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ORIGINAL ARTICLE

Adaption and preliminary validation of the Addenbrooke's Cognitive Examination-III as a screening test for mild cognitive impairment and dementia in hearing-impaired individuals

Courtney North[1] | Mary H. Heatley[1] | Nattawan Utoomprurkporn[2,3] | Doris Eva Bamiou[2,4] | Sergi G. Costafreda[5] | Joshua Stott[1]

[1]Faculty of Brain Sciences, UCL Division of Psychology and Language Sciences, London, UK

[2]UCL Ear Institute, London, UK

[3]Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

[4]NIHR Biomedical Research Centre Hearing and Deafness, London, UK

[5]UCL Division of Psychiatry, Maple House, London, UK

Correspondence
Joshua Stott, UCL Division of Psychology and Language Sciences, Faculty of Brain Sciences, 1–19 Torrington Place, Camden, London WC1E 7HB, UK.
Email: j.stott@ucl.ac.uk

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Abstract

Background: A large proportion of older adults assessed for cognitive impairment likely have hearing loss, potentially affecting accuracy of cognitive performance estimations. This study aimed to develop a hearing-impaired version of the Addenbrooke's Cognitive Examination-III (HI-ACE-III) and to assess whether the HI-ACE-III can accurately distinguish people with mild cognitive impairment (MCI) and dementia from cognitively intact controls.

Methods: The HI-ACE-III was developed by converting verbal instructions into a visual, timed PowerPoint presentation. Seventy-four participants over the age of 60 years were classified into three groups: 29 had MCI, 15 had mild to moderate dementia and 30 were cognitively intact controls. Receiver operating characteristic (ROC) curves were graphed to test screening accuracy. Concurrent validity was examined through correlations between HI-ACE-III domain scores and relevant, visually presented standardized neuropsychological measures.

Results: ROC analysis for dementia revealed an area under the curve (AUC) of 0.99, achieving excellent sensitivity (100%) and good specificity (93.3%) at an optimum cut-off of <87. The AUC for MCI was 0.86, achieving reasonable sensitivity (75.9%) and good specificity (86.7%) at an optimum cut-off of <92. HI-ACE-III subtests shared anticipated and statistically significant correlations with established measures of cognitive functioning. Internal consistency of the HI-ACE-III was excellent as verified with Cronbach's alpha (α = 0.904).

Conclusions: Preliminarily, the HI-ACE-III showed good reliability, validity and screening utility for MCI and dementia in older adults in a hearing-impairment context. The adapted HI-ACE-III may offer accurate and reliable indication of cognitive performance, supporting timely diagnosis and research examining links between hearing loss and cognitive decline.

KEYWORDS
dementia, cognitive screening, Addenbrooke's Cognitive Examination, hearing loss, HI-ACE-III, MCI, mild cognitive impairment

See commentary by L. Vita and D. Bruno on page 1795

INTRODUCTION

Cognitive decline and age-related hearing loss (ARHL) are both leading causes of chronic disability in older age [1,2]. While often underdiagnosed, an estimated two-thirds of adults over 70 years of age will suffer some degree of ARHL [3,4]. At present, screening tools for cognitive impairment implicitly assume intact hearing ability by including a strong auditory component. Older adults with hearing impairment perform worse on cognitive tests, even if hearing impairment is not severe enough to prohibit standard verbal administration, making inaccurate estimation of cognitive ability a significant concern [5].

Beyond changes resulting from normal cognitive ageing, up to 20% of adults over 65 years will be affected by mild cognitive impairment (MCI) [6] and the estimated age-standardized population prevalence of both diagnosed and undiagnosed dementia is 7.1% [7]. ARHL has been identified as a risk factor for developing MCI [8] and dementia [9,10]. However, despite this demonstrated association, current cognitive tests are inadequate to screen for cognitive decline in a hearing-impaired population [11].

In this study, we intended to develop a validated version of an existing cognitive screening tool adapted for individuals with hearing loss which would minimize underperformance related to auditory threshold. Given that a majority of older adults assessed for suspected cognitive impairment may have diagnosed or undiagnosed hearing loss, such a screening tool would be clinically useful. In addition, a screening tool that is not reliant on audibility and is unaffected by hearing status would support longitudinal research into the etiological link between MCI, dementia and hearing impairment, as well as inform the effectiveness of potential interventions intended to delay the progression of cognitive decline and onset of dementia, such as the application of hearing aids [12].

The Addenbrooke's Cognitive Examination-III (ACE-III) [13] represents a good option for a hearing-adapted tool. Originally designed to detect cognitive impairment, and to overcome omissions present in the Mini-Mental State Examination (MMSE) [14], the ACE-III offers a global cognitive overview as well as assessing attention, memory, language, fluency and visuospatial skills. The ACE-III has been shown to be superior to a number of widely used screening tools including the Montreal Cognitive Assessment (MoCA) and the MMSE for the screening of Alzheimer's disease (AD) [15]. The ACE-III has good discriminant ability for the screening of MCI, with demonstrated diagnostic properties comparative or superior to the MoCA and the MMSE [16–18]. The ACE-III is more sensitive to functional impairment [19] and offers a more comprehensive cognitive profile which can provide information on dementia subtype and support differential diagnosis [20,21].

The ACE-III has excellent screening utility in identifying cognitive impairment in a variety of clinical situations [13]. We aimed to develop a hearing-impaired version of the ACE-III (HI-ACE-III) using a visually presented, timed PowerPoint (Microsoft Corporation) presentation, as well as test the ability of the HI-ACE-III to distinguish between a group of hearing-impaired individuals with and without MCI or dementia and provide optimum cut-off points that maximize sensitivity and specificity for both diagnoses.

METHODS

Ethical approval

Ethical approval was granted by the National Health Service (NHS) Health Research Authority (HRA) Research Ethics Committee (REC) (Reference: 18/LO/1225; Integrated Research Application System [IRAS] identification 247176; Appendix B). Written information about the study was provided prior to participation and written informed consent was obtained from each participant.

Participants

Participants in the MCI with hearing-impairment group (MCI-HI) and dementia with hearing-impairment group (D-HI) had a diagnosis from psychiatrist-led memory clinics in England. The MCI group were diagnosed in accordance with Petersen criteria [22–24] and the dementia group were diagnosed in accordance with the International Statistical Classification of Diseases and Related Health Problems 10th edition (ICD-10; World Health Organization) [25]. The D-HI group (n = 15) comprised 11 individuals with AD, two with vascular dementia, one with frontotemporal dementia and one with mixed dementia. Participants in the D-HI group had mild to moderate dementia, determined by previous MMSE scores and clinical judgement, along with the capacity to consent to participate in the study.

Participants in the hearing-impaired without cognitive impairment group (HI) were recruited from an adult audiology clinic in England. The presence of hearing loss in all participants was determined using pure-tone air-conduction with a portable audiometer (MA41 from Maico Diagnostics GmbH) which has been validated for use with older adults in a natural environment [26]. Standard diagnostic procedures outlined by the British Society of Audiology were followed [27]. Hearing loss was considered as an average threshold of 30 decibels hearing level (dB HL) or more, taken as the pure-tone average (PTA) of the better hearing ear at frequencies of 0.5, 1, 2 and 4 KHz. In the HI group, normal cognition was verified using the General Practitioner Assessment of Cognition (CPCOG), a valid instrument for detecting cognitive impairment with good sensitivity (0.85) and specificity (0.86) [28]. To ensure participants in the HI group had normal cognition, only participants who scored 9 on the GPCOG-patient or between 5 and 8 with a GPCOG-informant score of between 4 and 6 were recruited.

Participants in all groups were over the age of 60 years, no upper age limit was in place. The inclusion criteria were intentionally broad in an attempt to recruit a representative sample. Exclusion criteria for all groups included: uncorrected visual impairment and/or a physical disability which might inhibit performance on written test

elements; and congenital or childhood-onset hearing loss. While there was no exclusion on the basis of years spent in education, the participants were required to be literate.

Development of the HI-ACE-III

With permission from Professor John Hodges, main developer and copyright owner, the verbal ACE-III instructions were transcribed onto a timed PowerPoint presentation to ensure standardized administration. The contrasting blue background and white characters were chosen based on guidelines regarding readability when using a computer screen [29]. A manual was developed to ensure standardization of administration across researchers.

The adapted test was piloted on a group of clinicians, specialist neuropsychologists, older adults and carers of people living with dementia and modified based on their commentary. The final version of the HI-ACE-III together with the administration instructions will be available as supplementary material and will also shortly be available on the website for the Brain and Mind Centre at the University of Sydney (https://www.sydney.edu.au/brain-mind/resources-for-clinicians/dementia-test.html).

Measures

All participants were examined using the hearing-impaired HI-ACE-III and standardized tests with established reliability and validity including the Rey–Osterrieth Complex Figure (ROCF) test [30], Spatial Span digit span forward and backwards (DSF and DSB) tests [31,32] and Graded Naming Test (GNT) [33] to assess convergent and divergent validity of the HI-ACE-III.

Where there was a need to give test instructions, PowerPoint presentations were developed to deliver instructions visually. Whilst there are not specific examples in the literature of using written instructions for these measures, incidences of creating visually presented versions for hearing-dependent items have been cited [9,11]. A version of the MoCA adapted for individuals with hearing impairment was also administered to participants as part of an associated project, and these results are reported elsewhere. The order of administration was counterbalanced.

Power calculation

Sample size was determined using the EasyROC tool [34]. Power was calculated for using ROC analysis. Alpha was set at 0.05 and beta was set at 0.8. The effect size was set at 0.7 based on the figure obtained from the predicted AUC for the ACE-III, which was 0.897 for the screening of dementia [15] and 0.906 for the screening of MCI [16]. This lower figure ensures a conservative estimate for sample size due to the possibility that the hearing-impaired version is not as accurate at distinguishing cognitive impairment as the established version [9]. The sample size calculation indicated 24 participants would be required for each group.

Statistical analysis

Demographic data were explored using descriptive statistics and frequency analysis as well as independent samples t-tests and a chi-square test of independence.

A ROC analysis was conducted to establish the AUC, which was used to determine the ability of the HI-ACE-III to correctly classify participants with and without MCI or dementia. An AUC value of 0.7–0.8 was considered acceptable, 0.8–0.9 was considered excellent and higher than 0.9 outstanding [35]. The optimal cut-off score for maximizing the detection of both MCI and dementia was established based on the largest Youden index (YI), a measure of diagnostic accuracy designed to maximize both sensitivity and specificity [36,37].

Correlation coefficients were used to investigate the association between subtests of the HI-ACE-III and outlined, non-verbal tests of cognitive function. An exploratory hierarchical multiple regression was used to examine the unique contribution of cognitive status to variation in total HI-ACE-III score over and above participant age and years of education. Finally, to check reliability the internal consistency of the HI-ACE-III subtests was confirmed with Cronbach's alpha correlation coefficient. The value of 0.70 was considered the minimum acceptable value [38].

RESULTS

Demographic characteristics and HI-ACE-III scores

The demographic characteristics of participants are shown in Table 1. Participants in the MCI-HI and D-HI groups were found to be significantly older (MCI-HI group: $t(57) = -5.61$, $p < 0.001$; D-HI group: $t(43) = -2.55$, $p = 0.014$), with fewer years of education (MCI-HI group: $t(57) = 2.78$, $p = 0.008$; D-HI group: $t(43) = 4.66$, $p < 0.001$) than participants in the HI group. No significant association between gender and cognitive status was found for any group. As would be anticipated, participants in the MCI-HI group, $t(38.2) = 25.4$, $p < 0.001$, had significantly lower HI-ACE-III total scores than their cognitively intact counterparts in the HI group. A similar trend was observed between the D-HI group and the HI group, $t(43) = 11.7$, $p < 0.001$.

Screening accuracy of the HI-ACE-III

The ROC curves for discriminating individuals with MCI and dementia from cognitively intact control participants with the HI-ACE-III are shown in Figure 1 and Table 2. The AUC value was excellent for MCI (0.856) and outstanding for dementia (0.994). Based on the

largest YI, an optimum cut-off score of <91.5 (sensitivity 75.9%, specificity 86.7%, YI 0.626) was established for MCI and <86.5 (sensitivity 100%, specificity 93.3%, YI 0.933) for dementia. As half marks are not awarded on the ACE-III, the cut-off is considered to be scores of <92 for MCI and <87 for dementia.

Exploration of convergent and divergent validity

The exploratory correlation matrices to determine associations between the HI-ACE-III composite subtests and relevant measures of cognitive functioning for each group are outlined in Table 3.

Anticipated correlations were observed between the HI-ACE-III attention composite and DSF in the HI and D-HI groups. HI-ACE-III memory was correlated with DSB as expected in MCI-HI and D-HI groups and also the ROCF, and ROCF 3-minute recall (ROCF 3 min) and 30-minute recall (ROCF 30 min) in the MCI-HI group alone. Performance on the HI-ACE-III fluency subscale was associated with performance on the GNT in the MCI-HI group. In every group, the HI-ACE-III language composite was correlated with the GNT. Finally, the HI-ACE-III visuospatial domain was found to be associated with the ROCF in the HI and MCI-HI groups and the ROCF 30 min in the MCI-HI group.

Less expected correlations included HI-ACE-III fluency and the ROCF in each group and HI-ACE-III memory with the GNT in the HI and MCI-HI groups.

Reliability of the HI-ACE-III

The internal consistency of the HI-ACE-III, as measured by Cronbach's alpha, was high (α = 0.904).

Exploratory hierarchical multiple regression

Given that groups differed in age and years of education, factors which are correlated with cognitive performance [39], an exploratory hierarchical regression was conducted to determine the unique contribution of cognitive status to HI-ACE-III scores over and above age and years of education (YoE) for all groups (Table 4).

Cognitive status was included as a variable in the first block (Step 1) and contributed significantly to the regression model, $F(1,72) = 103.62$, $p < 0.001$. The adjusted R^2 was 0.584, indicating that cognitive status accounted for approximately 58.4% of the variation in total HI-ACE-III score.

In the second and final block (Step 2), participant age and YoE were added to the analysis and the collective three variables contributed significantly to the regression model, $F(3,70) = 37.92$, $p = <0.001$. The adjusted R^2 was 0.603, suggesting that the age and YoE explained an additional 1.9% of the variation in total HI-ACE-III score for a total of 60.3%, which was not a statistically significant increase. Cognitive status was the only significant predictor of total HI-ACE-III score, $t(70) = -10.18$, $p < 0.001$.

TABLE 1 Participant demographics and Hearing Impaired Addenbrooke's Cognitive Examination-III (HI-ACE-III) scores

Group	Males (%)	YoE M (SD)	Age M (SD)	HI-ACE-III total M (SD)	HI-ACE-III attention M (SD)	HI-ACE-III memory M (SD)	HI-ACE-III fluency M (SD)	HI-ACE-III language M (SD)	HI-ACE-III visuospatial M (SD)
HI (n = 30)	60	16.1 (3.7)	75.3 (5.9)	94.4 (4.9)	17.5 (0.7)	24.4 (1.8)	12.1 (1.9)	24.9 (2.4)	15.4 (0.7)
MCI-HI (n = 29)	48	13.2 (4.2)	84.1 (6.3)	83*** (11.2)	16.2** (2)	19.7*** (5.2)	10.4** (2.6)	23.1* (3.3)	13.6*** (2.1)
D-HI (n = 15)	73	10.53 (3.87)	80.8 (8.52)	60.4*** (14.5)	13.6** (3.7)	12.3*** (5.9)	5.5*** (2.9)	18.5*** (4.7)	10.5*** (4.9)8

Note: Significance levels using Welch's independent samples t-tests comparing HI and MCI-HI and HI and D-HI.

Abbreviations: D-HI, dementia and hearing impairment; HI, cognitively intact with hearing impairment; HI-ACE-III, Hearing Impaired Addenbrookes Cognitive Examination-III; M, mean; MCI-HI, mild cognitive impairment and hearing impairment; SD, standard deviation; YoE, years of education.

$^{*}p < 0.05$.

$^{**}p < 0.01$.

$^{***}p < 0.001$.

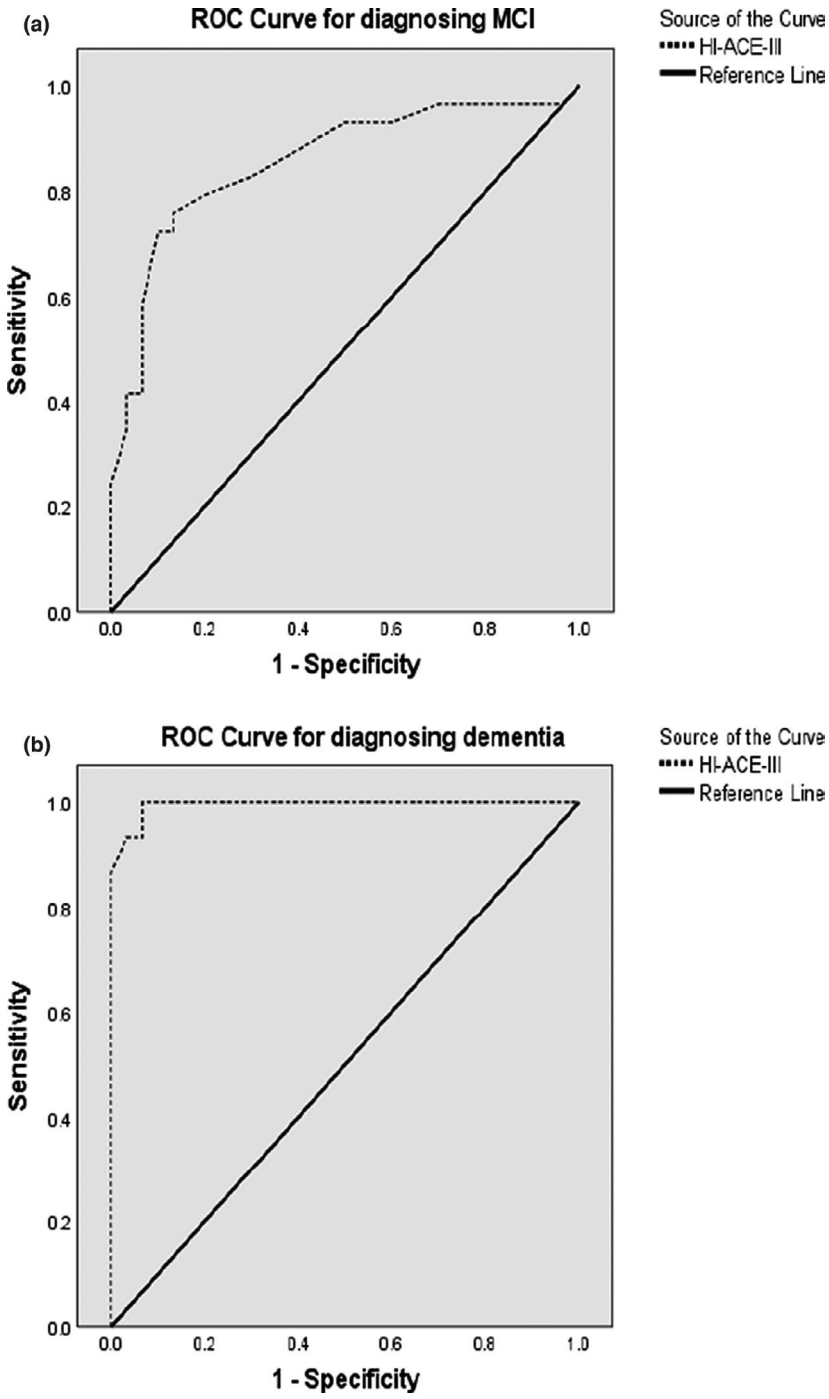

FIGURE 1 Receiver operating characteristic (ROC) curves of the Hearing Impaired Addenbrooke's Cognitive Examination-III (HI-ACE-III) for detecting mild cognitive impairment (MCI) (a) and dementia (b).

DISCUSSION

This study sought to address the recognized need for cognitive screening tests adapted for hearing loss [5,10] by developing a visually presented version of the ACE-III. The results indicate the HI-ACE-III is a sensitive and specific screening tool, with an outstanding ability to distinguish those with dementia from cognitively intact control participants (AUC = 0.99) and an excellent ability to distinguish those with MCI from control participants (AUC = 0.86) [40].

According to the ROC analysis results, the optimal cut-off for detecting dementia using the HI-ACE-III is <87 (sensitivity 100%, specificity 93.3%). This falls between previously recommended cut-off points, <88 (sensitivity 100%, specificity 96%) and <82 (sensitivity 93%, specificity 100%), for identifying dementia in the ACE-III validation for dementia study [13].

For detecting MCI, the optimal cut-off using the HI-ACE-III is <92 (sensitivity 75.9%, specificity 86.7%). This is in keeping with cut-off points for distinguishing individuals with MCI from individuals who are cognitively intact with associated versions of the ACE; the original ACE <92 (sensitivity 72%, specificity 79%) and the ACE-R < 94 (sensitivity 83%, specificity 73%) [41–43].

Studies evaluating the utility of the ACE-III for screening for cognitive impairment have highlighted the tool's usefulness in detecting MCI and dementia in a wide range of populations [13,44–47]. These

TABLE 2 Optimal cut-off scores and psychometric properties of the Hearing Impaired Addenbrooke's Cognitive Examination-III (HI-ACE-III) for detecting mild cognitive impairment and dementia

Psychometric properties	HI-ACE-III for detecting MCI	HI-ACE-III for detecting dementia
Optimal cut-off score	92.5	86.5
Sensitivity (%)	75.9%	100%
Specificity (%)	86.7%	93.3%
AUC (95% CI)	0.856 (0.756–0.957)	0.994 (0.981–1.000)
SE	0.051	0.007
PPV (%)	84.6%	88.2%
NPV (%)	78.8%	100%
YI	0.626	0.933
LR	5.69	15

Abbreviations: AUC, area under the curve; CI, confidence interval; HI-ACE-III, Hearing Impaired Addenbrookes Cognitive Examination-III; LR, likelihood ratio; MCI, mild cognitive impairment; NPV, negative predictive value; PV, positive predictive value; SE, standard error; YI, Youden index.

studies highlight the adaptability of the ACE-III and are consistent with our finding that modified versions of the ACE maintain original screening properties [48].

Measures of concurrent validity used in the current study show that the HI-ACE-III correlated in many anticipated ways with established tests of cognitive functioning, particularly within the MCI-HI group. The D-HI and HI groups also showed a broadly expected pattern of high correlation coefficients.

Performance on the HI-ACE-III attention subtest in each group and HI-ACE-III memory subtest in the MCI-HI and D-HI groups correlated with the DSB, an established measure of attention and working memory [31]. As anticipated, significant associations existed between the ROCF and the HI-ACE-III visuospatial subtest in the HI and MCI-HI groups [49]. ROCF recall conditions performance was associated with HI-ACE-III memory performance in the MCI-HI group, which is expected given these immediate and delayed recall conditions measure incidental memory [30].

In the HI and MCI-HI groups, HI-ACE-III memory correlated highly with the GNT. While not predicted, this association is supported by previous findings [50,51], citing the memory component

TABLE 3 Convergent and divergent validity of the Hearing Impaired Addenbrooke's Cognitive Examination-III (HI-ACE-III) composite domain scores

Group	DSF	DSB	ROCF	ROCF 3 min	ROCF 30 min	GNT
HI						
ACE attention	0.085	**0.373***	0.344	0.097	0.031	0.164
ACE memory	0.109	−0.028	0.220	0.173	0.080	**0.371***
ACE fluency	0.082	0.116	0.175	**0.371***	0.289	0.108
ACE language	−0.059	0.139	0.009	−0.004	−0.190	**0.373***
ACE visuospatial	0.054	0.194	0.243	**0.398***	0.328	0.356
MCI-HI						
ACE attention	−0.124	**0.407***	0.070	−0.069	−0.007	**0.387***
ACE memory	0.136	**0.481****	0.281	**0.537****	**0.516****	**0.502****
ACE fluency	0.286	0.336	**0.526****	0.345	0.368	**0.376***
ACE language	0.168	**0.417***	0.327	0.102	0.270	**0.627*****
ACE visuospatial	**0.473***	**0.409***	**0.515****	0.367	**0.385***	0.245
D-HI						
ACE attention	0.042	**0.634***	0.320	0.371	0.345	0.169
ACE memory	0.107	**0.576***	0.091	0.472	0.398	0.443
ACE fluency	0.389	**0.215***	**0.650***	0.119	0.226	0.279
ACE language	−0.2	0.1	0.1	−.0140	0.164	**0.783****
ACE visuospatial	0.321	0.150	0.271	0.127	0.183	**0.608***

Note: Data are presented as Spearman correlation coefficients.

Significant correlations are in bold type.

Abbreviations: ACE, Addenbrookes Cognitive Examination-III; D-HI, dementia and hearing impairment; DSB, Digit Span backward; DSF, Digit Span forward; GNT, Graded Naming Test; HI, cognitively intact with hearing impairment; MCI-HI, mild cognitive impairment and hearing impairment; ROCF 30 min, Rey–Osterrieth Complex Figure 30-minute recall; ROCF 3 min, Rey–Osterrieth Complex Figure 3-minute recall; ROCF, Rey–Osterrieth Complex Figure test.

*$p < 0.5$.

**$p < 0.01$.

***$p < 0.001$.

TABLE 4 Hierarchical regression analysis predicting total Hearing Impaired Addenbrooke's Cognitive Examination-III (HI-ACE-III) score

	Step 1			Step 2		
Predictor	***b***	**SE (*b*)**	**B**	***b***	**SE (*b*)**	**β**
Constant	95.96	1.75		101.99	15.56	
Cognitive status	−16.22	1.59	−0.768	−14.1***	1.8	−0.668
Age				−0.187	0.172	−0.09
YoE				0.521	0.316	0.144
Adjusted R^2	0.584			0.603		
F	103.62***			37.92***		
ΔR^2	0.590			0.029		
ΔF	2.67***			2.67		

Note: $n = 59$.

Abbreviations: ΔF, F change; ΔR^2, R^2 change; YoE, years of education.

*$p < 0.05$.

**$p < 0.01$.

***$p < 0.001$.

of word retrieval and the fact the ACE-III is considered a language-based memory test. The fluency subscale of the HI-ACE-III correlated highly with the ROCF subtest in each group, which is consistent with research evidence that phonemic and semantic fluency are related to frontal impairment [52] and executive dysfunction [53,54].

To our knowledge, this is the first study presenting data on validity of a cognitive screening tool adapted for individuals with age-related hearing loss. A promising adaptation of the MOCA, the hearing-impaired Montreal Cognitive Assessment (HI-MoCA) [55], has been developed, but formal validation is yet to be reported [11].

Limitations

Recruitment for the D-HI group was suspended early due to the COVID-19 outbreak and the vulnerable characteristic of the recruited population. While an excellent AUC was found, the limited sample size may reduce robustness and external validity of findings regarding screening utility of the HI-ACE-III. When interpreting exploratory correlations between HI-ACE-III subtests and relevant standardized measures, the small D-HI group likely resulted in an underpowered analysis. This precluded the use of Bonferroni correction for multiple comparisons due to the associated reduction in statistical power and criticism of Bonferroni as overly conservative [56]. In addition, the ceiling effect, in which a large proportion of participants achieve the largest possible test score [57], may have masked correlations in the HI group. Due to the small sample size, participants with dementia were not divided into groups based on dementia subtype. Previous research has indicated the ACE-III can discriminate between different dementia subtypes [13,58,59] and the ability of the HI-ACE-III to support differential diagnosis may be an interesting follow-up.

Another limitation is that the HI, MCI-HI and D-HI groups differed considerably in terms of age and YoE. This is important given both age and education are linked to differences in performance on cognitive tests [37]. We conducted an exploratory hierarchical regression and found adding age and education on top of group status did not result in a significant increase in variance in total HI-ACE-III scores, suggesting the diagnostic value of the HI-ACE-III was robust to the effects of age and education. Future research attention might be directed towards conducting studies with matched controls, in order to control for any potential contributions of these variables [60].

Clinical implications and directions for future research

This study supports the preliminary validation of the HI-ACE-III as a specific and sensitive screening tool for populations with MCI, dementia and comorbid hearing loss. The HI-ACE-III is potentially appropriate for clinical use when hearing impairments are diagnosed. However, hearing impairments in older adults are frequently unrecognized [3,61]. In instances where hearing impairment is reasonably expected, using the HI-ACE-III on a precautionary basis may offer the most accurate indication of cognitive performance provided the individual is able to process written instructions.

More extensive exploration of the psychometric properties of the HI-ACE-III might strengthen evidence supporting application in populations with hearing loss. This might include testing the sensitivity and specificity of the tool in larger sample sizes; using controls matched for age and education; as well as expanding the battery of neuropsychological assessments used for assessing the concurrent validity of the HI-ACE-III. Larger sample sizes may also support the validation of the HI-ACE-III in the differential diagnosis of various dementia subtypes.

Finally, whilst research already outlines promising steps towards tool development for other widely used screening instruments, such as the HI-MoCA [12], continued research attention is needed to validate these as screening tools for individuals with cognitive

impairment. This would offer practitioners more options, allowing for factors such as tool familiarity, length and ease of administration to contribute to clinical decision-making.

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CONFLICT OF INTEREST

The authors declare no financial or other conflicts of interest.

AUTHOR CONTRIBUTIONS

Courtney North: Conceptualization (supporting); Data curation (equal); Formal analysis (equal); Investigation (equal); Methodology (equal); Writing-original draft (equal); Writing-review & editing (equal). **Mary Hazel Heatley:** Conceptualization (supporting); Data curation (equal); Formal analysis (equal); Investigation (equal); Methodology (equal); Writing-original draft (equal); Writing-review & editing (equal). **Natatawan Utoomprurkporn:** Conceptualization (equal); Investigation (equal); Writing-review & editing (equal). **Doris-Eva Bamiou:** Conceptualization (equal); Funding acquisition (equal); Writing-review & editing (equal). **Sergei G. Costafreda:** Conceptualization (equal); Funding acquisition (equal); Writing-review & editing (equal). **Josh Stott:** Conceptualization (equal); Funding acquisition (equal); Supervision (lead); Writing-review & editing (equal).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Nattawan Utoomprurkporn https://orcid.org/0000-0001-6472-7573
Joshua Stott https://orcid.org/0000-0003-1361-053X

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