC reference:	**18/LO/1225**
Protocol number:	**18/0306**
IRAS project ID:	**247176**

Thank you for your letter of 31 August 2018 , responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further

information, or wish to make a request to postpone publication, please contact hra.studyregistration@nhs.net outlining the reasons for your request.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System, at www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering letter on headed paper [Cover letter : revision documents]	1.0	02 August 2018
Covering letter on headed paper [Cover letter : revision documents]	v1	02 August 2018
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [UCL insurance]	v1.0	29 May 2018
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only)	1	24 July 2017
HRA Schedule of Events	1	04 July 2018
HRA Statement of Activities	2	05 July 2018
IRAS Application Form [IRAS_Form_02072018]		02 July 2018
IRAS Application Form XML file [IRAS_Form_02072018]		02 July 2018
IRAS Checklist XML [Checklist_30082018]		30 August 2018
Letter from funder [funding letter]	v1.0	06 June 2018
Letters of invitation to participant [recruitment flyer]	v1.1	29 August 2018
Non-validated questionnaire [ACE-III written for hearing impaired]	1.0	29 June 2018
Participant consent form [consent]	1.1	31 July 2018
Participant consent form [consent_communication partner]	1.0	31 July 2018
Participant consent form [consent]	1.1	31 July 2018
Participant consent form [consent_communication partner]	1.0	31 July 2018
Participant information sheet (PIS) [PIS_normal cognition]	v1.2	29 August 2018
Participant information sheet (PIS) [PIS_communication partner]	v1.1	29 August 2018
Participant information sheet (PIS) [PIS_MCI]	v1.2	29 August 2018
Participant information sheet (PIS) [PIS_dementia]	v1.2	29 August 2018
Research protocol or project proposal [Project protocol]	1.1	31 July 2018
Research protocol or project proposal [Project protocol]	1.1	31 July 2018
Summary CV for Chief Investigator (CI) [CI summary CV]	v1.0	05 June 2018

Summary CV for student [student CV]	v1.0	15 May 2018
Summary CV for supervisor (student research) [first supervisor CV]	v1.0	05 June 2018
Summary CV for supervisor (student research) [second supervisor CV]	v1.0	05 June 2018
Validated questionnaire [MOCA for hearing impaired]	1.0	29 June 2018
Validated questionnaire [MOCA original]	8.1	01 July 2017
Validated questionnaire [ACE-III]	1.0	20 December 2012
Validated questionnaire [SSQ questionnairs]	v1.0	25 November 2012
Validated questionnaire [m-AIAD questionnairs]	v1.0	01 June 2013

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at
http://www.hra.nhs.uk/hra-training/

18/LO/1225	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

[redacted]

Sir Adrian Baillie
Chair

Email:nrescommittee.london-surreyborders@nhs.net

Enclosures: "After ethical review – guidance for researchers"

Copy to: *Ms Jessica Broni-Tabi*
Mr Joe Marley, University College London Hospital NHS Trust

Appendix B: REC amendment approval letter

NHS
Health Research Authority

London - Surrey Borders Research Ethics Committee
Research Ethics Committee (REC) London Centre
Ground Floor
Skipton House
80 London Road
London
SE1 6LH

Tel: 02071048052

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

02 November 2018

Miss Nattawan Utoomprurkporn
UCL Ear institute
332 Grays Inn Rd, Kings Cross, London
WC1X 8EE

Dear Miss Utoomprurkporn

Study title:	**Validation of the "Montreal Cognitive Assessment (MoCA) and Addenbrooke's Cognitive Examination III (ACE-III) " as cognitive screening tools for the hearing impaired.**
REC reference:	**18/LO/1225**
Protocol number:	**18/0306**
Amendment number:	**1**
Amendment date:	**03 October 2018**
IRAS project ID:	**247176**

Approval was sought for the following points:

An amendment was made to the inclusion and exclusion criteria to include the more severe to profound hearing loss group to cover all range of hearing loss population for the tools validation.

To exclude the congenital and childhood onset hearing loss population for the "normal cognition group" since there is evident that this group may have sub-clinical cognitive issue.

The above amendment was reviewed at the meeting of the Sub-Committee held on 17 October 2018 by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Notice of Substantial Amendment (non-CTIMP) [AmendmentForm_ReadyForSubmission]	1	03 October 2018
Research protocol or project proposal [cognitive validation tools_protocol version 1.2_3.10.2018_clean copy]	1.2	03 October 2018
Research protocol or project proposal [cognitive validation tools_protocol version 1.2_3.10.2018_highlighted]	1.2	03 October 2018

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our Research Ethics Committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

18/LO/1225:	**Please quote this number on all correspondence**

Yours sincerely

[redacted]

Ms. Christine Braithwaite
Chair

E-mail: nrescommittee.london-surreyborders@nhs.net

Enclosures: *List of names and professions of members who took part in the*

review

Copy to: *Mr Joe Marley, University College London Hospital NHS Trust*
miss nattawan utoomprurkporn

London - Surrey Borders Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 17 October 2018

Committee Members:

Name	*Profession*	*Present*	*Notes*
Mr. Hakam Abbass	Clinical Research Nurse	Yes	
Ms. Christine Braithwaite	Director of Standards and Policy	Yes	Chair

Also in attendance:

Name	*Position (or reason for attending)*
Ms Noorisha Rahman	REC Assistant

Appendix C: Health Research Authority (HRA) approval letter

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Professor Doris Bamiou
UCL ear institute
332 Grays Inn Rd, Kings Cross, London
WC1X 8EE

Email: hra.approval@nhs.net
Research-permissions@wales.nhs.uk

14 September 2018

Dear Professor Bamiou

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Validation of the "Montreal Cognitive Assessment (MoCA) and Addenbrooke's Cognitive Examination III (ACE-III) " as cognitive screening tools for the hearing impaired.**
IRAS project ID:	**247176**
Protocol number:	**18/0306**
REC reference:	**18/LO/1225**
Sponsor	**University College London**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

How should I continue to work with participating NHS organisations in England and Wales?
You should now provide a copy of this letter to all participating NHS organisations in England and Wales, as well as any documentation that has been updated as a result of the assessment.

Following the arranging of capacity and capability, participating NHS organisations should **formally confirm** their capacity and capability to undertake the study. How this will be confirmed is detailed in the "*summary of assessment*" section towards the end of this letter.

You should provide, if you have not already done so, detailed instructions to each organisation as to how you will notify them that research activities may commence at site following their confirmation of capacity and capability (e.g. provision by you of a 'green light' email, formal notification following a site initiation visit, activities may commence immediately following confirmation by participating organisation, etc.).

It is important that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details of the research management function for each organisation can be accessed here.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within the devolved administrations of Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) has been sent to the coordinating centre of each participating nation. You should work with the relevant national coordinating functions to ensure any nation specific checks are complete, and with each site so that they are able to give management permission for the study to begin.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?
The document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

I am a participating NHS organisation in England or Wales. What should I do once I receive this letter?
You should work with the applicant and sponsor to complete any outstanding arrangements so you are able to confirm capacity and capability in line with the information provided in this letter.

The sponsor contact for this application is as follows:

Ms Jessica Broni-Tabi
E-mail randd@uclh.nhs.uk
Telephone 02034472122

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **247176**. Please quote this on all correspondence.

IRAS project ID	247176

Yours sincerely

Catherine Adams
Senior Assessor
Email: hra.approval@nhs.net

Copy to: *Ms Jessica Broni-Tabi, Sponsor's Representative*
Mr Joe Marley, University College London Hospital NHS Trust

IRAS project ID	247176

List of Documents

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Covering letter on headed paper [Cover letter : revision documents]	1.0	02 August 2018
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [UCL insurance]	v1.0	29 May 2018
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only)	1	24 July 2017
HRA Schedule of Events	1	04 July 2018
HRA Statement of Activities	2	05 July 2018
IRAS Application Form [IRAS_Form_02072018]		02 July 2018
Letter from funder [funding letter]	v1.0	06 June 2018
Letters of invitation to participant [recruitment flyer]	v1.1	29 August 2018
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Participant consent form [consent]	1.1	31 July 2018
Participant information sheet (PIS) [PIS_normal cognition]	v1.2	29 August 2018
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Participant information sheet (PIS) [PIS_dementia]	v1.2	29 August 2018
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Validated questionnaire [SSQ questionnairs]	v1.0	25 November 2012
Validated questionnaire [m-AIAD questionnairs]	v1.0	01 June 2013

IRAS project ID	247176

Information for Sponsors and Participating NHS Organisations

The below provides all parties with information to support the arranging of capacity and capability with participating NHS organisations in England and Wales. This is intended to be an accurate reflection of the study at the time of issue of this letter. As part of the application process, details may change prior to a Letter of HRA and HCRW Approval being issued. NHS organisations should be assured that we will continue to work with the sponsor on any assessment criteria which are 'pending', and this should not impact on the arranging or capacity and capability.

Assessment criteria

Section	Assessment Criteria	Compliant with Standards?	Comments
1.1	IRAS application completed correctly	Yes	No comments
2.1	Participant information/consent documents and consent process	Yes	The information sheets have been update to comply with GDPR wording
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	A statement of activities will act as agreement of an NHS organisation to participate. The sponsor is not requesting and does not expect any other site agreement.
4.2	Insurance/indemnity arrangements assessed	Yes	Valid insurance certificate supplied
4.3	Financial arrangements assessed	Yes	No comments
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No comments
5.2	CTIMPS – Arrangements for compliance with the Clinical	Not Applicable	No comments

IRAS project ID	247176

Section	Assessment Criteria	Compliant with Standards?	Comments
	Trials Regulations assessed		
5.3	Compliance with any applicable laws or regulations	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Yes	No comments
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England and Wales

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.

All organisations will be undertaking the same activity (i.e. there is only one 'site-type') as detailed in the protocol and supporting documentation

The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England and Wales in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. Where applicable, the local LCRN contact should also be copied into this correspondence.

If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England and Wales which are not provided in IRAS or on the HRA or HCRW websites, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net, or HCRW at Research-permissions@wales.nhs.uk. We will work with these organisations to achieve a consistent approach to information provision.

IRAS project ID	247176

Principal Investigator Suitability

This confirms whether the sponsor's position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England and Wales, and the minimum expectations for education, training and experience that PIs should meet (where applicable).
A Principal Investigator is expected at participating organisations. GCP training is not a generic training expectation, in line with the HRA/HCRW/MHRA statement on training expectations.

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken.
Where arrangements are not already in place, research staff not employed by the NHS host organisation undertaking any of the research activities listed in the research application would be expected to obtain an honorary research contract from one NHS organisation (if university employed), followed by Letters of Access for subsequent organisations. This would be on the basis of a Research Passport (if university employed) or an NHS to NHS confirmation of pre-engagement checks letter (if NHS employed). These should confirm enhanced DBS checks, including appropriate barred list checks, and occupational health clearance. Where arrangements are not already in place, for research team members only administering questionnaires or surveys, a Letter of Access based on standard DBS checks and occupational health clearance would be appropriate.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales in study set-up.
The applicant has indicated that they intend to apply for inclusion on the NIHR CRN Portfolio. .

Appendix D: Participant information sheet for NC-HI cohort

University College London Hospitals NHS Foundation Trust

UCL

Participant information sheet

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of trial: Validation of "Montreal Cognitive Assessment (MoCA) and Addenbrooke's Cognitive Examination III (ACE-III)" as a cognitive screening tools for the hearing impaired.

Department: Ear institute, Faculty of Brain science

Name and contact details of the Trial Manager:

Nattawan Utoomprurkporn

Email : n.utoomprurkporn.12@ud.ac.uk

Tel : 020 34567870

Ear institute, Faculty of Brain science, University College London

We would like to invite you to take part in a research project

- Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve for you.
- Please take the time to read the following information carefully. Discuss it with friends and relatives if you wish. Take time to decide whether or not you wish to take part.
- Ask us if there is anything that is not clear or if you would like more information.
- Thank you for reading this information sheet.

1. Why are we doing this trial?

Hearing problems are very common in older adults, but we don't have good quality pencil and paper tests to identify whether people with hearing loss might have dementia or not. The purpose of this trial is to develop such tests.

Early and appropriate detection of dementia among older adult with hearing loss is very important. Early detection of dementia can help these older adults, who are at risk, to get timely intervention needed for them.

2. Why am I being asked to take part?

We have invited you to take part in this trial because you have a diagnosis of hearing loss and are aged 65 or over. 30 participants of hearing loss with normal cognition will be recruited from total of 90 participants in this trial.

We need people with hearing loss to take part in this trial because we need to know how easy they find our new tests in comparison to people with mild cognitive impairment or dementia.

3. Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You can withdraw at any time without giving a reason and without it affecting any benefits that you are entitled to.

If you do withdraw, any identifiable/personal information we have collected about you will be destroyed. Data which is not identifiable may be retained.

4. What will happen to me if I take part?

If you decide you would like to take part in the trial, a researcher will arrange a convenient time to meet with you to carry out a 'screening' visit. This initial visit will assess whether you are eligible to take part in the study. This assessment will involve doing a hearing test and answering some questions.

If the tests show that you are eligible to take part in the study then there will ask you to fill in some questionnaires and short tests of your memory, language and thinking abilities.

If you have a communication partner (someone you see on a near daily basis) they will also be invited to take part if you are happy for them to do so. If they do not formally want to take part, they do not have to.

The whole session will last about 2 hours, but you can take a break or do this over several visits if that suits you.

5. What are the possible benefits of taking part?

We believe participants could potentially benefit from the dementia tests and hearing tests, since they may pick up issues which were not previously known about and, which we may then be able to help.

More broadly, the information we get may lead good quality dementia tests for people with hearing loss, which could help to improve things for people with hearing loss in the future.

6. What are the possible disadvantages and risks of taking part?

We do not feel there are significant risks associated with this project.

You will spend about 2 hours completing the assessment. As mentioned, previously if you are tired, or wish to take a break for any reason you can do that before completing the rest of the study.

All the tests and questionnaires are routinely used in the NHS and are not known to cause upset or harm. However, if you feel upset or distressed by the assessments you can speak to the researcher. You can also withdraw from the trial at any point, without giving a reason.

7. What if something goes wrong?

If you have a concern about any aspect of this trial you should ask to speak to the researcher or you can contact the Chief Investigator, Nattawan Utoomprurkprurkporn (email n.utoomprurkporn.12@ucl.ac.uk).

If you feel your complaint has not been handled satisfactorily, please contact the Patient and Liaison Service (PALS) at your NHS Trust by email, uclh.pals@nhs.net or telephone, 020 3447 3042. PALS can provide information on Trust policies and put you in touch with the relevant people to help your resolve your concerns. PALS can also assist people in making formal complaints if necessary. You can find your nearest PALS office on the NHS choices website, or ask your GP surgery or hospital for the details (or phone NHS on 111).

8. Will my taking part in this project be kept confidential?

A copy of this information sheet and your signed consent form will be placed in your medical notes so that any health care professionals involved in your care are aware of your participation in the trial.

All the information that we collect about you during the course of the research will be stored at University College London and kept strictly confidential and only accessed by authorised members of the research team. All data collected about you will be anonymised by using participant ID numbers which will uniquely identify each individual and be stored in a locked filing cabinet. The anonymised data will also be stored electronically on password protected computers. Identifiable information is only kept for a short period where it is necessary for the conduct of the trial. You will not be able to be identified in any ensuing reports or publications. The research team will occasionally need to allow monitors from Regulatory Authorities to inspect the study paperwork, in order to meet legal, ethical and safety requirements. All individuals who have access to data will be bound by strict data protection and confidentiality rules.

Limits to confidentiality

If during the interview or assessments you tell the researcher something that makes them concerned for your safety, or the safety of others, they will have to share this information as appropriate with the safeguarding team.

9. What will happen to the results of this trial?

We intend to publish the results of this study in scientific journals and public platform. All results will have your personal information removed so you cannot be identified in any published articles.

10. Data Protection Privacy Notice

As a university (UCL), we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your

personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

The data controller for this project will be University College London (UCL). The UCL Data Protection Office provides oversight of UCL activities involving the processing of personal data, and can be contacted at data-protection@ucl.ac.uk. UCL's Data Protection Officer is Lee Shailer and he can also be contacted at data-protection@ucl.ac.uk.

Your personal data will be processed so long as it is required for the research project. If we are able to anonymise or pseudonymise the personal data you provide we will undertake this, and will endeavour to minimise the processing of personal data wherever possible.

University College London (UCL) is the sponsor for this study based in the United Kingdom. We will be using information from you and/or your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. UCL will destroy all identifiable information about you immediately after the study has finished (The duration of this study is 3 years, your identifiable data will be kept only until 2021).

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You can find out more about how we use your information, if you are concerned about how your personal data is being processed, please contact UCL in the first instance at data-protection@ud.ac.uk. If you remain unsatisfied, you may wish to contact the Information Commissioner's Office (ICO). Contact details, and details of data subject rights, are available on the ICO website at: https://ico.org.uk/for-organisations/data-protection-reform/overview-of-the-gdpr/individuals-rights/

UCLH/Camden and Islington NHS foundation trust will collect information from you and/or your medical records for this research study in accordance with our instructions.

UCLH/Camden and Islington NHS foundation trust will keep your name, NHS number and contact details confidential and will not pass this information to our sponsor UCL. UCLH/Camden and Islington NHS foundation trust will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from UCL and regulatory organisations may look at your medical and research records to check the accuracy of the research study. UCL will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

UCLH/Camden and Islington NHS foundation trust will destroy identifiable information about you from this study immediately after the study has finished (This study is intended to be for 3 years until 2021].

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

11. Who is organising and funding the trial?

This trial is sponsor and organised by University College London (UCL).

The funding of the trial is from "The national Brain Appeal" (Funding advances in neurology and neurology).

12. Who has reviewed the trial?

This trial has been reviewed by an independent group of people, called the Research Ethics Committee, to protect your safety, rights, well-being and dignity. The trial has been given a favourable opinion by (London - Surrey Borders Research Ethics Committee) Research Ethics Committee.

13. Contact for further information

Nattawan Utoomprurkporn

Ear institute, Faculty of Brain science, University College London
332 Grays inn road, Kings cross, London WC1X 8EE
Tel 020 34567870
Email: n.utoomprurkporn.12@ucl.ac.uk

Professor Doris Eva Bamiou (Chief investigator of the trial)

Ear institute, Faculty of Brain science, University College London
332 Grays inn road, Kings cross, London WC1X 8EE
Tel 020 34567870

Thank you for reading this information sheet and for considering to take part in this research trial.

Appendix E: Participant information sheet for the communication partner of NC-HI cohort

University College London Hospitals NHS Foundation Trust

UCL

Participant information sheet

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of trial: Validation of "Montreal Cognitive Assessment (MoCA) and Addenbrooke's Cognitive Examination III (ACE-III) " as a cognitive screening tools for the hearing impaired.

Department: Ear institute, Faculty of Brain science

Name and contact details of the Trial Manager:

Nattawan Utoomprurkporn

Email : n.utoomprurkporn.12@ucl.ac.uk

Tel : 020 34567870

Ear institute, Faculty of Brain science, University College London

We would like to invite you to take part in a research project

- Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve for you.
- Please take the time to read the following information carefully. Discuss it with friends and relatives if you wish. Take time to decide whether or not you wish to take part.
- Ask us if there is anything that is not clear or if you would like more information.
- Thank you for reading this information sheet.

1. Why are we doing this trial?

Hearing problems are very common in older adults, but we don't have good quality pencil and paper tests to identify whether people with hearing loss have dementia or not. The purpose of this trial is to develop such tests. This is

particularly important, because, if we can detect who has dementia or who may be at risk of dementia early, we can get timely intervention for them.

2. Why am I being asked to take part?

We have invited you to take part in this trial because you are a friend, carer, spouse or communication partner of someone who is participating in the research project.

3. Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You can withdraw at any time without giving a reason and without it affecting any benefits that you are entitled to.

If you do withdraw, any identifiable/personal information we have collected about you will be destroyed. Data which is not identifiable may be retained.

4. What will happen to me if I take part?

If you decide you would like to take part in the trial, a researcher will arrange a mutually convenient time to meet with you to answer a few questions about the person who is participating in this research project. The questions are routinely used by clinicians such as general practitioners. No personal data or any information about you will be collected by the researchers.

5. What are the possible benefits of taking part?

the information we get may lead good quality dementia tests for people with hearing loss, which could help to improve things for people with hearing loss in the future

6. What are the possible disadvantages and risks of taking part?

We do not feel there are any risks associated with this trial. You will spend about 5 minutes to complete the questionnaire. If at any time you are upset or wish to move on during the assessments, you can inform the researcher. If you feel upset or distressed by the assessments you can speak to the researcher immediately. You can also withdraw from the trial at any point, without giving a reason.

7. What if something goes wrong?

If you have a concern about any aspect of this trial you should ask to speak to the researcher or you can contact the Chief Investigator, Nattawan Utoomprurkprurkporn (email n.utoomprurkporn.12@ucl.ac.uk).

If you feel your complaint has not been handled satisfactorily, please contact the Patient and Liaison Service (PALS) at your NHS Trust. PALS can provide information on Trust policies and put you in touch with the relevant people to help your resolve your concerns. PALS can also assist people in making formal complaints if necessary. You can find your nearest PALS office on the NHS choices website, or ask your GP surgery or hospital for the details (or phone NHS on 111).

8. Will my taking part in this project be kept confidential?

A copy of this information sheet and your signed consent form will be placed in a secure place.

All the information that we collect from you during the course of the research will be stored at University College London and kept strictly confidential and only accessed by authorised members of the research team. All data collected about you will be anonymised by using participant ID numbers which will uniquely identify each individual and be stored in a locked filing cabinet. The anonymised data will also be stored electronically on password protected

computers. Identifiable information is only kept for a short period where it is necessary for the conduct of the trial. You will not be able to be identified in any ensuing reports or publications. The research team will occasionally need to allow monitors from Regulatory Authorities to inspect the study paperwork, in order to meet legal, ethical and safety requirements. All individuals who have access to data will be bound by strict data protection and confidentiality rules.

Limits to confidentiality

If during the interview or assessments you tell the researcher something that makes them concerned for your safety, or the safety of others, they will have to share this information as appropriate with the safeguarding team.

9. What will happen to the results of this trial?

We intend to publish the results of this study in scientific journals and public platform. All results will have your personal information removed so you cannot be identified in any published articles.

10. Data Protection Privacy Notice

As a university (UCL), we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

The data controller for this project will be University College London (UCL). The UCL Data Protection Office provides oversight of UCL activities involving the processing of personal data, and can be contacted at data-protection@ucl.ac.uk. UCL's Data Protection Officer is Lee Shailer and he can also be contacted at data-protection@ucl.ac.uk.

Your personal data will be processed so long as it is required for the research project. If we are able to anonymise or pseudonymise the personal data you provide we will undertake this, and will endeavour to minimise the processing of personal data wherever possible.

University College London (UCL) is the sponsor for this study based in the United Kingdom. We will be using information from you and/or your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. UCL will destroy all identifiable information about you immediately after the study has finished (The duration of this study is 3 years, your identifiable data will be kept only until 2021).

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the

information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information, if you are concerned about how your personal data is being processed, please contact UCL in the first instance at data-protection@ucl.ac.uk. If you remain unsatisfied, you may wish to contact the Information Commissioner's Office (ICO). Contact details, and details of data subject rights, are available on the ICO website at: https://ico.org.uk/for-organisations/data-protection-reform/overview-of-the-gdpr/individuals-rights/

UCLH/Camden and Islington NHS foundation trust will collect information from you and/or your medical records for this research study in accordance with our instructions.

UCLH/Camden and Islington NHS foundation trust will keep your name, NHS number and contact details confidential and will not pass this information to our sponsor UCL. UCLH/Camden and Islington NHS foundation trust will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from UCL and regulatory organisations may look at your medical and research records to check the accuracy of the research study. UCL will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

UCLH/Camden and Islington NHS foundation trust will destroy identifiable information about you from this study immediately after the study has finished (This study is intended to be for 3 years until 2021].

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by

organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

11. Who is organising and funding the trial?

This trial is sponsor and organised by University College London (UCL).

The funding of the trial is from "The national Brain Appeal" (Funding advances in neurology and neurology).

12. Who has reviewed the trial?

This trial has been reviewed by an independent group of people, called the Research Ethics Committee, to protect your safety, rights, well-being and dignity. The trial has been given a favourable opinion by (London - Surrey Borders Research Ethics Committee) Research Ethics Committee.

13. Contact for further information

Nattawan Utoomprurkporn

Ear institute, Faculty of Brain science, University College London
332 Grays inn road,Kings cross, London WC1X 8EE
Tel 020 34567870
Email: n.utoomprurkporn.12@ucl.ac.uk

Professor Doris Eva Bamiou (Chief investigator of the trial)

Ear institute, Faculty of Brain science, University College London

University College London Hospitals NHS Foundation Trust

UCL

332 Grays inn road,Kings cross, London WC1X 8EE
Tel 020 34567870

Thank you for reading this information sheet and for considering to take part in this research trial.

Appendix F: Participant information sheet for the MCI-HI cohort

University College London Hospitals NHS Foundation Trust

UCL

Participant information sheet

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of trial: Validation of "Montreal Cognitive Assessment (MoCA) and Addenbrooke's Cognitive Examination III (ACE-III) " as a cognitive screening tools for the hearing impaired.

Department: Ear institute, Faculty of Brain science

Name and contact details of the Trial Manager:

Nattawan Utoomprurkporn

Email : n.utoomprurkporn.12@ucl.ac.uk

Tel : 020 34567870, 020 76798884

Ear institute, Faculty of Brain science, University College London

We would like to invite you to take part in a research project

- Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve for you.
- Please take the time to read the following information carefully. Discuss it with friends and relatives if you wish. Take time to decide whether or not you wish to take part.
- Ask us if there is anything that is not clear or if you would like more information.
- Thank you for reading this information sheet.

1. Why are we doing this trial?

Hearing problems are very common in older adults, but we don't have good quality pencil and paper tests to identify whether people with hearing loss might have dementia or not. The purpose of this trial is to develop such tests.

Early and appropriate detection of dementia among older adult with hearing loss is very important. Early detection of dementia can help these older adults, who are at risk, to get timely intervention needed for them.

2. Why am I being asked to take part?

We have invited you to take part in this trial because you have a diagnosis of hearing loss and are aged 65 or over. 30 participants of mild cognitive impairment with hearing loss will be recruited from total of 90 participants in this trial.

We need people with mild cognitive impairment to take part in this trial because we need to know how easy they find our new tests in comparison to people without mild cognitive impairment or dementia.

3. Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You can withdraw at any time without giving a reason and without it affecting any benefits that you are entitled to.

If you do withdraw, any identifiable/personal information we have collected about you will be destroyed. Data which is not identifiable may be retained.

4. What will happen to me if I take part?

If you decide you would like to take part in the trial, a researcher will arrange a convenient time to meet with you to carry out a 'screening' visit. This initial visit will assess whether you are eligible to take part in the study. This assessment will involve doing a hearing test and answering some questions.

If the tests show that you are eligible to take part in the study then there will ask you to fill in some questionnaires and short tests of your memory, language and thinking abilities.

If you have a communication partner (someone you see on a near daily basis) they will also be invited to take part if you are happy for them to do so. If they do not formally want to take part, they do not have to.

The whole session will last about 2 hours, but you can take a break or do this over several visits if that suits you.

Then we will ask for your permission to contact your key worker in the memory clinic about your results at your next routine annual follow up. This is to examine whether there has been any change in your memory, intellectual or language abilities over the course of the year.

5. What are the possible benefits of taking part?

We believe participants could potentially benefit from the dementia tests and hearing tests, since they may pick up issues which were not previously known about and, which we may then be able to help.

More broadly, the information we get may lead good quality dementia tests for people with hearing loss, which could help to improve things for people with hearing loss in the future.

6. What are the possible disadvantages and risks of taking part?

We do not feel there are significant risks associated with this project.

You will spend about 2 hours completing the assessment. As mentioned, previously if you are tired, or wish to take a break for any reason you can do that before completing the rest of the study.

All the tests and questionnaires are routinely used in the NHS and are not known to cause upset or harm. However, if you feel upset or distressed by the assessments you can speak to the researcher. You can also withdraw from the trial at any point, without giving a reason.

7. What if something goes wrong?

If you have a concern about any aspect of this trial you should ask to speak to the researcher or you can contact the Chief Investigator, Nattawan Utoomprurkprurkporn (email n.utoomprurkporn.12@ucl.ac.uk).

If you feel your complaint has not been handled satisfactorily, please contact the Patient and Liaison Service (PALS) at your NHS Trust by email, uclh.pals@nhs.net or telephone, 020 3447 3042. PALS can provide information on Trust policies and put you in touch with the relevant people to help your resolve your concerns. PALS can also assist people in making formal complaints if necessary. You can find your nearest PALS office on the NHS choices website, or ask your GP surgery or hospital for the details (or phone NHS on 111).

8. Will my taking part in this project be kept confidential?

A copy of this information sheet and your signed consent form will be placed in your medical notes so that any health care professionals involved in your care are aware of your participation in the trial.

All the information that we collect about you during the course of the research will be stored at University College London and kept strictly confidential and only accessed by authorised members of the research team. All data collected about you will be anonymised by using participant ID numbers which will uniquely identify each individual and be stored in a locked filing cabinet. The anonymised data will also be stored electronically on password protected computers. Identifiable information is only kept for a short period where it is necessary for the conduct of the trial. You will not be able to be identified in any ensuing reports or publications. The research team will occasionally need to allow monitors from Regulatory Authorities to inspect the study paperwork, in order to meet legal, ethical and safety requirements. All individuals who have access to data will be bound by strict data protection and confidentiality rules.

Limits to confidentiality

If during the interview or assessments you tell the researcher something that makes them concerned for your safety, or the safety of others, they will have to share this information as appropriate with the safeguarding team.

9. What will happen to the results of this trial?

We intend to publish the results of this study in scientific journals and public platform. All results will have your personal information removed so you cannot be identified in any published articles.

10. Data Protection Privacy Notice

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If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your

personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

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UCLH/Camden and Islington NHS foundation trust will collect information from you and/or your medical records for this research study in accordance with our instructions.

UCLH/Camden and Islington NHS foundation trust will keep your name, NHS number and contact details confidential and will not pass this information to our sponsor UCL. UCLH/Camden and Islington NHS foundation trust will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from UCL and regulatory organisations may look at your medical and research records to check the accuracy of the research study. UCL will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

UCLH/Camden and Islington NHS foundation trust will destroy identifiable information about you from this study immediately after the study has finished (This study is intended to be for 3 years until 2021].

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

11. Who is organising and funding the trial?

This trial is sponsor and organised by University College London (UCL).

The funding of the trial is from "The national Brain Appeal" (Funding advances in neurology and neurology).

12. Who has reviewed the trial?

This trial has been reviewed by an independent group of people, called the Research Ethics Committee, to protect your safety, rights, well-being and dignity. The trial has been given a favourable opinion by (London - Surrey Borders Research Ethics Committee) Research Ethics Committee.

13. Contact for further information

Nattawan Utoomprurkporn

Ear institute, Faculty of Brain science, University College London
332 Grays inn road, Kings cross, London WC1X 8EE
Tel 020 34567870
Email: n.utoomprurkporn.12@ucl.ac.uk

Professor Doris Eva Bamiou (Chief investigator of the trial)

Ear institute, Faculty of Brain science, University College London
332 Grays inn road, Kings cross, London WC1X 8EE
Tel 020 34567870

Thank you for reading this information sheet and for considering to take part in this research trial.

Appendix G: Consent form

IRAS ID:247176

Centre Number: Study Number:

Participant Identification Number for this trial:

CONSENT FORM

Title of Project: Validation of "Montreal Cognitive Assessment (MoCA) and the Addenbrooke's Cognitive Examination III (ACE-III)" as a cognitive screening tool for the hearing impaired.

Name of Researcher:

	Please initial box
1. I confirm that I have read the information sheet dated 29/8/2018 (version 1.2.) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	☐
3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from University College London, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. This includes data being collected at follow-up clinic visits about the progression of my medical conditions during the 3 years study period.	☐
4. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.	☐
5. I understand that the information held and maintained by the Health and Social Care Information Centre (or amend as appropriate) and other central UK NHS bodies may be used to help contact me or provide information about my health status.	☐
6. I agree to take part in the above study.	☐

Name of Participant	Date	Signature
Name of Person taking consent	Date	Signature

When completed: 1 for participant; 1 for researcher site file; 1 to be kept in medical notes.

Appendix H: Dichotic digits scoring sheet

EXTENDED DICHTOIC DIGIT TEST [Frank Musiek, Ph.D.]

TEST #1

10	3	9	2
6	10	1	2
9	2	3	4
9	3	4	1
3	8	5	9
1	8	3	6
5	8	6	9
5	10	4	8
9	4	5	6
5	6	3	1
2	9	1	6
3	5	1	4
2	1	4	6
9	1	3	10
5	9	1	6
2	8	6	5
4	10	8	6
3	10	4	8
1	5	6	2
9	6	3	4

Left Ear _____ Right Ear Score _____

TEST #2

1	9	2	3
5	9	1	6
4	2	1	8
5	6	8	9
5	10	2	8
3	2	1	4
5	2	3	6
2	1	10	3
4	10	5	3
6	8	4	9
2	5	3	4
3	9	2	10
2	8	1	3
5	4	8	6
1	5	2	6
4	3	1	5
6	1	10	4
10	1	5	4
6	4	3	5
9	5	6	3

Left Ear _____ Right Ear Score _____

TEST #3

10	2	1	3
5	1	10	2
8	9	1	2
9	1	6	10
1	4	2	10
6	1	2	10
1	2	3	8
2	10	9	3
1	9	8	4
10	9	3	1
9	4	5	1
2	5	6	1
3	6	8	10
9	5	6	2
1	9	4	8
6	2	3	9
8	1	3	6
8	6	5	3
1	4	10	5
4	5	2	3

Left Ear _____ Right Ear Score _____

TEST #4

6	5	10	8
10	6	3	2
10	3	9	8
2	5	10	6
8	10	2	4
3	2	1	10
9	6	8	1
5	1	10	8
6	5	4	8
8	4	2	3
8	4	1	5
2	9	4	6
1	9	10	5
4	3	8	2
2	4	9	6
9	5	6	8
10	3	4	6
8	3	9	10
2	1	8	5
2	8	4	9

Left Ear _____ Right Ear Score _____

Appendix I: Modified Amsterdam Inventory for Auditory Disability and Handicap

Participant ID: _ _ _ _-_ _ _ _ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

Modified Amsterdam Inventory for Auditory Disability and Handicap

1. Can you understand a shop assistant in a crowded shop?

1a. At present

☐ Almost never ☐ occasionally ☐ frequently ☐ almost always

1b. Before

☐ Almost never ☐ occasionally ☐ frequently ☐ almost always

2. Can you carry on a conversation with someone in a quiet room?

2a. At present

☐ Almost never ☐ occasionally ☐ frequently ☐ almost always

2b. Before

☐ Almost never ☐ occasionally ☐ frequently ☐ almost always

3. Do you immediately hear from which direction a car is approaching when outside?

3a. At present

☐ Almost never ☐ occasionally ☐ frequently ☐ almost always

3b. Before

☐ Almost never ☐ occasionally ☐ frequently ☐ almost always

4. Can you hear cars passing by?

4a. At present

□ Almost never □ occasionally □ frequently □ almost always

4b. Before

□ Almost never □ occasionally □ frequently □ almost always

5. Do you recognise members of your family by their voices?

5a. At present

□ Almost never □ occasionally □ frequently □ almost always

5b. Before

□ Almost never □ occasionally □ frequently □ almost always

6. Can you recognise melodies in music or songs?

6a. At present

□ Almost never □ occasionally □ frequently □ almost always

6b. Before

□ Almost never □ occasionally □ frequently □ almost always

7. Can you carry on a conversation with someone in a crowded meeting?

7a. At present

□ Almost never □ occasionally □ frequently □ almost always

7b. Before

□ Almost never □ occasionally □ frequently □ almost always

8. Can you carry on a telephone conversation in a quiet room?

8a. At present

□ Almost never □ occasionally □ frequently □ almost always

8b. Before

□ Almost never □ occasionally □ frequently □ almost always

9. Can you hear from which corner of a lecture room someone is asking a question during a meeting?

9a. At present

□ Almost never □ occasionally □ frequently □ almost always

9b. Before

□ Almost never □ occasionally □ frequently □ almost always

10. Can you hear someone approaching from behind?

10a. At present

□ Almost never □ occasionally □ frequently □ almost always

10b. Before

□ Almost never □ occasionally □ frequently □ almost always

11. Do you recognise a presenter on TV by his/her voice?

11a. At present

□ Almost never □ occasionally □ frequently □ almost always

11b. Before

□ Almost never □ occasionally □ frequently □ almost always

12. Can you understand text that is being sung?

12a. At present

□ Almost never □ occasionally □ frequently □ almost always

12b. Before

□ Almost never □ occasionally □ frequently □ almost always

13. Can you easily carry on a conversation with somebody in a car or bus?

13a. At present

□ Almost never □ occasionally □ frequently □ almost always

13b. Before

□ Almost never □ occasionally □ frequently □ almost always

14. Can you understand the presenter of the news on TV?

14a. At present

□ Almost never □ occasionally □ frequently □ almost always

14b. Before

□ Almost never □ occasionally □ frequently □ almost always

15. Do you immediately look in the right direction when somebody calls you in the street?

15a. At present

□ Almost never □ occasionally □ frequently □ almost always

15b. Before

□ Almost never □ occasionally □ frequently □ almost always

16. Can you hear noises in the house like running water, vacuuming, a washing machine?

16a. At present

□ Almost never □ occasionally □ frequently □ almost always

16b. Before

□ Almost never □ occasionally □ frequently □ almost always

17. Can you discriminate between the sound of a car and a bus?

17a. At present

□ Almost never □ occasionally □ frequently □ almost always

17b. Before

□ Almost never □ occasionally □ frequently □ almost always

18. Can you follow a conversation between a few people during dinner?

18a. At present

□ Almost never □ occasionally □ frequently □ almost always

18b. Before

□ Almost never □ occasionally □ frequently □ almost always

19. Can you understand the presenter of the news on the radio?
19a. At present
□ Almost never □ occasionally □ frequently □ almost always
19b. Before
□ Almost never □ occasionally □ frequently □ almost always

20. Can you hear from which corner of the room someone is talking to you in a quiet house?
20a. At present
□ Almost never □ occasionally □ frequently □ almost always
20b. Before
□ Almost never □ occasionally □ frequently □ almost always

21. Can you hear the doorbell at home?
21a. At present
□ Almost never □ occasionally □ frequently □ almost always
21b. Before
□ Almost never □ occasionally □ frequently □ almost always

22. Can you distinguish between male and female voices?
22a. At present
□ Almost never □ occasionally □ frequently □ almost always
22b. Before
□ Almost never □ occasionally □ frequently □ almost always

23. Can you hear rhythm in music or songs?
23a. At present
□ Almost never □ occasionally □ frequently □ almost always
23b. Before
□ Almost never □ occasionally □ frequently □ almost always

24. Can you carry on a converstation with someone in a busy street?
24a. At present
□ Almost never □ occasionally □ frequently □ almost always
24b. Before
□ Almost never □ occasionally □ frequently □ almost always

25. Can you distinguish intonation and inflections in people's voices?
25a. At present
□ Almost never □ occasionally □ frequently □ almost always
25b. Before
□ Almost never □ occasionally □ frequently □ almost always

26. Do you hear from which direction a car horn is coming?
26a. At present
□ Almost never □ occasionally □ frequently □ almost always
26b. Before
□ Almost never □ occasionally □ frequently □ almost always

27. Do you hear birds singing outside?
27a. At present
□ Almost never □ occasionally □ frequently □ almost always
27b. Before
□ Almost never □ occasionally □ frequently □ almost always

28. Can you recognise and distinguish between different musical instruments by their sound?

28a. At present

□ Almost never □ occasionally □ frequently □ almost always

28b. Before

□ Almost never □ occasionally □ frequently □ almost always

Appendix J: Speech Spatial Qualities questionnaires

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

Speech Spatial Qualities

Advice about answering the questions

The following questions inquire about aspects of your ability and experience hearing and listening in different situations.

For each question, put a mark, such as a cross (x), anywhere on the scale shown against each question that runs from 0 through to 10. Putting a mark at 10 means that you would be perfectly able to do or experience what is described in the question. Putting a mark at 0 means you would be quite unable to do or experience what is described.

As an example, question 1 asks about having a conversation with someone while the TV is on at the same time. If you are well able to do this then put a mark up toward the right-hand end of the scale. If you could follow about half the conversation in this situation put the mark around the mid-point, and so on.

We expect that all the questions are relevant to your everyday experience, but if a question describes a situation that does not apply to you, put a cross in the "not applicable" box. Please also write a note next to that question explaining why it does not apply in your case.

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

Please check one of these options:

☐ I have no hearing aid/s
☐ I use one hearing aid (left ear) I use one hearing aid (right ear)
☐ I use two hearing aids (both ears)

If you have been using hearing aid/s, for how long?

_____ years

_____ months

or

_____ weeks

If you have two aids and have used them for different lengths of time, please write down both.

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

S[peech] **S**[patial] **Q**[ualities] **version 3.1.2**

I. Speech hearing rating scale

1. You are talking with one other person and there is a TV on in the same room. Without turning the TV down, Can you follow what the person you're talking to says?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐ Tick if not applicable
2. You are talking with one other person in a quiet, carpeted lounge-room. Can you follow what the other person says?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐ Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

3. You are in a group of about five people, sitting round a table. It is an otherwise quiet place. You can see everyone else in the group. Can you follow the conversation?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐ Tick if not applicable
4. You are in a group of about five people in a busy restaurant. You can see everyone else in the group. Can you follow the conversation?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐ Tick if not applicable
5. You are talking with one other person. There is continuous background noise, such as a fan or running water. Can you follow what the person says?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐ Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

6. You are in a group of about five people in a busy restaurant. You cannot see everyone else in the group. Can you follow the conversation?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐ Tick if not applicable
7. You are talking to someone in a place where there are a lot of echoes, such as a church or railway terminus building. Can you follow what the other person says?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐ Tick if not applicable
8. Can you have a conversation with someone when another person is speaking whose voice is the same pitch as the person you're talking to?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐ Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

9. Can you have a conversation with someone when another person is speaking whose voice is different in pitch from the person you're talking to?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
10. You are listening to someone talking to you, while at the same time trying to follow the news on TV. Can you follow what both people are saying?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
11. You are in conversation with one person in a room where there are many other people talking. Can you follow what the person you are talking to is saying?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

12. You are with a group and the conversation switches from one person to another. Can you easily follow the conversation without missing the start of what each new speaker is saying?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐ Tick if not applicable
13. Can you easily have a conversation on the telephone? [using one, none, or both aids?]	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐ Tick if not applicable
14. You are listening to someone on the telephone and someone next to you starts talking. Can you follow what's being said by both speakers?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐ Tick if not applicable

Participant ID: _ _ _ -_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

SSQ3.1 II. Spatial Rating Scale

1. You are outdoors in an unfamiliar place. You hear someone using a lawnmower. You can't see where they are. Can you tell right away where the sound is coming from?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
2. You are sitting around a table or at a meeting with several people. You can't see everyone. Can you tell where any person is as soon as they start speaking?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

3. You are sitting in between two people. One of them starts to speak. Can you tell right away whether it is the person on your left or your right, without having to look?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
4. You are in an unfamiliar house. It is quiet. You hear a door slam. Can you tell right away where that sound came from?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
5. You are in the stairwell of a building with floors above and below you. You can hear sounds from another floor. Can you readily tell where the sound is coming from?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

6. You are outside. A dog barks loudly. Can you tell immediately where it is, without having to look?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
7. You are standing on the footpath of a busy street. Can you hear right away which direction a bus or truck is coming from before you see it?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
8. In the street, can you tell how far away someone is, from the sound of their voice or footsteps?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

9. Can tell how far away a bus or a truck is, from the sound?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
10. Can you tell from the sound which direction a bus or truck is moving, for example, from your left to your right or right to left?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
11. Can you tell from the sound of their voice or footsteps which direction a person is moving, for example, from your left to your right or right to left?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

12. Can you tell from their voice or footsteps whether the person is coming towards you or going away?	Not at all — Perfectly  0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
13. Can you tell from the sound whether a bus or truck is coming towards you or going away?	Not at all — Perfectly  0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
14. Do the sounds of things you are able to hear seem to be inside your head rather than out there in the world?	Inside my head — Out there  0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

15. Do the sounds of people or things you hear, but cannot see at first, turn out to be closer than expected when you do see them?	Much closer — Not closer 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
16. Do the sounds of people or things you hear, but cannot see at first, turn out to be further away than expected when you do see them?	Much further — Not further 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
17. Do you have the impression of sounds being exactly where you would expect them to be?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

SSQ3.1 Ill Sound Qualities Rating Scale

1. Think of when you hear two things at once, for example, water running into a basin [a power-tool being used] [a plane flying past] and, at the same time, a radio playing [the sound of hammering] [a truck driving past]. Do you have the impression of these as sounding separate from each other?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

2. When you hear more than one sound at a time, do you have the impression that it seems like a single jumbled sound? * *If you have this experience, can you give examples of the sounds in question?	Jumbled — Not jumbled 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
3. You are in a room and there is music on the radio. Someone else in the room is talking. Can you hear the voice as something separate from the music?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
4. Do you find it easy to recognise different people you know by the sound of each one's voice?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

5. Do you find it easy to distinguish different pieces of music that you are familiar with?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
6. Can you tell the difference between different sounds, for example, a car versus a bus; water boiling in a pot versus food cooking in a frying pan?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
7. When you listen to music, can you make out which instruments are playing?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable

Participant ID: _ _ _ -_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

8. When you listen to music, does it sound clear and natural?	Not at all ... Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min ... Max ☐Tick if not applicable
9. Do everyday sounds that you can hear easily seem clear to you (not blurred)?	Not at all ... Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min ... Max ☐Tick if not applicable
10. Do other people's voices sound clear and natural?	Not at all ... Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min ... Max ☐Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

11. Do everyday sounds that you hear seem to have an artificial or unnatural quality?	Unnatural — Natural 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
12. Does your own voice sound natural to you?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
13. Can you easily judge another person's mood from the sound of their voice?	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

14. Do you have to concentrate very much when listening to someone or something?	Concentrate hard — Not need to concentrate 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
15. [for long-term bilateral hearing aids/implants user only] If you turn one hearing aid/implant off, and do not adjust the other, does everything sound unnaturally quiet?	Too quiet — Not too quiet 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
16. When you are the driver in a car can you easily hear what someone is saying who is sitting alongside you? [if use one aid, which one, why?]	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable

Participant ID: _ _ _-_ _ _ _ Date (DD/MM/YYYY) _ _/_ _/_ _
Completed by: _ _ _

17. When you are a passenger can you easily hear what the driver is saying sitting alongside you? [if use one aid, which one, why?]	Not at all — Perfectly 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
18. Do you have to put in a lot of effort to hear what is being said in conversation with others?	Lot of effort — No effort 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable
19. Can you easily ignore other sounds when trying to listen to something?	Not easily ignore — Easily ignore 0 1 2 3 4 5 6 7 8 9 10 Min — Max ☐Tick if not applicable

20. [long-term bilateral hearing aids/implant user] What are the quietest sounds that you are aware you do not hear ?	
21. Are there contexts where you definitely prefer not to use/to use only one hearing aid/implant?	
22. Are there contexts where you definitely prefer to use a/two hearing aid/s/implant/s?	