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# The Mexican Cognitive Aging Ancillary Study (Mex-Cog): Study Design and Methods

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## Abstract

**Objective—**Describe the protocol sample and instruments of the Cognitive Aging Ancillary Study in Mexico (Mex-Cog). The study performs an in-depth cognitive assessment in a subsample of older adults of the ongoing Mexican Health and Aging Study (MHAS). The Mex-Cog is part of the Harmonized Cognitive Assessment Protocol (HCAP) design to facilitate cross-national comparisons of the prevalence and trends of dementia in aging populations around the world, funded by the National Institute on Aging (NIA).

**Methods—**The study protocol consists of a cognitive assessment instrument for the target subject and an informant questionnaire. All cognitive measures were selected and adapted by a team of experts from different ongoing studies following criteria to warrant reliable and comparable cognitive instruments. The informant questionnaire is from the 10/66 Dementia Study in Mexico.

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Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: Silvia Mejia-Arango, Rene Nevarez, Alejandra Michaels-Obregon, Rebeca Wong.

Conflict of Interest

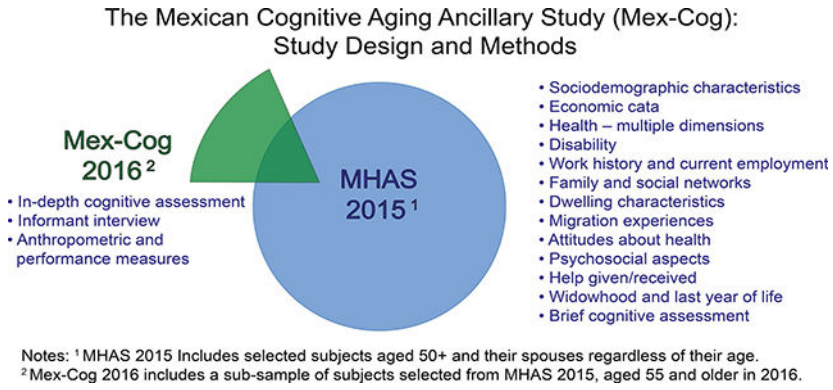
The authors have no conflicts of interest to declare.

Disclosure Statement

**Results—**A total of 2,265 subjects aged 55–104 years participated, representing a 70% response rate. Validity analyses showed the adequacy of the content validity, proper quality-control procedures that sustained data integrity, high reliability, and internal structure.

**Conclusions—**The Mex-Cog study provides in-depth cognitive data that enhances the study of cognitive aging in two ways. First, linking to MHAS longitudinal data on cognition, health, genetics, biomarkers, economic resources, health care, family arrangements, and psychosocial factors expands the scope of information on cognitive impairment and dementia among Mexican adults. Second, harmonization with other similar studies around the globe promotes cross-national studies on cognition with comparable data. Mex-Cog data is publicly available at no cost to researchers.

## Graphical Abstract




### Keywords

Cognitive aging; Epidemiologic studies; Population-based studies; Mexico; MHAS

## Introduction

Cognitive aging has emerged as a global research interest as population aging continues to advance, and a general concern has risen over the consequences of accelerated aging in societies with low institutional assistance for old-age economic and social support. This is important as there is no cure for Alzheimer's disease and related dementias, and it is projected that, by the year 2050, two-thirds of older adults with dementia in the world will live in low-and middle-income countries. Longitudinal studies have emerged that follow national samples of older adults over time to understand the multiple dimensions of aging and health, including cognition.

The Mexican Health and Aging Study (MHAS) is a longitudinal cohort study of adults aged 50 and older in Mexico, with national and urban-rural representation. The baseline survey was completed with a sample of adults born in 1951 or earlier in 2001, and follow-ups were conducted in 2003, 2012, 2015, and 2018, having interviewed more than 25,000 individuals aged 50 and older [1]. Another wave is planned for 2021. The MHAS content includes a wide variety of health and socioeconomic aspects such as self-reports of diagnosed diseases, physical function, depressive symptoms, and cognitive assessment; time use and life

satisfaction; childhood socioeconomic and health conditions, work and migration history; characteristics of children, help given to and received from children; and dwelling conditions, income, pensions, and assets. The MHAS is part of a group of longitudinal studies on aging with similar protocols and content in more than 40 countries around the world. Direct interviews with the target subjects are sought, but proxy interviews are also allowed when the target subject cannot complete the interview for health reasons or temporary absence. The MHAS interviews are applied to the selected person, and his/her spouse is also recruited for the study regardless of age. All interviews are conducted in Spanish, hence non-Spanish speaking population is excluded from the study. Once recruited for the study, subjects are followed over time until their death, even if they relocate within Mexico or if they form new unions, divorce, separate, or become widowed. After death, a next-of-kin exit interview is completed regarding the last year of life of the deceased.

For direct interviews, MHAS cognitive section includes the Cross-Cultural Cognitive Examination (CCCE) [2]. This instrument has been adapted and modified for the different MHAS waves to cover more cognitive domains and include a more sensitive scoring system. The last adaptation of the CCCE includes nine tasks to assess: 1) verbal learning, 2) verbal recall, 3) visuospatial abilities, 4) visuospatial recall, 5) visual scanning, 6) orientation, 7) backward counting, 8) verbal fluency, and 9) serial 7. Based on reference norms by age and education, scores on each task are classified as normal, mild, or severe impaired [3]. For proxy interviews, cognition is assessed through the brief version of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) [4]. As a screening tool for dementia in population settings, a cut-point score of 3.4 had a sensitivity of 0.84 and specificity of 0.80 [5].

The cognitive section of the MHAS has been previously used to examine cognition of Mexican elders and its association with different health and social conditions, applying cross-sectional and longitudinal analysis methods [6–15]. Published works portray an overall picture of disparities in cognitive aging in Mexico, describing the burden of cognitive impairment and dementia in the population, and its association with other diseases and conditions in old age and over the life course, as well as the consequences for caregiving and health systems. Results have pointed towards a need to address this public health problem through public policies that consider modifiable risk factors such as educational attainment, access to health services, environmental exposures, and cardiovascular diseases, among others. Studies comparing cognitive aging in Mexico with other countries [16–18] have also added information regarding health, economic, social, and cultural aspects that differentiate cognitive aging among Mexican origin populations. Despite improvements made over time to the MHAS cognitive instrument, the battery is short by necessity, given that the MHAS is a multi-purpose study of aging, and cannot fully cover the multidimensionality of the cognitive system, limiting the assessment of different cognitive domains to one or two tasks each. In addition, because different cognitive tests are used in different countries with studies like the MHAS, cross-national comparisons are limited.

To incorporate a more in-depth cognitive assessment of older individuals and at the same time contribute to global harmonization in the study of dementia and cognitive aging, researchers from the Health and Retirement Study (HRS), a long-standing longitudinal study

of older adults in the United States, proposed the Harmonized Cognitive Assessment Protocol (HCAP) project to study cognition, collaborating with a network of longitudinal aging studies around the world (https://hrs.isr.umich.edu/about/international-sister-studies). The HCAP project seeks the administration of an expanded battery of cognitive tasks to target subjects and informant reports, using a sub-sample of participants from the respective national studies. The cognitive assessment is highly comparable across countries, and incorporates three sections with increasing difficulty: the first part for the detection of dementia, and the second and third parts for the detection of mild cognitive impairment (MCI). An additional questionnaire is applied to a knowledgeable informant, who reports on the target individual's cognitive status. The cognitive assessment includes well-known neurocognitive measures of memory, attention, language, visuospatial abilities, executive function, and cognitive decline [19–24]. The application of more sensitive instruments, with more tasks to assess cognitive domains, are intended to solve issues related to floor effects in low educated subjects and ceiling effects in subjects with MCI or early stages of dementia. In addition, the use of an informant-based report for all the participants provides another important source of information for the detection of cognitive impairment. While maximum harmonization across countries was sought, each country adapted the questionnaires to fit the language, social context, and culture of their respective populations.

As part of these efforts, the MHAS launched the Cognitive Aging Ancillary Study in Mexico (Mex-Cog) in 2016, applied to a sub-sample of the national MHAS 2015. The primary goal was to expand the knowledge about cognitive aging in Mexico through an in-depth cognitive protocol harmonized with other international studies to allow cross-national comparisons. In addition, as a secondary purpose, the Mex-Cog included a sub-group for which biomarkers and anthropometric measures were collected, with the goal of enhancing further the potential for comparative studies. These were: non-fasting intravenous blood for genetic analysis, and for vitamin D, cholesterol, C-reactive protein, thyroid hormone; plus capillary blood for glucose using HbA1c. Anthropometric and performance measures included blood pressure, height, weight, walking speed, and grip strength. These markers were selected because they required no fasting, they had relatively low cost and could be applied in urban and rural settings, and support the assessment of the presence of the metabolic syndrome in the Mexican population. The objective of this article is to describe the protocol, sample, and instruments of the Mex-Cog ancillary study.

## 2. MEX-COG Protocol

The study protocol comprises an in-home interview with the target person and the informant, conducted by trained interviewers as follows: 1) in-depth cognitive assessment administered to the target person with an approximate duration of 60 minutes, 2) interview with a knowledgeable informant with a duration of 20 minutes, and 3) anthropometric and performance measurements for the target person, as well as blood samples for biomarkers in a sub sample. The selection criterion for the knowledgeable informant was that it should be an adult, capable of answering questions, familiar with the behavior and health of the target subject, most frequently a spouse or an adult child, a resident of the household or caregiver. Interviewers are instructed to seek and select the most adequate informant. The informant is

asked to provide their perception regarding the functionality and behavior of the target subject.

The assessments and interviews were completed using a computer-assisted personal interview (CAPI) for the majority of the survey, although paper and pencil were used for six cognitive exercises that required the use of paper to complete (sentence writing and copy of a figure, visual scan, symbol-digit, copy and recall a copy of three figures). Similar to the MHAS protocol, both spouses in a household were included if they were eligible. If an individual was going to serve as Informant for his/her spouse and was also going to complete a cognitive assessment for him/herself, the interviewers first applied the informant questionnaire regarding the spouse, and then conducted the person's own cognitive assessment.

## 2.1. Cognitive Assessment Measures

The cognitive assessment battery included a version of the Mini-Mental State Examination (MMSE) validated in Mexico [25] and adapted by our team of clinicians and researchers after the Mex-Cog pilot study (see below). For the adaptation, two orientation questions were excluded (What floor are we on? In which neighborhood are we?) because they were deemed inapplicable for the general rural and urban population of Mexico. The question about the name of the city was replaced by a question on the name of the state. The final adapted MMSE was a 10-item scale with a total score of 28.

After the adapted MMSE, the assessment battery includes a series of 21 cognitive tasks divided into seven domains (see Appendix Table 1), selected by the HRS/HCAP team working in collaboration with the Mex-Cog team. The adaptation sought to incorporate measures suitable to the Mexican context and to rural and less educated groups of Mexican elders. As previously mentioned, the cognitive battery is divided into three parts. The first one intends to detect dementia and includes the adapted MMSE, followed by measures of verbal learning, verbal fluency, visual scan, backward counting, naming, and delayed verbal recall. The second part incorporates tests with higher cognitive demands for the detection of MCI, such as immediate and delayed logical memory, list word recognition, copy and recall constructional praxis, and symbol-digit. For the third part, we added two tasks of executive function that measure abstract reasoning and inhibition control. Three cognitive scores can be calculated in the Mex-Cog: an individual score for each task, a composite score for the different cognitive tasks within each domain, and a total composite score from the sum of all tasks across domains (see Appendix Table 1 for details of tasks grouped by cognitive domains).

**2.1.1 Cognitive Assessment Structure—**To minimize the burden on impaired respondents [26], the study subjects completed a short or a long cognitive assessment depending on their performance on the adapted-MMSE score (maximum 28 points); more details of this battery are provided below. If the individual scored 10 points or less, a short version of the interview was applied. The selection of this cut-point was based on the diagnostic accuracy of the MMSE at various cut points for dementia in community settings [27]. For short interviews, in addition to the adapted MMSE, interviewers continued

administering the assessment until the end of the first part, which was designed to ensure the detection of dementia. If the score was 11 points or more on the adapted MMSE, the second and third parts with higher cognitive demands were administered. In both short and long interviews, at the end of the cognitive assessment, questions about self-reported memory, history of lead exposure, history of traumatic brain injury, and a depressive symptoms scale from the MHAS [28] were also included. These items were included as part of the country-specific interest in environmental exposures and brain health for older adults in Mexico.

### 2.2. Informant Measures and Structure

The informant questionnaire incorporated the Community Screening Interview for Dementia (CSI'D) [29], an informant scale used in the 10/66 Dementia studies. The questionnaire asks about the target person's cognitive and functional performance on an everyday basis. The original version of the CSI'D had 27 items; however, we separated the question about incontinence into two different questions on urine and bowel control, for a total of 28 items.

The interview with informants also had a short or long version, depending on the answers to the CSI'D. A positive response to two or more of six selected questions capturing impairment severity determined that a long interview would be applied. The six items were: a general decline in mental function; serious problem remembering things; forgetting what happened the day before; forgetting where he/she is; change in the ability to think or reason; and difficulty getting dressed. In the long interview cases, interviewers continued by asking the informant about the target person's decline process using an adapted version of the History and Aetiology Schedule (HAS) [30]. Eleven of the items were selected and adapted by our team, to establish the type of cognitive deterioration (gradual or sudden onset of symptoms, symptoms progression, and presence of mental and behavioral disorders). At the end of the informant interview, a selection of care needs of the target subject, as well as their activities inside and outside of the household, were also included. See Appendix Table 2 for details of the questionnaire items.

## 3. Material and Methods

### 3.1. Sample Selection

The Mex-Cog 2016 sample was selected using the MHAS wave 4 (2015) as a sampling frame. The latter survey was conducted in October to December of 2015, as a follow-up of a sample with a national and urban-rural representation of adults aged 50 and older, distributed over all 32 states of Mexico. Following the survey protocol, trained interviewers from the Mexican Statistical Bureau (Instituto Nacional de Estadística y Geografía, INEGI) conducted the interviews. The MHAS 2015 included 13,850 direct interviews, 929 proxy interviews, and 1,209 next-of-kin interviews.

From the MHAS sample, the criteria for eligibility for Mex-Cog were: first, aged 55 and older in the MHAS 2015; and completed a direct interview or a proxy interview for health reasons in the MHAS 2015. A total of 12,926 subjects distributed in the 32 states were eligible. Second, the sample was distributed in 8 of the 32 states, which were selected using stratified sampling procedures. As mentioned above, this is because the Mex-Cog 2016

included collection of biomarkers, anthropometric and performance measures in a sub-group. The 8 states were selected aiming to represent the national population using strata of states according to the following criteria: socioeconomic (percent urban, rural, number of residents who are former migrants to the U.S.) and health exposures (percent with obesity, diabetes, mine industry, and pottery industry). These criteria cover the variety of socioeconomic and health exposures over the life course that are associated with cognitive function in old age. Once the 8 states were selected, all MHAS 2015 subjects who were eligible in each state were included as the sample for Mex-Cog 2016.

The total Mex-Cog target sample included 3,250 individuals. The fieldwork was conducted in two phases, in the spring and the fall of 2016. Interviewers from the National Institute of Public Health in Mexico conducted the Mex-Cog interviews, and their health teams collected blood samples and completed the anthropometric and performance measures. Study subjects provided oral or written consent to participate in Mex-Cog and to provide each biomarker. The study was approved by the Institutional Review Boards of the University of Texas Medical Branch (UTMB) in the United States and the National Institute of Public Health in Mexico.

### 3.2. Response Rates

Mex-Cog interviews were completed for 2,265 subjects, representing a response rate of 69.7 percent. See Figure 1 for the distribution of cases according to the type of interviews completed. Of this total, there were 193 cases for which only the cognitive assessment was obtained and 223 for which only the informant interview was obtained. In both cases, the main reason for the missing interview was the absence of the target person (160/193) or absence of the adequate informant (163/223), respectively. Of the 2,042 subjects who carried out the cognitive assessment, only 5.6% (115) completed a short interview. Of the 2,072 cases with an informant questionnaire, 62% (1,292) did a short interview.

Table 1 reveals that the distribution of the Mex-Cog sample (column 3) by sociodemographic factors and depressive symptoms does not differ significantly from the distribution in the target Mex-Cog sample (column 2) and the eligible sample from the larger MHAS study (column 1). Similarly, the average cognitive function scores do not differ significantly. Further analysis comparing Mex-Cog responders (69.7%) and non-responders (30.3%) showed no statistical differences ($p<.05$).

Table 2 presents the response rates by main characteristics of the target sample. Overall, the response rates were similar (around 70%) across groups defined by sex, age, education, community of residence, and cognitive status in MHAS 2015. One noticeable exception is the response rate by type of interview completed in MHAS 2015, where only 53% of those who completed a proxy interview in 2015 also completed an interview for Mex-Cog 2016. This result implies that the proxy respondents from the parent MHAS sample are under-represented in the Mex-Cog study.

### 3.3. Sample Characteristics

Table 1 column 3 shows the characteristics of the 2,265 individuals who participated in the Mex-Cog study. Nearly 60% of Mex-Cog subjects were female; 79% were aged 60 and

older, while 40% were aged 70 and older; 70% had fewer than 7 years of formal education, while 18% had zero; and about 56% lived in urban areas, while 29% lived in semi-rural or rural communities. A total of 2,072 informants completed an interview. Of these, 42% were spouses and 36% were adult children; 35% had elementary school and 7% had no formal education; and 79% lived in the same household as the study subject (results not shown).

## 4. Validity Analysis

To examine validity, we followed Messick's [31] approach endorsed by the American Educational Research Association and the American Psychological Association [32], based on the validity of the inferences made from scores. For the Mex-Cog cognitive instrument, the underlying constructs are cognitive status and, more specifically, cognitive domain status inferred from scores. For the informant's questionnaire, cognitive status and cognitive deterioration processes are the underlying constructs inferred from the answers given by the informants. We analyzed four of the five sources of validity proposed by Messick [33, 34]: 1) content, 2) response process, 3) internal structure, and 4) relationship with other variables. The fourth source of validity, consequences of the assessment, does not apply given the cross-sectional design of the Mex-Cog study.

### 4.1. Content of the Instruments

Researchers from the MHAS and 10/66 Dementia studies contributed to the selection of the items to be included in the cognitive assessment and the informant's questionnaire based on the proposal from HRS researchers [35]. We followed four criteria for selection of the cognitive tasks: 1) items that can identify profiles of impairment across different cognitive domains and levels of impairment from MCI to dementia, 2) items suitable for in-home application by trained interviewers, and that could be culturally adapted for rural and low-educated populations in the context of Mexico, 3) items that overlap those used in the MHAS cognition section as a matter of comparability, and 4) the same or similar items to those used in the HRS/HCAP study, to maximize harmonization. All items and measures included in the Mex-Cog cognitive instrument are used by population-based studies of dementia and cognitive impairment [36–41]. They are part of well-known neuro-cognitive scales and batteries (CERAD, WMS, Digit-Symbol, Brief CSI'D, FAB, CCCE) [2, 19, 21–24] used to measure different cognitive domains and subdomains (orientation, immediate memory, delayed memory, attention, language, processing speed, visuospatial abilities, and executive function). This neuropsychological approach is based on a model of brain functioning in which domain assessment yields a performance profile to detect dysfunctions of different neural networks caused by dementia [42]. As previously mentioned, the informant questionnaire items were selected from the Informant items used by the 10/66 Dementia studies [38]. Specifically, we included the CSI'D [29] to assess cognitive status and several questions from the HAS [30], to assess the process of deterioration. All selected questions and task instructions were translated into Spanish and adapted as needed to be applicable to the Mexican rural and urban context. To pretest the Mex-Cog protocol, a group of geriatricians, psychiatrists, and neuropsychologists from the National Institute of Geriatrics in Mexico City conducted a pilot study with 21 older adults and 17 informants.

Modifications to the wording of the instructions and survey questions were then further incorporated in the final version of the instruments and protocol.

### 4.2. Response Process

The response process is defined here as evidence of data integrity [34]. To control sources of error associated with the cognitive assessment application, interviewers from the National Institute of Public Health in Mexico (Instituto Nacional de Salud Publica, INSP) who had experience in other home-based surveys (e.g., the National Health and Nutrition Survey in Mexico [43]) were trained by the principal investigator of the study and by a neuropsychologist during 6-hour daily sessions for a week, including practice sessions with older adults from the community. An interviewer manual was prepared (available from the MHAS website) and provided to each of the interviewers. The manual was followed throughout the training sessions to address any issues. Standardization for the assessment application was established by implementing uniform procedures for the interviews, using a CAPI for most of the interview, which incorporated direct instructions to move back and forth between paper-pencil and CAPI. Instructions for each measure were read by the interviewer directly from the CAPI, ensuring the same wording for all individuals. The CAPI provided all expected response options for the interviewer to register the answer, with the goal of avoiding differences in interpretation and ensuring the accuracy of responses. After the fieldwork, the survey unit of the National Institute of Public Health in Mexico processed the data and sent a database to the MHAS team at UTMB for further data cleaning and scoring of tasks as needed. Based on the original source of each task (e.g., CERAD, WMS, etc.), scoring instructions were adapted for each measure to construct the final score variables. Also, paper and pencil measures were scored by two different scorers previously trained by a neuropsychologist, who served as a third scorer in case of discrepancies. Additional documentation on scoring and programming of scores are available from the MHAS study website.

### 4.3. Internal Structure of the Instruments

The structure of the cognitive instrument was based on the multidimensional nature of neurocognitive functions. Domain scores were the sum of individual task scores in each domain, while the total composite score was the sum of all the domains. Reliability coefficients for individual cognitive domains were calculated to evaluate internal structure and correlations between age, education, and part-whole correlations with the adapted MMSE. Reliability analysis using the seven cognitive domain scores showed high internal consistency (Cronbach’s alpha = 0.93). Corrected Item-total correlation for each of the seven domains was: Orientation (0.70); Immediate Memory (0.77); Delayed Memory (0.83); Attention (0.78); Language (0.73); Visuospatial Abilities (0.73); and Executive Function (0.86). Deletion of any domain score did not increase the reliability coefficient, showing a high correlation among the domain scores.

To study variations of cognitive abilities by demographic characteristics, we examined the association between domain scores and age (Figure 2a) and years of education (Figure 2b). As expected, we found a negative correlation with age and a positive correlation with years of education. Finally, considering that the MMSE has been used as a measure of global

cognition, we estimated the correlation between the adapted-MMSE group of items (total=28 points) and the respondent's total Mex-Cog score excluding these MMSE items (total=356 points), and found a strong positive association (r=0.83); see Figure 3a.

For reliability analysis of the informant questionnaire, we examined the CSI'D scores. We found high internal consistency (Cronbach's alpha = 0.88), with a corrected Item-total correlation for each of the 28 items ranging between 0.37 and 0.61, while deletion of any item did not increase the reliability coefficient. Finally, we examined the correlation between the respondent's total Mex-Cog score (total=384 points) and the CSI'D informant's score (total=52 points); see Figure 3b. As expected, we found a negative association, showing that lower cognitive performance by the target subject was associated with a higher rating of the subject's cognitive decline provided by the informant.

## 5. Conclusions

We provided a summary of the in-depth cognitive aging ancillary study (Mex-Cog) conducted in 2016 using a rural and urban sub-sample of the MHAS wave 4 completed in Mexico in 2015. A clear strength of the Mex-Cog is its use of a comprehensive assessment protocol, evaluating all cognitive functions necessary for a research diagnosis and classification of normal cognition, MCI, and dementia in Mexico. The multi-domain measurement of cognitive function offers a more precise assessment of cognition than the current practice used in most population-based surveys. Because of cost and time-demands, this type of in-depth cognitive assessments cannot be conducted in every large study of aging or in every wave of the MHAS. However, the Mex-Cog design allows cross-walking between the sub-sample and the MHAS longitudinal assessments completed before and after the Mex-Cog, as well as between the Mex-Cog sub-sample and the full 2015 sample of the MHAS from which the sub-sample was selected. This feature will enable the research community to contribute to population-based studies of cognitive function incorporating a wide variety of socioeconomic and health information. For longitudinal follow-up, it is worth mentioning that, among those who completed the Mex-Cog in 2016, 60% (n=1,362) had completed the four waves of the MHAS from 2001 to 2015 and 99% had completed at least two of these previous interviews. Furthermore, the richness and potential impact of the data are enhanced by the availability of biomarkers. Of those who participated in the Mex-Cog in 2016, a large proportion provided blood samples to obtain biomarkers as follows: 88% for HbA1C; 82% for Vitamin D, Cholesterol, C-reactive protein, and thyroid hormone; and 81% provided an EDTA sample for genotyping.

Another strength of the Mex-Cog is that the cognitive assessment was applied in person to the target subjects, by trained interviewers who applied the protocol in the target subject's home. In addition, the protocol included an interview with an informed person who provided an assessment of the respondent's performance and history of cognitive decline. This is useful information to improve the classification of the cognitive status of subjects, both to corroborate or supplement the subject's assessment and to provide information when subjects are unwilling or unable to complete the assessments themselves. Also, the in-home survey facilitated the interview with the knowledgeable informant, who often was the spouse or an adult co-resident child of the target person. The structure of a short and long interview

in Mex-Cog permitted the cognitive assessment to move along items that give progressively more in-depth information on the target subject's cognitive function while taking into consideration the burden attributable to cognitive assessments in those with severe impairment. A similar short or long structure used for the informant interview allowed gathering of complementary information about the cognitive deterioration of the target subject only for those subjects considered by the informant to be cognitively impaired.

We presented four sources of validity evidence that support meaningful interpretation of the assessment scores used in the Mex-Cog from the perspective of validity as a unitary concept and construct validity as the whole validity [31, 34]. We emphasized the use of domain scores, considering that the interpretation of single task scores may lead to inaccurate inferences due to intra-individual performance variability [44]. Cognitive profiles based on domain scores contribute substantially to the diagnosis of neurocognitive disorders based on criteria proposed by the Diagnostic and Statistical Manual of Mental Disorders [45] and the recommendations of the National Institute on Aging and the Alzheimer's Association [46]. However, future studies may contribute with additional methods of classifying cognitive domains through statistical measurement models like item response theory, factor analysis, or other approaches. Further, a diagnostic algorithm using Mex-Cog data to assign a research diagnosis of cognitively normal, MCI, and dementia is being developed by the Mex-Cog research group and will be published in a future paper.

Limitations of the Mex-Cog worth mentioning include the relatively small sample size, which may limit the analysis of in-depth cognitive function stratified by sub-groups of the population. Another limitation is the low educational achievement of the sample, which resulted in a relatively high number of missing values in difficult tasks such as subtract-7 (see Appendix Table 1), or inability to complete tasks that involved literacy or numeracy, or inability to complete tasks that involved drawing or writing due to motor limitations or vision or hearing impairment. This limitation implies that researchers will have to decide on the proper scoring of such items. Careful considerations of these features in the application of the protocol in low-income countries will be topics of future research for the harmonized cross-country efforts.

Lastly, one of the most important features of the Mex-Cog instruments and protocol is that these were harmonized with other similar studies around the globe, as part of the HCAP, a group of studies which should enable population-based research on cognitive function with a cross-national perspective. More details of this cross-national project can be found in the HCAP/HRS publication [47].

Like the MHAS, the databases from the Mex-Cog and the respective questionnaires and documentation are available to the research community without cost at www.MHASweb.org in English and www.ENASEM.org in Spanish.

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# Appendix

**Appendix Table 1.**

Tasks of Cognitive Assessment, Scores, and Missing Values by Cognitive Domain *

| Domain | Task | Number of Items | Possible Score |
|---|---|---|---|
| **. Orientation** | 1. Day of the month | 1 | 1 |
| | 2. Month | 1 | 1 |
| | 3. Year | 1 | 1 |
| | 4. Day of the week | 1 | 1 |
| | 5. What time is it? | 1 | 1 |
| | 6. Where are we now? | 1 | 1 |
| | 7. How can I get to store to buy a soda? | 1 | 1 |
| | 8. Country | 1 | 1 |
| | 9. State | 1 | 1 |
| | **Subtotal** | **9** | **9** |
| **2. Immediate Memory** | 1. Repeat 3 words | 3 | 3 |
| | 2.1– 2.3 Repeat 10 words / 3 trials | 30 | 30 |
| | 2.4 Total *(***)* | | *30* |
| | 2.5 Average *(***)* | | *10* |
| | 3.1 Immediate recall of short story | 6 | 12 |
| | 3.2 Immediate recall short story – Approx. *(***)* | | *6* |
| | 3.3 Immediate recall short story – Exact *(***)* | | *6* |
| | 4.1 Immediate recall of long story | 25 | 50 |
| | 4.2 Immediate recall of long story – Approx. *(***)* | | *12* |
| | 4.3 Immediate recall of long story – Exact *(***)* | | *12* |
| | **Subtotal** | **64** | **95** |
| **3. Delayed Memory** | 1. Delayed recall of 3 words | 3 | 3 |
| | 2. Delayed recall of 10 words | 10 | 10 |
| | 3.1 Delayed recall of short story | 6 | 12 |
| | 3.2 Delayed recall short story – Approx. *(***)* | | *6* |
| | 3.3 Delayed recall of short story – Exact *(***)* | | *6* |
| | 4.1 Delayed recall of long story | 25 | 50 |
| | 4.2 Delayed recall of long story – Approx. *(***)* | | *25* |
| | 4.3 Delayed recall of long story – Exact *(***)* | | *25* |
| | 5. Recall by recognition of 10 words | 20 | 20 |
| | 6. Delayed recall of 4 figures | 4 | 11 |
| | **Subtotal** | **68** | **106** |
| **4. Attention** | 1. Visual scan | 1 | 60 |

| Domain | Task | Number of Items | Possible Score |
|---|---|---|---|
| | 2. Backward counting | 1 | 5 |
| | **Subtotal** | **2** | **65** |
| **5. Language** | 1. Following instructions 3 steps | 3 | 3 |
| | 2. Following instructions 2 steps | 2 | 2 |
| | 3. Naming shoe | 1 | 1 |
| | 4. Naming pencil | 1 | 1 |
| | 5. Naming Elbows | 1 | 1 |
| | 6. Define Bridge | 1 | 1 |
| | 7. Use of Hammer | 1 | 1 |
| | 8. Use of Scissors | 1 | 1 |
| | 9. Repetition | 1 | 1 |
| | 10. Reading | 1 | 1 |
| | 11. Writing | 1 | 1 |
| | **Subtotal** | **14** | **14** |
| **6. Constructional Praxis** | 1. Copy one figure | 1 | 1 |
| | 2. Copy 4 figures | 4 | 11 |
| | **Subtotal** | **5** | **12** |
| **7. Executive Function** | 1. Serial 3 | 5 | 5 |
| | 2. Serial 7 | 5 | 5 |
| | 3. Verbal Fluency | 1 | 4 |
| | 4. Symbols and Digits | 1 | 56 |
| | 5. Similarities | 3 | 3 |
| | 6. Go no Go | 10 | 10 |
| | **Subtotal** | **25** | **83** |
| **TOTAL** | | **187** | **384** |

*(*)*The grouping of tasks by domain is suggested by the Mex-Cog project. Users can group tasks differently.

*(**)*r. = does not respond; .i = incomplete; .l = physical or visual limitation; .c = short interview; .s = skip; .m = no response [Frequencies out of n = 2,042].

*(***)*Variables also available in the database, but not considered in the calculation of Total Score.

## Appendix Table 2.

Informant Interview Items, Scores, and Missing Values by Domain

| | | Possible Items or Points |
|---|---|---|
| **1. Cognitive Decline** | 1. Change in daily activities | 3 |
| | 2. Change in mental functioning. | 1 |
| | 3. Serious problems remembering. | 1 |
| | 4. Forgets where she/he put things. | 2 |

| | | Possible Items or Points |
|---|---|---|
| | 5. Forgets where things are usually kept | 2 |
| | 6. Forgets friend's names | 2 |
| | 7. Forgets names of family members | 2 |
| | 8. Forgets what to say in the middle of conversation | 2 |
| | 9. Forgets words when speaking | 2 |
| | 10. Uses wrong words | 2 |
| | 11. Talks more about the past | 2 |
| | 12. Forgets when she saw you last time | 2 |
| | 13. Forgets what happened day before | 2 |
| | 14. Forgets where he/she is | 2 |
| | 15. Gets lost in the neighborhood | 2 |
| | 16. Gets lost at home | 2 |
| | 17. Difficulty adjusting to changes in daily routine. | 2 |
| | 18. Changes in the ability to think or reason. | 1 |
| | 19. Mistaken a family member or friend for another person | 1 |
| | 20. Difficulty making decisions about daily life. | 1 |
| | 21. Thought process is confusing or illogic | 1 |
| | **Subtotal** | **37** |
| **2.Functional Decline** | 1. Difficulty with usual household chores | 2 |
| | 2. Stopped doing usual activities or hobbies | 1 |
| | 3. Difficulty managing money | 2 |
| | 4. How is the ability to eat | 3 |
| | 5. How is the ability to get dressed | 3 |
| | 6. Difficulty controlling urine | 2 |
| | 7. Difficulty controlling bowel movement | 2 |
| | **Subtotal** | **15** |
| **TOTAL** | | **52** |

(**) r. = does not respond; .i = incomplete; .l = physical or visual limitation; .c = short interview; .s = skip; .m = no response [Frequencies out of n = 2,072].

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## Highlights

- Mex-Cog is a data source for cognitive aging in Mexico linked to the larger MHAS
- Combines measurements of multiple domains of cognition and informant interviews
- Cross-walking to the MHAS extends the scope with longitudinal data and biomarkers
- Mex-Cog forms part of a multi-country Harmonized Cognitive Aging Protocol (HCAP)
- Supports cross-national population-based research on cognitive aging and dementia

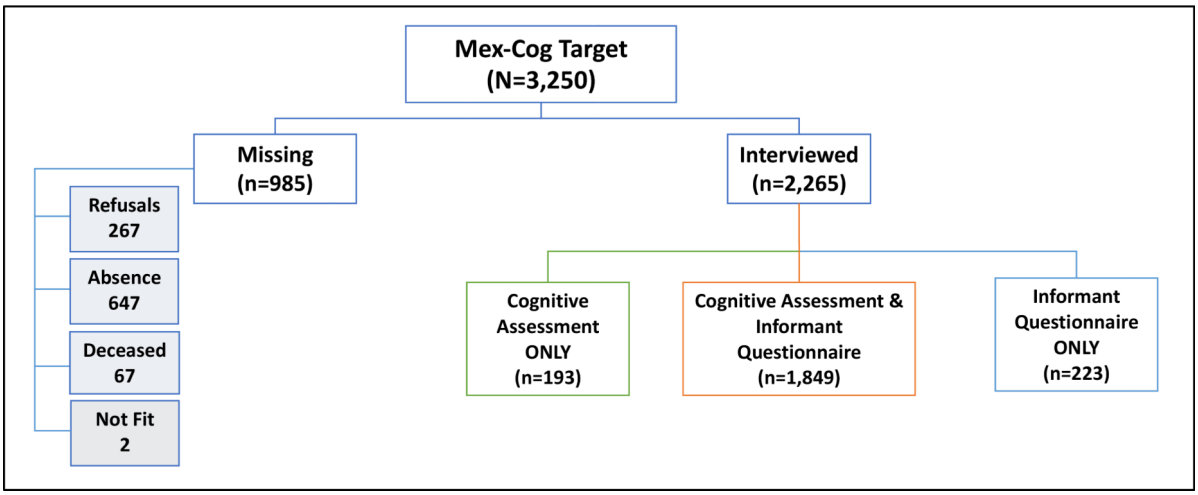


**Figure 1.**
Mex-Cog Sample Distribution by Type of Instrument Completed

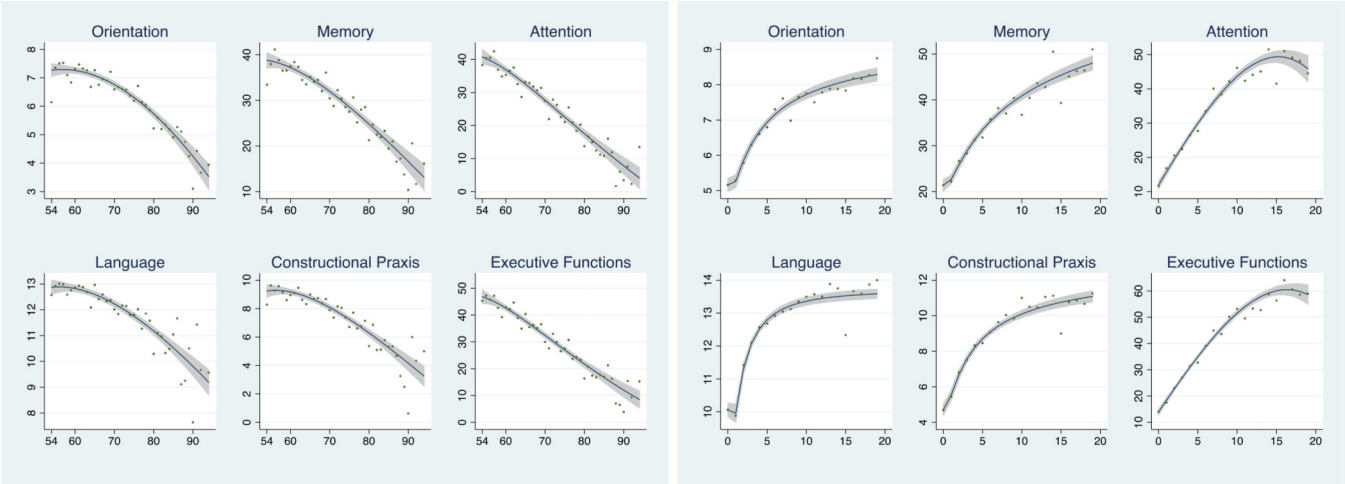


**Figure 2.**

a. Mex-Cog Score in Cognitive Domains by Age[1]

b. Mex-Cog Score in Cognitive Domains by Years of Education

Note: Each dot represents the mean score (of each domain) by the variable of interest (age or years of education, respectively). The curve represents the predicted values using fractional polynomials to regress the total score by the variable of interest; the gray area indicates the confidence interval of the mean.

[1]Using a STATA command to calculate the prediction of each domain score as the dependent variable using a fractional polynomial of the independent variable, and plots the resulting curve along with the confidence interval of the mean predicted value.

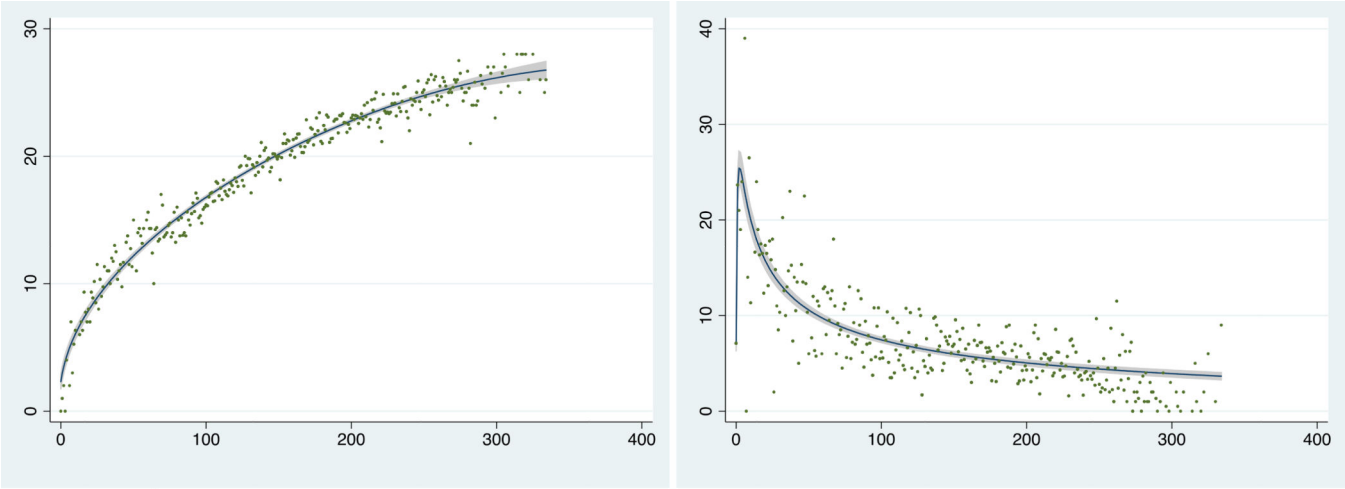


**Figure 3.**

a. Adapted-MMSE score by total cognitive cognitive score[1]

b. Informant score by total score[2]

Notes: [1] In Figure 3a, each dot represents the mean of the Adapted-MMSE score (maximum 28 points) by the total cognitive score excluding the MMSE items. The Mex-Cog total score (excluding the MMSE items) maximum possible score is 356. [2] In Figure 3b, each dot represents the mean of the CSI'D Informant score (maximum 52 points) by the total cognitive score (including all items; the maximum score is 384).

The curves represent the predicted values using fractional polynomials to regress the Y-axis variable by the X-axis variable; the gray area indicates the confidence interval for the mean of the Y-axis variable.

**Table 1.**

Demographic characteristics of the MHAS eligible sample, target subsample for Mex-Cog, and Mex-Cog completed interviews[1].

| Variables | MHAS sample [2] (1) N=12,926 | Target Mex-Cog (2) N=3,250 | Mex-Cog sample [3] (3) N=2,265 | p-value [4] (1) vs (2) | p-value [4] (2) vs (3) |
|---|---|---|---|---|---|
| *Sex – n (%)* | | | | | |
| Men | 5,604 (43.4) | 1,421 (43.7) | 976 (43.1) | p>0.05 | p>0.05 |
| Women | 7,322 (56.6) | 1,849 (56.3) | 1,289 (56.9) | p>0.05 | p>0.05 |
| *Age – Mean (SD)* | *68.1 (9.3)* | *67.8 (9.2)* | *68.1 (9.0)* | p>0.05 | p>0.05 |
| Age groups – n (%) | | | | | |
| 54–59 | 2,758 (21.3) | 721 (22.2) | 477 (21.1) | | |
| 60–69 | 4,943 (38.2) | 1,284 (39.5) | 886 (39.1) | | |
| 70–79 | 3,556 (27.5) | 839 (25.8) | 622 (27.5) | | |
| 80+ | 1,665 (12.9) | 405 (12.5) | 279 (12.3) | | |
| *Years of Education – Mean (SD)* | *5.6 (4.7)* | *5.7 (4.7)* | *5.3 (4.4)* | **p<0.05** | **p<0.05** |
| Education Groups – n (%) | | | | | |
| 0 years | 2,299 (18.0) | 514 (15.8) | 400 (17.8) | | |
| 1–6 years | 6,689 (53.3) | 1,724 (53.0) | 1,238 (55.2) | | |
| 7+ years | 3,794 (29.7) | 974 (30.0) | 603 (26.9) | | |
| *Occupation – n (%)* | | | | | |
| Currently Working | 4,598 (35.7) | 1,163 (35.8) | 793 (35.1) | p>0.05 | p>0.05 |
| Looking for Work | 204 (1.6) | 48 (1.5) | 30 (1.3) | p>0.05 | p>0.05 |
| Household Work | 3,603 (27.9) | 968 (29.8) | 706 (31.2) | p>0.05 | p>0.05 |
| Retired, Disabled, Doesn't Work | 4,484 (34.8) | 1,067 (32.9) | 733 (32.4) | p>0.05 | p>0.05 |
| *Marital Status – n (%)* | | | | | |
| Married/Union | 8,349 (64.6) | 2,070 (63.7) | 1,483 (65.5) | p>0.05 | p>0.05 |
| Separated/Divorced | 1,316 (10.2) | 354 (10.9) | 222 (9.8) | p>0.05 | p>0.05 |
| Widowed | 2,706 (20.9) | 677 (20.8) | 458 (20.2) | p>0.05 | p>0.05 |
| Single | 555 (4.3) | 149 (4.6) | 102 (4.5) | p>0.05 | p>0.05 |
| *Living Arrangements – n (%)* | | | | | |
| Living Alone | 1,107 (8.6) | 286 (8.8) | 185 (8.2) | p>0.05 | p>0.05 |
| With Spouse | 2,024 (15.7) | 484 (14.9) | 353 (15.6) | p>0.05 | p>0.05 |
| With Family or Others (spouse)[5] | 9,795 (75.8) | 2,480 (76.3) | 1,727 (76.3) | p>0.05 | p>0.05 |
| *Depressed – n (%)*[6] | *3,837 (31.2)* | *974 (31.2)* | *708 (32.3)* | p>0.05 | p>0.05 |
| *Community of Residence – n (%)* | | | | | |
| Urban (Population of 100,000+) | 7,466 (57.8) | 1,904 (58.6) | 1,265 (55.8) | p>0.05 | p>0.05 |
| Semi-Urban (15,000 – 99,999) | 1,759 (13.6) | 458 (14.1) | 339 (15.0) | p>0.05 | p>0.05 |
| Semi-Rural (2,500 – 14,999) | 1,217 (9.4) | 286 (8.8) | 203 (9.0) | p>0.05 | p>0.05 |
| Rural (<2,500) | 2,484 (19.2) | 601 (18.5) | 458 (20.2) | p>0.05 | p>0.05 |
| *MHAS 2015 Type of Interview – n (%)* | | | | | |
| Direct | 12,367 (95.7) | 3,134 (96.4) | 2,204 (97.2) | p>0.05 | p>0.05 |

| Variables | MHAS sample [2] (1) N=12,926 | Target Mex-Cog (2) N=3,250 | Mex-Cog sample [3] (3) N=2,265 | p-value [4] (1) vs (2) | p-value [4] (2) vs (3) |
|---|---|---|---|---|---|
| Proxy | 559 (4.3) | 116 (3.6) | 61 (2.8) | p>0.05 | p>0.05 |
| *MHAS 2015 Cognitive Score – Mean (SD)* | | | | | |
| Direct Interviews [7] | 56.6 (20.9) | 57.7 (20.7) | 56.3 (20.6) | p>0.05 | p>0.05 |
| Proxy Interviews [8] | 3.7 (0.03) | 3.7 (0.06) | 3.6 (0.09) | p>0.05 | p>0.05 |

Notes:

[1] Sample sizes vary due to missing values.

[2] Includes all subjects from the MHAS sample eligible for the Mex-Cog: aged 55 and older with a direct or proxy interview (for health reasons) during the MHAS 2015 fieldwork

[3] Includes Mex-Cog completed assessments and/or interviews.

[4] Differences between MHAS sample, Target Mex-Cog, and Mex-Cog Sample were estimated comparing 95% confidence intervals (using ci mean and ci proportions) for each category.

[5] Includes living with children, extended family or other non-relatives and spouse if any.

[6] Using a modified version of the CES-D scale and indicating 5 o more depressive symptoms in MHAS 2015.

[7] Using the MHAS CCCE; includes nine tasks to asses: verbal learning, verbal recall, visuospatial abilities, visuospatial recall, visual scanning, orientation, backward counting, verbal fluency, and serial 7.

[8] Using the MHAS version of IQCODE.

**Table 2.**

Mex-Cog Study Response Rates. [1]

| Variables | Response Rate |
|---|---|
| *Sex* | |
| Men | 68.7% |
| Women | 70.5% |
| *Age Groups* | |
| 54–59 | 66.2% |
| 60–69 | 69.0% |
| 70–79 | 74.1% |
| 80+ | 68.9% |
| *Education Groups* | |
| 0 years | 77.8% |
| 1–6 years | 71.8% |
| 7+ years | 61.9% |
| *Community of Residence* | |
| Urban (Population of 100,000+) | 66.4% |
| Semi-Urban (15,000 – 99,999) | 74.0% |
| Semi-Rural (2,500 – 14,999) | 71.2% |
| Rural (<2,500) | 76.2% |
| *MHAS 2015 Type of Interview* | |
| Direct | 70.3% |
| Proxy | 52.6% |
| *MHAS 2015 Cognitive Status* | |
| Normal | 70.2% |
| CIND | 68.9% |
| Dementia | 67.1% |

Note:

[1] Own calculation using Mex-Cog 2016

[2] Response rates calculated as: Number of completed interviews in Mex-Cog (cognitive assessment and/or informant interview) divided by number of cases selected for Target Mex-Cog (n=3,250).