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Comparison of the Telephone-Montreal Cognitive Assessment (T-MoCA) and Telephone Interview for Cognitive Status (TICS) as screening tests for early Alzheimer's disease

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Abstract

INTRODUCTION: Remote screening for cognitive impairment associated with Alzheimer's disease (AD) has grown in importance with the expected rise in prevalence of AD in an aging population and new potential treatment options.

METHODS: The Telephone Instrument for Cognitive Screening (TICS) and new Telephone Adaptation of the Montreal Cognitive Assessment (T-MoCA) were administered to participants independently classified through in-person clinical evaluation as cognitively normal (CN; n=167), mild cognitive impairment (MCI; n=25), or dementia (n=23). Cerebrospinal fluid AD biomarkers were measured (n=79).

RESULTS: TICS and T-MoCA were highly correlated ($r=.787$; $p<.001$), groups differed on both (CN<MCI<Dementia; TICS: $F(2,212)=156.66$; $p<.001$; T-MoCA: $F(2,210)=143.72$; $p<.001$), both effectively detected cognitive impairment (ROC AUC: TICS=.889; T-MoCA=.902), and both negatively correlated with a composite AD biomarker (Tau/A β 1-42; TICS: $r=-.372$; $p=.001$; T-MoCA: $r=-.480$; $p<.001$).

DISCUSSION: TICS and T-MoCA are effective for remotely detecting cognitive impairment associated with AD in older adults. Strong correlation between tests provides construct validity for the newer T-MoCA.

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Keywords

Cognitive Screening; Cognition; Remote Cognitive Assessment; Alzheimer's disease; Mild

Background

Efficient and accurate screening for cognitive impairment associated with Alzheimer's disease (AD) has grown in importance with the development of treatment options that may be most effective early in the course of disease¹. It is estimated that 6.2 million Americans age 65 and older are currently living with AD, and this number may rise to nearly 14 million by 2060². The need for early detection of cognitive impairment in such a large and rapidly growing population led to the creation of brief, structured mental status screening examinations that can be administered remotely using telephone and videoconferencing technology. One of the first and most widely used of these is the Telephone Interview for Cognitive Screening (TICS)³. The TICS is a 41-point cognitive screening test developed from the Mini-Mental State Exam (MMSE)⁴ that consists of verbal questions and mental tasks that briefly assess orientation, concentration, short-term memory, language, praxis and simple calculation abilities. The TICS and its modified version with word-list delayed recall were validated against extensive in-person neuropsychological assessment and shown to be effective at detecting mild dementia or mild cognitive impairment (MCI)^{5,6}. A recent meta-analysis showed that the recommended cut-off score of <31 of 41 possible points on the TICS provides 92% sensitivity and 66% specificity for the detection of dementia⁷.

The Telephone-Montreal Cognitive Assessment (T-MoCA)⁸ is a newer structured mental status screening examination that consists of 15 non-visual items from the widely-used Montreal Cognitive Assessment (MoCA)⁹. Originally developed for the visually impaired¹⁰, the T-MoCA is a 22-point scale that briefly assesses auditory attention, mental flexibility, verbal fluency, sentence repetition, word-list memory, and orientation to time and place. The T-MoCA was validated against in-person administration of the full MoCA in a diverse population of elderly individuals with normal cognition or MCI¹¹: T-MoCA and MoCA scores were significantly correlated and had similar sensitivity for detecting cognitive impairment identified through an extensive in-person cognitive evaluation. An optimal T-MoCA cut-off score of 17 provided 72% sensitivity and 59% specificity for detection of MCI, compared to 70% sensitivity and 77% specificity for the full MoCA¹¹.

Zietemann and colleagues¹² showed that optimal cut-off scores for the TICS (i.e., <37) and T-MoCA (i.e., <19) had similar sensitivity (i.e., 82% and 81%, respectively) for detecting cognitive impairment verified by in-person neuropsychological assessment of patients with vascular disease or stroke; however, specificity was higher for the T-MoCA than the TICS (73% and 44%, respectively). Pendlebury and colleagues⁸ found similar areas under the curve (AUC) for the T-MoCA (.75) and TICS (.79) in Receiver Operating Characteristic (ROC) analyses differentiating no-cognitive impairment from mild cognitive impairment in patients with transient ischemic attack (TIA) or stroke. These results support the construct validity of both measures versus independently-verified vascular cognitive impairment, and provide concurrent validity for the T-MoCA against the more established TICS.

The relative validity and effectiveness of the T-MoCA and TICS for detecting cognitive impairment related to AD has not been examined. Although the two measures are similarly effective for detecting vascular cognitive impairment, the same may not be true for AD-related cognitive decline given differences in cognitive deficit profiles associated with AD and cerebrovascular disease¹³ and in some aspects of cognition assessed by the TICS and T-MoCA. Thus, the present study directly compared the effectiveness of the TICS and T-MoCA for detecting independently-verified cognitive impairment related to AD, examined the relationship between each screening measure and cerebrospinal fluid (CSF) levels of AD biomarkers beta-amyloid ($A\beta_{1-42}$), total tau and phosphorylated tau (p-tau), and examined the correlation between T-MoCA scores and scores on the well-established TICS to demonstrate concurrent validity of the T-MoCA as an effective remote cognitive screening method.

Methods

Participants

The study included 215 participants from the ongoing longitudinal study of the University of California, San Diego (UCSD) Shiley-Marcos Alzheimer's Disease Research Center (ADRC) who completed remote clinical and cognitive assessments between June 2020 and June 2021. The ADRC cohort consists of approximately 450 volunteer participants in a longitudinal observational study of the clinical course, cognitive decline, biomarker changes, and pathology of AD and related disorders. Individuals were recruited for the cohort through advertisements, community presentations, community memory screening events for those with memory concerns, regional neurology and geriatric medicine clinics, and the UCSD Memory Disorders Clinic. Inclusion criteria for the cohort included age 60 or older (unless there is a diagnosis of AD or related disorder), ambulatory, no current alcohol or drug abuse, no major visual or hearing impairment, no major psychoses (e.g., schizophrenia), no major systemic or severe medical conditions, and no history of strokes that cause significant deficits. Only participants who completed the T-MoCA and TICS within 30 days of each other were included in the present study. All 215 participants had completed a comprehensive in-person ADRC evaluation within an average of 16.32 (s.d.=7.55) months before the remote assessments. Based on this extensive in-person evaluation, 167 participants had been classified as cognitively normal (CN), 25 as mild cognitive impairment (MCI) (19 single or multi-domain amnesic, 6 single or multi-domain non-amnesic), and 23 as Dementia (21 probable AD, 1 dementia with Lewy bodies (DLB), and 1 frontotemporal dementia (FTD)). At the time of T-MoCA and TICS administration, groups did not differ significantly in age ($F(2,212)=1.58$; $p=.208$), years of education ($F(2,212)=1.35$; $p=.261$), sex/gender distribution ($X^2(2)=5.08$; $p=.080$), or percentage of Hispanic participants ($X^2(2)=2.05$; $p=.360$). Groups did not differ in percentage of individuals with history of depression, anxiety disorder, or various chronic medical conditions (e.g., cancer, diabetes, coronary artery disease, hypertension, hypercholesterolemia) (all p -values > 0.40), or in the percentage of individuals currently using antidepressants, anxiolytics, or antipsychotic medications (all p -values > 0.15). A higher percentage of participants with MCI or Dementia were using AD medications (e.g., donepezil, memantine, rivastigmine) compared to cognitively normal individuals ($X^2(2)=47.26$; $p<.001$). Groups did not differ in number of

days between the T-MoCA and TICS ($F(2,212)=0.22$; $p=.800$), or months between the last in-person ADRC evaluation and the T-MoCA or TICS ($F(2,212)=1.57$; $p=.210$) (see Table 1).

Procedure

Remote ADRC evaluation.—Remote clinical and neuropsychological evaluations were carried out by telephone ($n=121$) or videoconference (e.g., Zoom; $n=92$) (missing modality information $n=2$). Prior to each evaluation the participant's ability to hear the examiner was assessed. Those who could not hear clearly were not further tested. Participants were asked to complete the evaluations alone in a room free of distractions and possible aids such as pens, paper, newspapers, watches, or calendars. The validity of the assessment in the opinion of the examiner was rated as very valid, questionably valid, or invalid. Only participants with both evaluations considered very valid ($n=187$) or, at worst, questionably valid ($n=28$) were included in analyses (1 participant was dropped due to invalid assessment).

The remote clinical evaluation included the TICS and versions of the interval medical history questions, Functional Assessment Questionnaire (FAQ), Clinical Dementia Rating (CDR), Geriatric Depression Scale (GDS), and Neuropsychiatric Inventory (NPI) adapted for telephone use. The remote neuropsychological evaluation included the T-MoCA and the remainder of the Telephone Cognitive (T-COG) Assessment Battery for the Uniform Data Set (UDS) of the National Alzheimer's Coordinating Center (NACC). The T-COG battery included a Story Recall test (immediate and delayed gist and verbatim recall), forward and backward Number Span tests, the Oral Trial-Making test (i.e., alternating between counting and saying the alphabet), and verbal fluency tests for phonemic ("F" and "L") and semantic ("animals" and "vegetables") categories. The remote clinical and neuropsychological evaluations were usually carried out on separate days within 1 week of each other and varied as to which occurred first. Approximately 80% of participants completed the T-COG and T-MoCA battery first, and 20% completed the clinical evaluation and TICS first.

Telephone Instrument for Cognitive Screening.—The TICS³ is a brief test of global mental status designed for in-person or telephone administration that includes items that assess personal orientation (first and last name, age), orientation to time (month, day, year, day of week, season), orientation to place (street address, city, state, zip code), attention (counting backwards, serial subtraction, finger tapping), episodic memory (10-word list recall), and language and semantic memory (naming, repetition, antonyms, name of president and vice president) (see Supplemental Table 1). Total scores range from 0 (worst) to 41 (best) and are classified as non-impaired (ranging 33–41), ambiguously impaired (26–32), mildly impaired (21–25) or moderately to severely impaired (< 20). Administration time is approximately 10 minutes.

Telephone Adaptation of the Montreal Cognitive Assessment Scale.—The T-MoCA is a brief mental status test designed for use with visually impaired individuals or for telephone administration⁸. The test includes all items from the MoCA⁹ that do not require drawing, writing or visual stimuli including items that assess episodic memory (5-word list

immediate and delayed recall), attention (forward and backward digit span, finger tapping in response to a target stimulus, serial subtraction), language (sentence repetition, phonemic fluency), abstraction (similarities), and orientation to place and time (see Supplemental Table 2). Total scores range from 0 (worst) to 22 (best). Scores ≤ 18 are considered impaired. Administration time is approximately 10 minutes.

Comprehensive in-person ADRC evaluation.—One to two years prior to the remote evaluation, all participants had completed in-person standardized clinical, neurological, and neuropsychological evaluations (previously described)¹⁴ as part of their participation in the ADRC longitudinal study. Clinical assessment included a review of medical history, mental status testing, assessment of psychiatric symptoms (e.g., depression, psychosis including hallucinations) with the GDS and NPI, assessment of functional abilities using the FAQ and CDR, and a physical neurological examination. Neuropsychological assessment included objective tests of global cognitive function, verbal and non-verbal memory, language, executive functions, attention, and visuospatial abilities. Results were reviewed by board-certified neurologists and neuropsychologists with expertise in cognitive disorders to reach a consensus clinical diagnosis. This was a two-step procedure with classification as cognitively normal, MCI¹⁵, or dementia followed by assignment of a presumed etiology based on published criteria for AD¹⁶, DLB¹⁷, FTD¹⁸ or other neurological disease. A research lumbar puncture (LP) was completed for CSF biomarker analysis on a sub-set of participants at this or a previous in-person ADRC evaluation. Biomarker information was not used in making the clinical diagnosis. All participants in the ADRC cohort are asked to complete an LP, but it is not a requirement for participation in the longitudinal study. Of those ADRC participants who agreed to an LP, 79 were also participants in the present study and had had the LP within 48 months of completing the TICS and T-MoCA. While not a random subsample, the participants in the present study providing CSF (n=79) were representative of the entire group and did not differ from those who did not provide CSF (n=136) in age ($t(213)=1.23$; $p=.222$), education ($t(213)=-0.15$; $p=.881$), sex distribution ($\chi^2(2)=0.37$; $p=.542$), diagnostic group distribution ($\chi^2(2)=2.83$; $p=.243$), TICS score ($t(213)=-0.25$; $p=.691$), T-MoCA score ($t(213)=0.03$; $p=.977$), CDR-sum of boxes ($t(213)=0.71$; $p=.482$), or any of the TCOG neuropsychological test measures (all p -values $> .10$).

Biomarker Acquisition and Analysis.—Research LP and preanalytical preparation and storage of CSF were performed using standardized procedures¹⁹ following recommended best practices²⁰. CSF (15–25 mL) was collected by routine LP early in the morning after overnight fasting. Samples were processed, aliquoted into 500 μ L fractions in polypropylene microtubes, snap frozen, and stored at -80°C until assayed. Samples were analyzed locally at UCSD on an automated Lumipulse platform using assays developed with established monoclonal antibodies (Fujirebio Inc.)²¹. CSF AD biomarkers measured included $\text{A}\beta_{1-40}$, $\text{A}\beta_{1-42}$, total Tau, and p-Tau. The ratio of total Tau over $\text{A}\beta_{1-42}$ (Tau/ $\text{A}\beta_{42}$) was calculated and used as a composite biomarker of AD. A cut-point for biomarker positivity in Lumipulse space was derived for the ratio from CSF samples from 462 unique UCSD ADRC participants (ranging from cognitively normal to severely demented). A Tau/ $\text{A}\beta_{42}$ cut-point of .609 provided the best classification of individuals without dementia into those with or

without pre-clinical AD. This cut-point is highly consistent with a published Lumipulse assay cut-point ($\text{Tau}/\text{A}\beta_{42} > 0.540$) for AD biomarker positivity derived against clinical reads of amyloid PET scans²¹ with validation in multiple cohorts. For the current study, AD biomarker data were used if CSF had been collected within 48 months of the remote ADRC evaluation given the stability of CSF biomarkers over several years²².

Statistical Analyses

Group comparisons across demographic, cognitive, and biomarker variables were made with one-way Analysis of Variance (ANOVA) followed by post-hoc pair-wise comparisons using Tukey's Least Significant Difference (LSD) test ($p < .05$ for significance). Categorical variables were compared with χ^2 analyses. Ability of T-MoCA or TICS to differentiate between individuals with or without independently-verified cognitive impairment was examined using ROC curves with calculation of area under the curve (AUC). Optimal sensitivity and specificity were determined by the Youden J index. Pearson product-moment correlation or linear regression analyses examined associations between TICS and T-MoCA scores, or between cognitive scores and biomarker values.

Consent Statement

The research protocol was reviewed and approved by the UCSD human subjects review board. Informed consent was obtained at the point of entry into the longitudinal study from all patients or their caregivers consistent with California State law.

Results

Subgroups tested by videoconference or telephone within the MCI and Dementia groups did not differ in age, education, TICS scores, T-MoCA scores, or T-COG neuropsychological test battery scores with the exception of Verbal Fluency for "L" within the MCI group. Those tested by videoconference within the NC group had more education and better T-MoCA, Oral Trail-Making Test Part A, and Verbal Fluency Test for "L" scores than those tested by telephone. Only the difference in T-MoCA scores remained after controlling for education and this difference was not judged to be clinically meaningful (videoconference T-MoCA mean = 19.8 ± 1.66 ; telephone T-MoCA mean = 18.8 ± 2.29). Therefore, data were collapsed across modality of remote testing for all further analyses.

Groups differed significantly on TICS ($F(2,212)=156.66$; $p < .001$) and T-MoCA ($F(2,210)=143.72$; $p < .001$) scores (see Table 2). Post-hoc pairwise comparisons showed the Dementia group scored worse than the MCI and NC groups on the TICS and the T-MoCA, and the MCI group scored worse than the NC group on both measures (all p 's $< .001$). The three groups also differed on all measures from the T-COG neuropsychological test battery (all p 's $< .001$, see Table 2). Post-hoc pair-wise comparisons showed the Dementia group scored worse than the NC group on all cognitive measures, and worse than the MCI group on all measures except the Oral Trail-Making Test Part A, and the Verbal Fluency Tests for "F" and "L" categories. The MCI group scored worse than the NC group on all cognitive measures except the Forward Number Span Test.

ROC curves depicting the diagnostic utility of the TICS and T-MoCA for distinguishing between cognitively normal and cognitively impaired (collapsed across the MCI and Dementia groups) individuals are shown in Figure 1. Both tests had excellent discriminability with an AUC of .902 for the T-MoCA and .889 for the TICS. An optimal cut-off score of <17 on the T-MoCA, determined by the Youden J statistic, provided 90.4% sensitivity and 76.6% specificity for detection of cognitive impairment. An optimal cut-off score of <34 on the TICS provided 91.0% sensitivity and 74.5% specificity for detection of cognitive impairment.

T-MoCA scores were correlated with TICS scores across the entire sample ($r=.787$, $p<.001$) and specifically within the MCI ($r=.657$, $p<.001$), Dementia ($r=.673$, $p=.001$) and CN ($r=.309$, $p<.001$) groups (See Figure 2). T-MoCA scores can be used to estimate TICS scores with the following regression equation: Estimated TICS = $.949(\text{T-MoCA score}) + 17.38$. Conversely, TICS scores can be used to estimate T-MoCA scores with the following linear regression equation: Estimated T MoCA = $.652(\text{TICS score}) - 4.48$. Estimated scores were highly correlated with actual scores for both the TICS ($r=.787$; $p<.001$) and T-MoCA ($r=.787$; $p<.001$; Supplemental Figure 1).

The CN, MCI and Dementia groups differed in $A\beta_{1-42}$ ($F(2,76)=3.88$; $p=.025$) and the $A\beta_{1-42}/A\beta_{1-40}$ ratio ($F(2,76)=10.01$; $p<.001$), total Tau ($F(2,76)=19.22$; $p<.001$) and p-Tau ($F(2,76)=15.62$; $p<.001$), and the ratio of total Tau/ $A\beta_{1-42}$ ($F(2,76)=21.15$; $p<.001$) (see Table 3). Groups did not differ in $A\beta_{1-40}$ ($F(2,76)=2.65$; $p=.077$). Post-hoc pairwise comparisons showed that the Dementia subgroup had a lower $A\beta_{1-42}/A\beta_{1-40}$ ratio ($p<.001$), higher total Tau ($p<.001$) and p-Tau ($p<.001$), and a lower total Tau/ $A\beta_{1-42}$ ratio ($p<.001$), than the CN subgroup. The MCI subgroup had lower $A\beta_{1-42}$ ($p=.019$), $A\beta_{1-42}/A\beta_{1-40}$ ratio ($p=.004$) and total Tau/ $A\beta_{1-42}$ ratio ($p=.013$) than the NC subgroup. The Dementia subgroup had higher levels of total Tau ($p<.001$) and p-Tau ($p<.001$) than the MCI subgroup.

Across the subgroup that provided CSF ($n=79$), CSF levels of $A\beta_{1-42}$ were marginally correlated with T-MoCA ($r=.240$, $p=.033$) but not TICS ($r=.163$, $p=.152$) scores, total Tau was negatively correlated with both T-MoCA ($r=-.398$, $p<.001$) and TICS ($r=-.451$, $p<.001$) scores, and p-Tau was negatively correlated with both T-MoCA ($r=-.390$, $p<.001$) and TICS ($r=-.424$, $p<.001$) scores. The Tau/ $A\beta_{1-42}$ ratio (a composite biomarker of AD) was negatively correlated with TICS ($r = -.372$; $p=.001$) and T-MoCA ($r = -.480$; $p<.001$) scores, indicating worse cognitive performance in the face of a stronger “AD” biomarker profile (see Figure 3). In those who were “amyloid positive” on the basis of an $A\beta_{1-42}/A\beta_{1-40}$ ratio greater than 0.056 ($n=29$), total Tau level was negatively correlated with TICS ($r = -.417$; $p=.024$) and T-MoCA ($r = -.379$; $p=.043$) scores, indicating worse cognitive performance with increasing tau in those with AD (see Figure 4).

Discussion

The T-MoCA and the TICS are similarly effective at detecting independently-verified cognitive impairment in elderly individuals assessed remotely via telephone or videoconference. Average scores were worse for patients with MCI than for CN individuals on both tests, and worse for those with dementia than for MCI or CN participants.

Furthermore, the T-MoCA and TICS provided similarly high levels of sensitivity (>90%) and good levels of specificity (> 74%) for differentiating between CN and cognitively impaired (i.e., MCI or dementia) individuals. The level of sensitivity and specificity observed for the TICS is consistent with the 92% sensitivity and 66% specificity for detecting dementia reported from a meta-analysis that pooled results of 6 studies using the TICS⁷. Similarly, the observed sensitivity and specificity for the T-MoCA is consistent with the pooled 98% sensitivity and 69% specificity obtained across 2 studies that used the T-MoCA to differentiate mild vascular cognitive impairment from normal cognition^{7,8,12}. The present results confirm the comparability of the two measures and show that both measures favor sensitivity over specificity as desired for their potential role as screens for cognitive impairment early in the course of AD⁷.

The optimal TICS (< 34/41) and T-MoCA (< 17/22) cut-off scores obtained in the present study are generally consistent with those previously reported. A pooled meta-analysis⁷ suggested a TICS cut-off score of <31/41 for detecting dementia versus normal cognition. The slightly higher cut-point obtained in the present study may reflect the high education (average > 16 years) of our convenience sample. Supporting this possibility, the original sample used to develop the TICS had approximately 13–15 years of education³, and a diverse population-based sample with less education (average <12 years) produced lower TICS cut-off scores for differentiating cognitive impairment (<26/41) or MCI (<29/41) from normal cognition⁶. Similar to the present results, previous studies of the T-MoCA proposed cut-off scores of 17/22¹¹ or 18/22^{7,10} for detecting cognitive impairment in the context of aging or cerebrovascular disease.

Across the spectrum of cognitive decline TICS and T-MoCA scores decreased with increasing CSF levels of total Tau, p-Tau, and the Tau/A β ₁₋₄₂ ratio (a composite AD biomarker). Degree of association with these biomarkers were similar for the two cognitive tests. Although TICS scores were not associated with CSF levels of A β ₁₋₄₂, and T-MoCA scores only marginally so, total Tau was significantly negatively correlated with scores on both tests in those individuals who were “amyloid positive” based on the CSF A β ₁₋₄₀/A β ₁₋₄₂ ratio. These results are consistent with a pathology study that showed correlations between TICS scores 3 to 7 years before death and severity of tangle (i.e., Braak stage) and neuritic plaque (i.e., CERAD pathology score) pathology, but not overall A β pathology (i.e., Thal phase)²³. Correlations between CSF AD biomarkers and TICS and T-MoCA scores suggest the tests may be useful in screening specifically for individuals with cognitive impairment related to AD when other potential causes of cognitive decline (e.g., depression, stroke, delirium) can be clinically excluded.

T-MoCA scores were strongly correlated with TICS scores across the entire sample ($r>0.78$) and specifically within the MCI and Dementia subgroups (both $r's>0.65$). This provides concurrent validity for the T-MoCA as an effective remote cognitive screening method relative to the well-established and well-validated TICS²⁴ and supports that it can be used as an alternative screening test. This option is strengthened by the finding that the two screening tests were equally effective at detecting cognitive impairment that had been verified through detailed in-person cognitive assessment. Because the relationship between the two measures is relatively linear through much of their scales (see Figure 1), regression

models provide a way to estimate scores on one measure by performance on the other to facilitate comparisons across studies. It should be cautioned, however, that linear model-based estimates may not work as well at the lower end of the scale where T-MoCA scores may over-estimate TICS scores and TICS scores under-estimate T-MoCA scores.

Several limitations of the study should be considered. First, the interval between in-person neuropsychological evaluation and administration of the TICS and T-MoCA was more than a year and there could have been diagnostic change during the interval. Second, there was an imbalance in test order between the T-MoCA and TICS with approximately 80% of the participants tested on the T-MoCA first. However, none of the participants were test naïve since all had received a comprehensive in-person neuropsychological assessment (including the MMSE and MoCA) at least a year earlier. Third, the sample was not representative of the population at large, consisting primarily of highly-educated, non-Hispanic white individuals already participating in a longitudinal study of cognitive decline. Previous studies have shown education can affect optimal cut-off scores on cognitive screening tests²⁵, including remote assessment by the TICS⁶. Further research is needed to confirm that the T-MoCA and TICS are equally effective and valid remote cognitive screening methods in diverse populations and across education levels. Fourth, CSF was available from only a subset of participants who agreed to LP (a convenience sample) rather than from a random sample of all study participants. However, those who provided CSF were reasonably representative of the entire group and did not differ from those who did not provide CSF in age, education, sex distribution or cognitive test performance. Finally, it should be noted that the lack of test items that assess visuoconstructional ability, confrontation naming, and visual executive functions may reduce the ability of the TICS and T-MoCA to detect rare variants of AD presenting as posterior cortical atrophy or frontal variant AD. Nevertheless, the present results provide evidence that both the TICS and T-MoCA can effectively serve the growing numbers of patients opting to be seen remotely by their providers²⁶ and add to this growing aspect of health care^{27–29}.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Cummings J, Lee G, Zhong K, Fonseca J, Taghva K. Alzheimer's disease drug development pipeline: 2021. *Alzheimers Dement.* 2021;7:e12179.
2. Alzheimer's Association, 2021 Alzheimer's disease facts and figures. *Alzheimers Dement.* 2021;17(3):327–406. [PubMed: 33756057]

3. Brandt J, Spencer M, Folstein M. The telephone interview for cognitive status. *Neuropsychiatry, Neuropsychol Behav Neurol.* 1988;1(2):111–117
4. Folstein MF, Folstein SE, McHugh PR. “Mini-Mental State”: A Practical Method for Grading the Cognitive State of Patients for the Clinician. *J Psychiatr Res.* 1975;12:189–198. [PubMed: 1202204]
5. Knopman DS, Roberts RO, Geda YE, Pankratz VS, Christianson TJ, Petersen RC, Rocca WA. Validation of the telephone interview for cognitive status-modified in subjects with normal cognition, mild cognitive impairment, or dementia. *Neuroepidemiology.* 2010;34(1):34–42. [PubMed: 19893327]
6. Manly JJ, Schupf N, Stern Y, Brickman AM, Tang M-X, Mayeux R. Telephone-based identification of mild cognitive impairment and dementia in a multicultural cohort. *Arch Neurol.* 2011;68(5):607–614. [PubMed: 21555635]
7. Elliott E, Green C, Llewellyn DJ, Quinn TJ. Accuracy of Telephone-Based Cognitive Screening Tests: Systematic Review and Meta-Analysis. *Curr Alzheimer Res.* 2020;17(5):460–471. [PubMed: 32589557]
8. Pendlebury S, Welch S, Cuthbertson F, Mariz J, Mehta Z, Rothwell P. Telephone assessment of cognition after TIA and stroke: TICS_m and telephone MoCA vs face-to-face MoCA and neuropsychological battery. *Stroke.* 2013;44(1):227–229. [PubMed: 23138443]
9. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, Cummings JL, Chertkow H. The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool for Mild Cognitive Impairment. *J Am Geriatr Soc.* 2005;53(4):695–699. [PubMed: 15817019]
10. Wittich W, Phillips N, Nasreddine ZS, Chertkow H. Sensitivity and specificity of the Montreal Cognitive Assessment modified for individuals who are visually impaired. *J Vis Impair Blind.* 2010;104(6):360–368.
11. Katz MJ, Wang C, Nester CO, Derby CA, Zimmerman ME, Lipton RB, Sliwinski MJ, Rabin LA. T-MoCA: A valid phone screen for cognitive impairment in diverse community samples. *Alzheimers Dement.* 2021;13(1):e12144. doi: 10.1002/dad2.12144.
12. Zietemann V, Kopczak A, Müller C, Wollenweber FA, Dichgans M. Validation of the Telephone Interview of Cognitive Status and Telephone Montreal Cognitive Assessment Against Detailed Cognitive Testing and Clinical Diagnosis of Mild Cognitive Impairment After Stroke. *Stroke.* 2017;48(11):2952–2957. [PubMed: 29042492]
13. Ramirez-Gomez L, Zheng L, Reed B, Kramer J, Mungas D, Zarow C, Vinters H, Ringman JM, Chui H. Neuropsychological Profiles Differentiate Alzheimer Disease from Subcortical Ischemic Vascular Dementia in an Autopsy-Defined Cohort. *Dement Geriatr Cogn Disord.* 2017;44(1–2):1–11. [PubMed: 28595184]
14. Smirnov DS, Galasko D, Edland SD, Filoteo JV, Hansen LA, Salmon DP. Cognitive decline profiles differ in Parkinson disease dementia and dementia with Lewy bodies. *Neurology.* 2020;94(20):e2076–e2087. [PubMed: 32332125]
15. Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer’s disease: Recommendations from the National Institute on Aging–Alzheimer’s Association workgroups on diagnostic guidelines for Alzheimer’s disease. *Alzheimers Dement.* 2011;7(3):270–279. [PubMed: 21514249]
16. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer’s disease: Recommendations from the National Institute on Aging–Alzheimer’s Association workgroups on diagnostic guidelines for Alzheimer’s disease. *Alzheimers Dement.* 2011;7:263–269. [PubMed: 21514250]
17. McKeith IG, Boeve BF, Dickson DW, et al. Diagnosis and management of dementia with Lewy bodies. *Neurology.* 2017;89:88–100. [PubMed: 28592453]
18. Rascovsky K, Hodges JR, Knopman D, et al. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain.* 2011;134(Pt 9):2456–2477. [PubMed: 21810890]
19. Xiao MF, Xu D, Craig MT, Pelkey KA, Chien CC, Shi Y, Zhang J, Resnick S, Pletnikova O, Salmon D, Brewer J, Edland S, Wegiel J, Tycko B, Savonenko A, Reeves RH, Troncoso JC, McBain CJ, Galasko D, Worley PF. NPTX2 and cognitive dysfunction in Alzheimer’s Disease. *Elife.* 2017;6:e23798. doi: 10.7554/eLife.23798. [PubMed: 28440221]

20. Vanderstichele H, Bibl M, Engelborghs S, Le Bastard N, Lewczuk P, Molinuevo JL, Parnetti L, Perret-Liaudet A, Shaw LM, Teunissen C, Wouters D, Blennow K. Standardization of preanalytical aspects of cerebrospinal fluid biomarker testing for Alzheimer's disease diagnosis: a consensus paper from the Alzheimer's Biomarkers Standardization Initiative. *Alzheimers Dement.* 2012;8(1):65–73. [PubMed: 22047631]
21. Kaplow J, Vandijck M, Gray J, Kanekiyo M, Huyck E, Traynham CJ, Esquivel R, Fagan AM, Luthman J. Concordance of Lumipulse cerebrospinal fluid t-tau/A β 42 ratio with amyloid PET status. *Alzheimers Dement.* 2020;16(1):144–152. [PubMed: 31914216]
22. Lleó A, Alcolea D, Martínez-Lage P, et al. Longitudinal cerebrospinal fluid biomarker trajectories along the Alzheimer's disease continuum in the BIOMARKAPD study. *Alzheimers Dement.* 2019;15(6):742–753. [PubMed: 30967340]
23. Robinson AC, Davidson YS, Roncaroli F, Minshull J, Tinkler P, Cairns M, Horan MA, Payton A, Mann DMA. Telephone Interview for Cognitive Status Scores Associate with Cognitive Impairment and Alzheimer's Disease Pathology at Death. *J Alzheimer's Dis.* 2021;84(2):609–619. [PubMed: 34602485]
24. Herr M, Ankri J. A critical review of the use of telephone tests to identify cognitive impairment in epidemiology and clinical research. *J Telemed Telecare.* 2013;19(1):45–54. [PubMed: 23390209]
25. Uhlmann RF, Larson EB. Effect of education on the mini-mental state examination as a screening test for dementia. *J Am Geriatr Soc.* 1991;39(9):876–880. [PubMed: 1885862]
26. Koonin LM, Hoots B, Tsang CA, Leroy Z, Farris K, Jolly T, Antall P, McCabe B, Zelis CBR, Tong I, Harris AM. Trends in the Use of Telehealth During the Emergence of the COVID-19 Pandemic - United States, January-March 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(43):1595–1599. [PubMed: 33119561]
27. Brearly TW, Shura RD, Martindale SL, Lazowski RA, Luxton DD, Shenal BV, Rowland JA. Neuropsychological Test Administration by Videoconference: A Systematic Review and Meta-Analysis. *Neuropsychol Rev.* 2017;27(2):174–186. [PubMed: 28623461]
28. Castanho TC, Amorim L, Zihl J, Palha JA, Sousa N, Santos NC. Telephone-based screening tools for mild cognitive impairment and dementia in aging studies: A review of validated instruments. *Front Aging Neurosci.* 2014;6:16–26. [PubMed: 24611046]
29. Geddes MR, O'Connell ME, Fisk JD, Gauthier S, Camicioli R, Ismail Z, for the Alzheimer Society of Canada Task Force on Dementia Care Best Practices for COVID-19. Remote cognitive and behavioral assessment: Report of the Alzheimer Society of Canada Task Force on dementia care best practices for COVID-19. *Alzheimers Dement.* 2020;12:e12111.

Highlights

- Construct validity for the T-MoCA was newly established against the TICS.
- TICS and T-MoCA effectively detected cognitive impairment with remote administration.
- Both tests negatively correlated with a composite CSF AD biomarker (Tau/A β 1–42).
- T-MoCA has potential to screen specifically for AD-related early cognitive decline.

Research in Context

Systematic review:

The authors reviewed literature on the efficacy of cognitive screening tests that can be administered remotely by telephone or videoconferencing to elderly individuals with normal cognition, mild cognitive impairment, or dementia. Little information was found on correlations between two of the most widely-used remote cognitive screening measures, the TICS and T-MoCA, their relative classification accuracy, or their correlation with markers of AD pathology.

Interpretation:

The TICS and T-MoCA are highly correlated and both tests effectively detect cognitive impairment with remote administration. This provides new construct validity for the T-MoCA. Scores on both tests are negatively correlated with a composite CSF AD biomarker (Tau/A β 1-42) suggesting potential to specifically screen for cognitive impairment related to AD.

Future directions:

Additional research is needed to confirm that the T-MoCA and TICS are equally effective and valid as remote cognitive screening methods in a diverse population and across education levels.

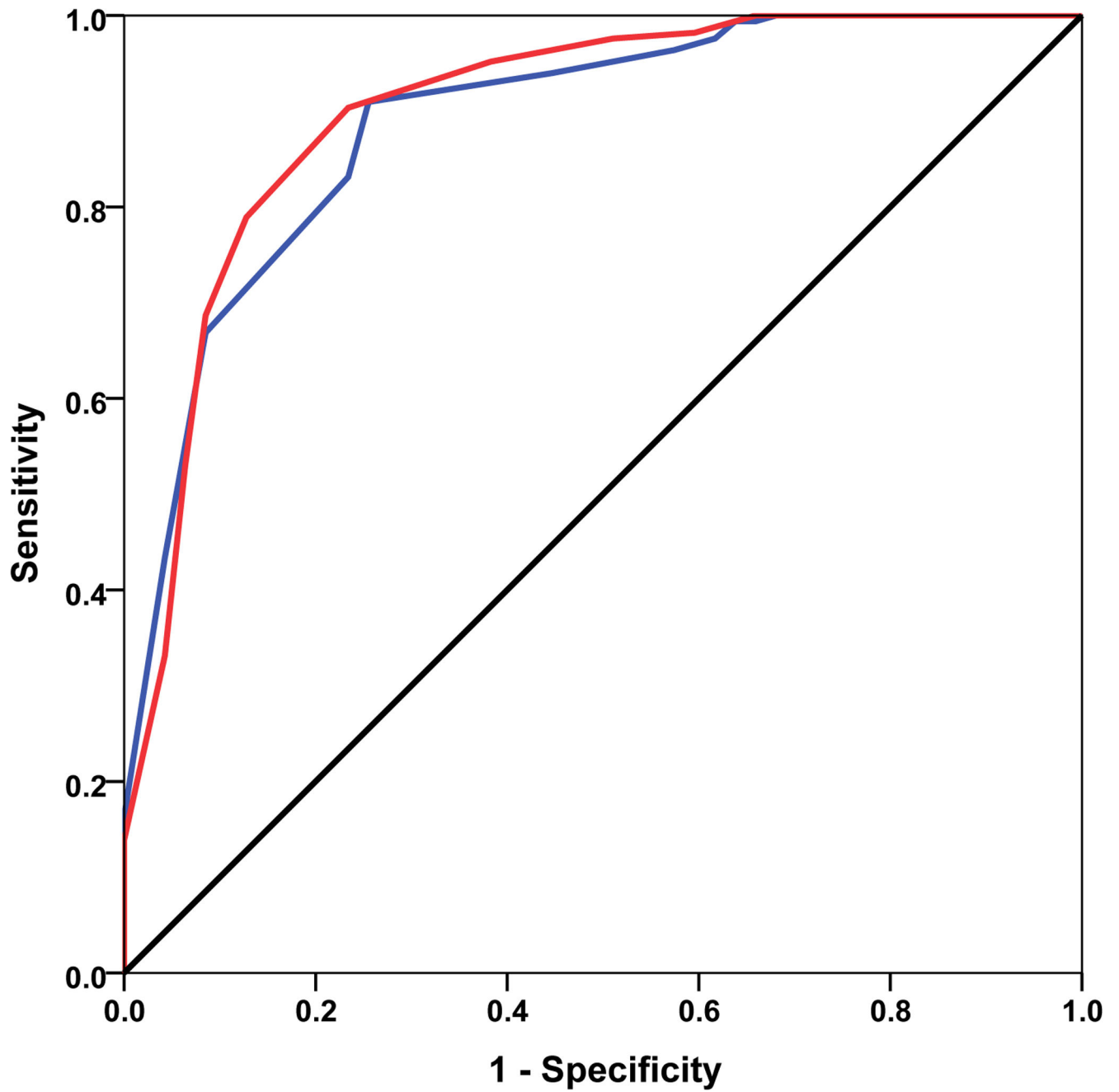


Figure 1. Receiver operating characteristic (ROC) curves comparing sensitivity and 1-specificity in distinguishing Cognitively Normal participants from those with cognitive impairment (Mild Cognitive Impairment or Dementia) for the Telephone Interview for Cognitive Screening (TICS; in blue) and the Telephone version of the Montreal Cognitive Assessment (T-MoCA; in red). Area under the curve for the TICS (.889) and T-MoCA (.902) indicates that both tests were highly accurate.

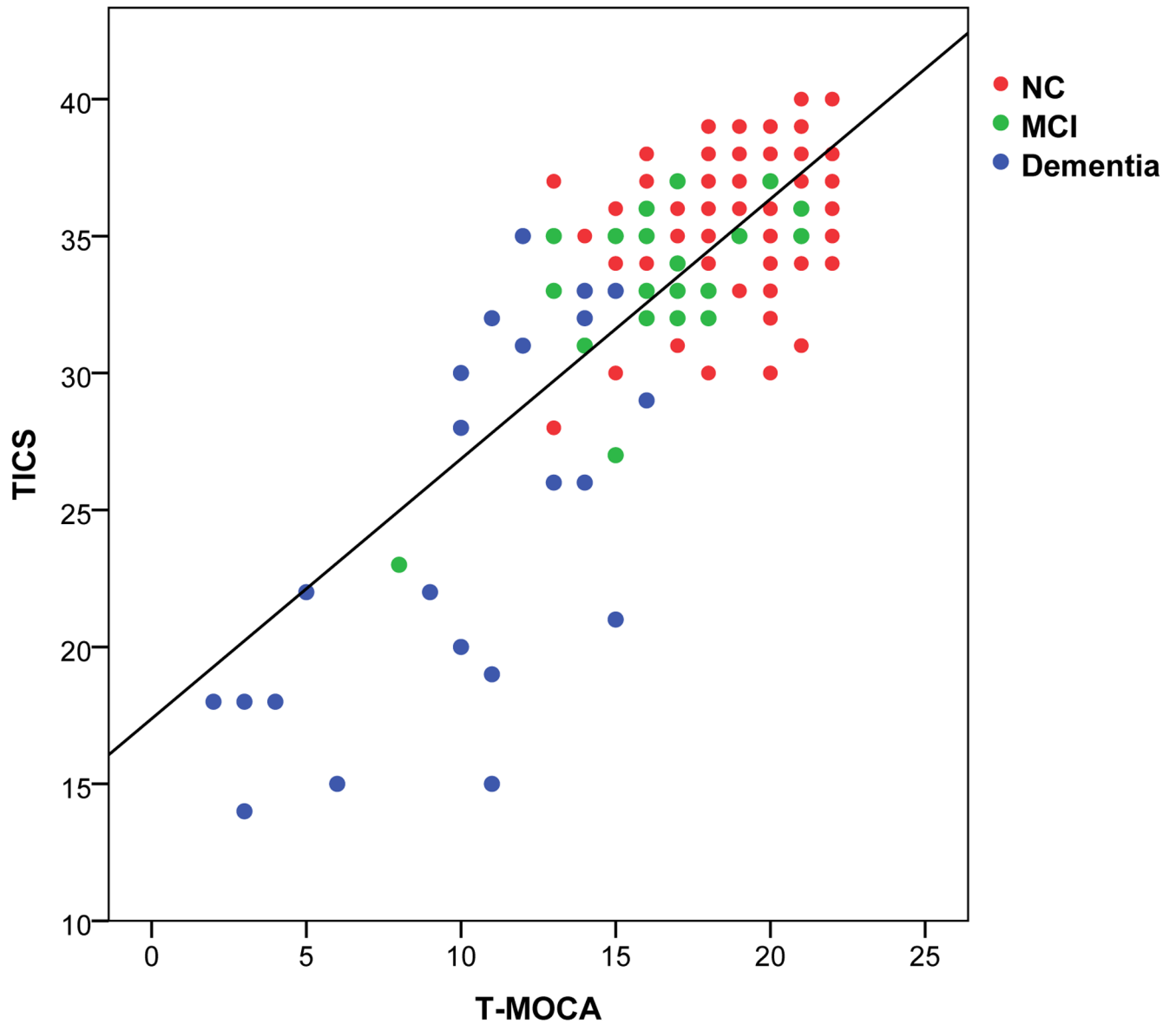


Figure 2. Scores on the Telephone Interview for Cognitive Screening (TICS) as a function of scores on the Telephone version of the Montreal Cognitive Assessment (T-MoCA). Scores were highly correlated ($R^2 = .619$; $p < .001$). The linear line of best fit is shown. Scores for individuals in the Cognitively Normal, Mild Cognitive Impairment (MCI), and Dementia groups are color coded.

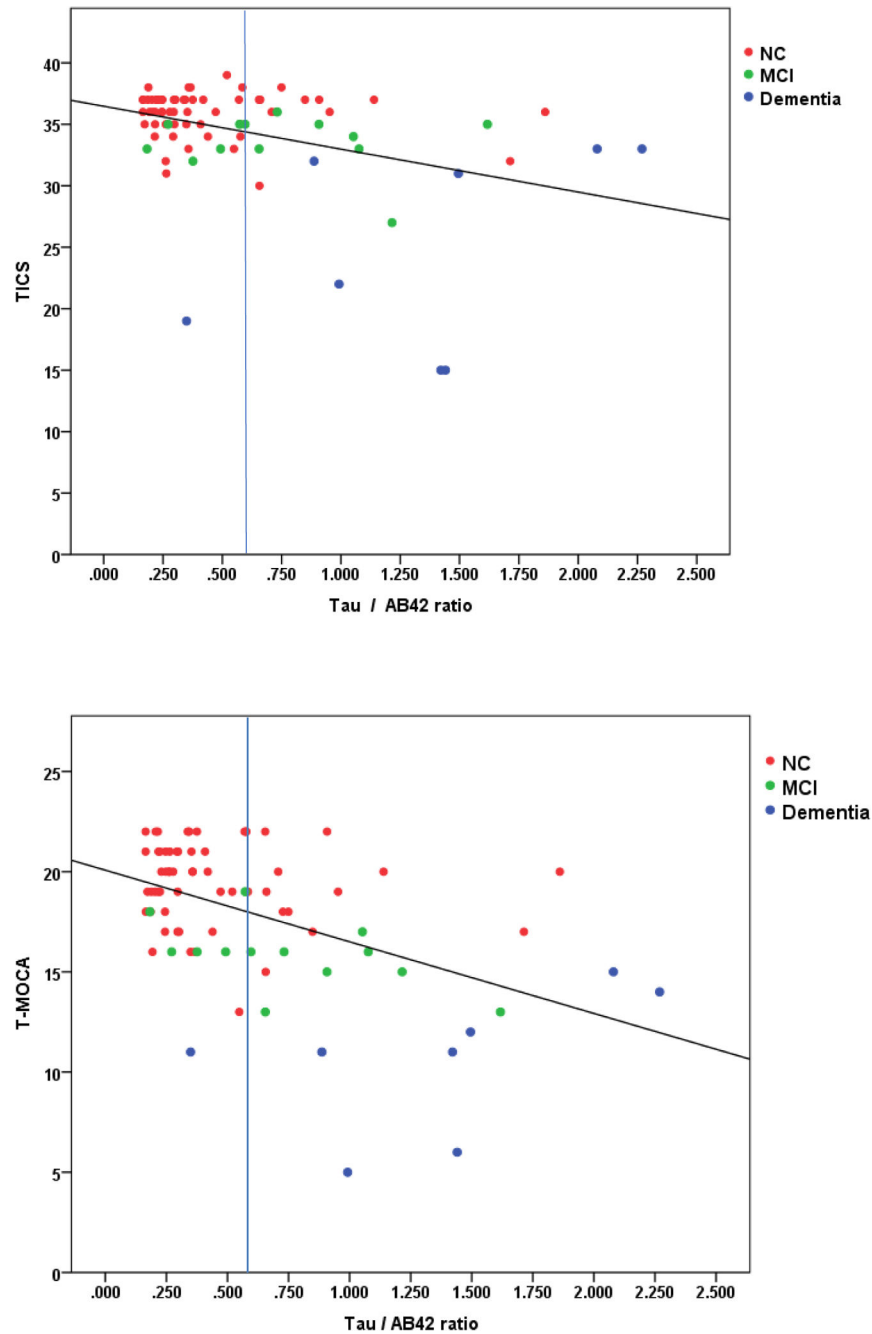


Figure 3. Scores on the Telephone Interview for Cognitive Screening (TICS; upper panel) and the Telephone version of the Montreal Cognitive Assessment (T-MoCA; lower panel) as a function of the total Tau/ $A\beta_{1-42}$ ratio in the subgroup of participants that provided cerebrospinal fluid (CSF). Scores on the TICS ($R^2 = .139$; $p=.001$) and T-MoCA ($R^2 = .230$; $p<.001$) were significantly correlated with the biomarker. The linear line of best fit is shown for each test. A vertical line marks the point at which the total Tau/ $A\beta_{1-42}$ ratio was considered “positive” for Alzheimer’s disease (to the right of the line). Scores for

individuals in the Cognitively Normal, Mild Cognitive Impairment (MCI), and Dementia groups are color coded.

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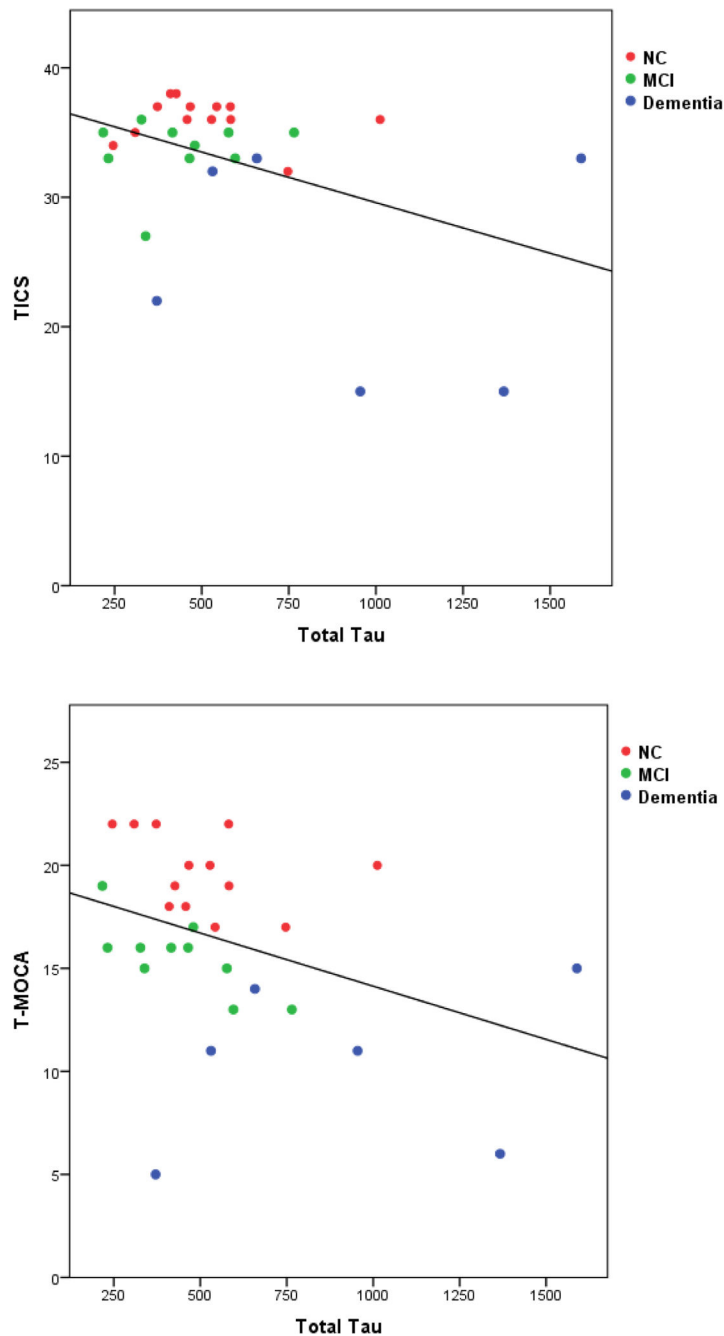


Figure 4. Scores on the Telephone Interview for Cognitive Screening (TICS; upper panel) and the Telephone version of the Montreal Cognitive Assessment (T-MoCA; lower panel) for participants who were “amyloid positive” based on a the $A\beta_{1-42}/A\beta_{1-40}$ ratio as a function of level of total Tau in the subgroup of participants that provided cerebrospinal fluid (CSF). Scores on the TICS ($R^2 = .174$; $p=.024$) and T-MoCA ($R^2 = .143$; $p=.043$) were significantly correlated with total Tau in these subgroups. The linear line of best fit is shown for each test.

Scores for individuals in the Cognitively Normal, Mild Cognitive Impairment (MCI), and Dementia groups are color coded.

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Table 1

Mean (and standard deviation) age, education and Clinical Dementia Rating Sum of Boxes scores of the Cognitively Normal, MCI and Dementia groups. The percentage of females, percentage of Hispanic participants, percentage of participants with history of various chronic diseases and psychiatric disorders, and percentage of participants using various psychoactive medications in each group is also shown. The mean number of days between the TICS and T-MoCA, and mean number of months between the most recent diagnosis made after an extensive in-person evaluation and testing on the Telephone Cognitive (T-COG) assessment battery (which contained either the T-MoCA or TICS) are shown.

	Cognitively Normal n=167	MCI n=25	Dementia n=23
Age (yrs.)	76.78 (6.11)	79.01 (5.62)	78.07 (8.77)
Education (yrs.)	16.69 (2.41)	16.08 (2.89)	15.91 (3.36)
Sex (% Female)	55.7%	32.0%	47.8%
Race/Ethnicity (% Hispanic)	11.4%	20.8%	8.7%
Medical History: Depression	18.6%	32.0%	21.7%
Medical History: Anxiety Disorder	1.8%	4.0%	4.3%
Medical History: Cancer	18.0%	16.7%	17.4%
Medical History: Diabetes (Type II)	8.4%	12.5%	13.0%
Medical History: CAD	10.2%	12.5%	8.7%
Medical History: Hypertension	46.7%	45.8%	34.8%
Medical History: HCL	49.7%	58.3%	43.5%
AD Medication Use	0.6%	20.8%*	34.8%*
Antidepressant Use	28.1%	36.0%	56.5%
Antipsychotic Use	1.8%	4.0%	8.7%
Anxiolytics Use	1.8%	0%	0%
CDR-Sum of Boxes	0.13 (0.32)	1.58 (1.58)*	7.13 (3.72)* [†]
Months between Dx & TCOG	16.61 (7.05)	16.80 (12.29)	13.70 (2.67)
Days between TICS & T-MoCA	4.34 (5.22)	3.88 (3.87)	4.91 (7.44)

* p<.05 vs. CN;

[†] p<.05 vs. MCI.

Abbreviations: AD = Alzheimer's disease; CAD = Coronary Artery Disease; CDR = Clinical Dementia Rating; CN = Cognitively Normal; Dx = most recent diagnosis; HCL = Hypercholesterolemia; MCI = Mild Cognitive Impairment; T-COG = Telephone Cognitive assessment battery; TICS = Telephone Interview for Cognitive Screening; T-MoCA = Telephone version of the Montreal Cognitive Assessment

Table 2

Mean (and standard deviation) scores achieved by the Cognitively Normal (CN), Mild Cognitive Impairment (MCI) and Dementia groups on the Telephone Interview for Cognitive Screening (TICS), the Telephone version of the Montreal Cognitive Assessment (T-MoCA), and tests from the Telephone Cognitive (T-COG) assessment battery.

	Cognitively Normal n=167	MCI n=25	Dementia n=23
TICS (41 points)	35.92 (1.96)	33.20 (3.01) [*]	23.74 (7.38) ^{*†}
T-MoCA (22 points)	19.29 (2.08)	16.24 (2.71) [*]	10.00 (4.33) ^{*†}
Telephone Cognitive Battery (T-COG)			
Forward Span Length	6.68 (1.24)	6.20 (1.16)	5.39 (1.53) ^{*†}
Backward Span Length	5.15 (1.12)	4.36 (1.11) [*]	3.50 (1.14) ^{*†}
Oral Trail-Making A (sec)	9.07 (2.55)	12.24 (6.06) [*]	11.25 (4.33) [*]
Oral Trail-Making B (sec)	35.87 (20.38)	59.00 (38.96) [*]	86.29 (72.16) ^{*†}
Verbal Fluency (F)	15.71 (4.50)	13.46 (5.06) [*]	11.38 (4.90) [*]
Verbal Fluency (L)	14.99 (4.32)	12.17 (4.65) [*]	9.57 (5.70) [*]
Verbal Fluency (“Animals”)	21.87 (5.13)	15.72 (4.31) [*]	10.59 (4.09) ^{*†}
Verbal Fluency (“Vegetables”)	14.19 (4.44)	10.12 (3.10) [*]	5.18 (2.06) ^{*†}
Story Recall Immediate (gist)	16.99 (3.42)	13.04 (4.34) [*]	6.13 (5.17) ^{*†}
Story Recall Delayed (gist)	16.02 (3.55)	9.96 (5.52) [*]	2.91 (4.52) ^{*†}

^{*}p<.05 vs. CN;

[†]p<.05 vs. MCI.

Table 3

Mean (and standard deviation) of Alzheimer's disease biomarkers measured in cerebrospinal fluid (CSF) of subgroups of the Cognitively Normal (CN), Mild Cognitive Impairment (MCI) and Dementia groups. Biomarkers of amyloid beta (A β) 1–40 (A β _{1–40}), A β _{1–42} and their ratio, total Tau and phosphorylated Tau (P-Tau), and the total Tau/A β _{1–42} ratio are shown.

	Cognitively Normal n=58	MCI n=13	Dementia n=8
A β _{1–40}	11409.64 (3539.77)	10940.77 (3315.19)	14767.38 (7666.65) ^{*†}
A β _{1–42}	866.28 (392.79)	601.85 (246.19) [*]	627.13 (210.35)
A β ₄₂ /A β ₄₀ ratio	.0763 (.0219)	.0567 (.0214) [*]	.0465 (.0153) [†]
Tau (total)	330.34 (170.12)	394.31 (177.17)	840.00 (475.77) ^{*†}
P-Tau	45.13 (25.83)	57.63 (26.44)	144.59 (72.26) ^{*†}
Tau/A β ₄₂ ratio	.449 (.340)	.750 (.410) [*]	1.367 (.627) ^{*†}

^{*} p<.05 vs. CN;

[†] p<.05 vs. MCI.