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Late Life Depressive Symptoms and Cognitive Function among Older Mexican Adults: The Past and the Present

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Abstract

Objective: To evaluate associations between depression and individual cognitive domains and how changes in depressive symptoms relate to cognition three years later in the context of Mexico, a developing country experiencing rapid aging.

Method: Data comes from waves 3 (2012) and 4 (2015) of the Mexican Health and Aging Study (n=12,898, age 50+). Depression is ascertained using a modified Center for Epidemiologic Studies – Depression Scale. Cognition is assessed using verbal learning, verbal memory, visual scanning, verbal fluency, visuospatial ability, visual memory, and orientation tasks. Depressive symptoms and cognitive functioning were both measured in 2012 and 2015. Scores across cognitive domains are modeled using ordinary least squares regression, adjusting for demographic, health, and economic covariates.

Results: When depression and cognition were measured concurrently in 2015, depression exhibited associations with all cognitive domains. When considering a respondent's history of depression, individuals who had elevated depressive symptoms in 2012 and recovered by 2015 continued to exhibit poorer cognitive function in 2015 in verbal learning, verbal memory, visual scanning, and verbal fluency tasks compared to individuals who were neither depressed in 2012 nor 2015.

Conclusions: Depression was associated with cognition across cognitive domains among older Mexican adults. Despite improvements in depressive symptomatology, formerly depressed respondents continued to perform worse than their counterparts without a history of depression on several cognitive tasks. In addition to current mental health status, researchers should consider an individual's history of depression when assessing the cognitive functioning of older adults.

Background:

Rapid population aging in Mexico has made the mental health, including late-life depression and cognitive functioning, of older adults an important public health and health policy priority. An estimated one out of every eight older adults in Mexico have major depressive

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symptoms (García-Peña et al., 2008), and the prevalence of cognitive impairment with no dementia (CIND) and dementia among older Mexican adults are estimated to be 28.7% and 6.1% respectively (Mejia-Arango & Gutierrez, 2011). While these are unique clinical entities, depression and cognitive impairment often co-occur (Afridi, Hina, Qureshi, & Hussain, 2011; Butters et al., 2004; Korczyn & Halperin, 2009; Potter & Steffens, 2007). This has been observed in several cross-sectional and longitudinal analyses that have noted significant negative correlations between depression and cognition (Diniz, Butters, Albert, Dew, & Reynolds, 2013; González, Bowen, & Fisher, 2008; Goveas et al., 2014; Mourao, Mansur, Malloy-Diniz, Costa, & Diniz, 2016; Richard et al., 2013). In Mexico, the prevalence of cognitive impairment among older adults is estimated to be approximately 38% higher in depressed individuals compared to the non-depressed (García-Peña et al., 2008). To this end, some have suggested late-life depression can be a preventable risk factor for mild cognitive impairment and dementia (Byers & Yaffe, 2011; Diniz et al., 2013; Mourao et al., 2016; Steenland et al., 2012).

Due to their common co-occurrence, previous work has suggested multiple mechanisms that may plausibly connect late-life depression to cognitive ability. For example, various brain regions may be negatively affected by depression which may lead to diminished cognitive ability. The hippocampus may play a role in diminished cognitive function, particularly in memory tasks, among depressed adults (Potter & Steffens, 2007). In addition, depression is associated with activity of the hypothalamic-pituitary-axis (HPA) (Nemeroff & Vale, 2005; Sapolsky, 2001) and increases in glucocorticoid hydrocortisone which may contribute to damage in the hippocampus and reduced hippocampal volumes (Sapolsky, 1996). Although depression and hippocampal atrophy do not always co-occur, depression has been found to be associated with decreased hippocampal volume in several studies (Campbell, Marriott, Nahmias, & MacQueen, 2004; Sawyer, Corsentino, Sachs-Ericsson, & Steffens, 2012; Steffens, McQuoid, Payne, & Potter, 2011; Videbech & Ravnkilde, 2004). Further, prolonged activation of the HPA has also been found to be associated with release and deposition of amyloid-beta in animal models (Dong & Csernansky, 2009). Depression is also associated with reduction in the volume of other brain regions important to cognitive functioning, including the prefrontal cortex (Bremner et al., 2002; Drevets et al., 1997) and greater white matter atrophy in the temporal and parietal lobes (Lee et al., 2012).

In addition to these intermediary mechanisms, researchers have hypothesized that depression is the result of early signs of cognitive deterioration as individuals notice cognitive changes (Jorm, 2001) or that both changes in cognition and depression may be driven by shared risk factors such as cerebrovascular diseases (Richard et al., 2013). Other investigators have argued that depression represents a prodromal feature of dementia, thus explaining their co-occurrence (Brommelhoff et al., 2009; Yaffe et al., 1999). Recent findings from the Whitehall II revealed that although older adults with and without dementia experienced similar depressive symptoms in middle age, older adults with dementia exhibited increased depressive symptomology 11-years prior to a dementia diagnosis (Singh-Manoux et al., 2017). These findings provide evidence that increasing depressive symptoms are part of the dementia prodrome (Singh-Manoux et al., 2017; Steffens, 2017).

While prior studies have evaluated the association between depression and cognition in order to identify mechanisms through which they may be related, less research has examined whether the cognitive profiles of individuals with a history of depression differ from individuals without a history of depression. Previous studies have emphasized the importance of considering depression history when modeling cognitive function and decline (Jorm, 2001; Potter & Steffens, 2007) as cognitive deficits may persist after depressed individuals have recovered from past episodes of depression (Bhalla et al., 2006; Neu et al., 2005; Reppermund, Ising, Lucae, & Zihl, 2009; Richard et al., 2013). Persistence of cognitive deficits among the formerly depressed has also been found in meta-analyses (Hasselbalch, Knorr, & Kessing, 2011; Rock, Roiser, Riedel, & Blackwell, 2014). Further, decreased volume of the hippocampus has been observed in formally depressed patients who have been depression-free for months to decades (Sheline, Wang, Gado, Csernansky, & Vannier, 1996). Moreover, persistently elevated depressive symptoms have been associated with poorer executive function and an accelerated decline in memory and attention (Dotson, Resnick, & Zonderman, 2008), greater declines in memory, verbal knowledge, and verbal fluency (Goveas et al., 2014), and incident dementia (Richard et al., 2013). Overall, these studies suggest that depression may lead to an increased risk of cognitive decline independent of other risk factors including vascular disease (Barnes, Alexopoulos, Lopez, Williamson, & Yaffe, 2006; Goveas et al., 2014). Taken together, these findings suggest a greater need to consider how current depression and history of depression may interact to impact cognitive function.

Most work on depression and cognition has focused on countries in later stages of economic development including European countries and the United States. For instance, a meta-analysis using data primarily from higher-income countries has found cross-sectional associations between depression and episodic memory, executive function, as well as processing speed but not semantic or visuospatial memory (McDermott & Ebmeier, 2009). Another meta-analysis found negative associations between depression and executive function, memory, and attention (Rock et al., 2014) when comparing the currently depressed to non-depressed controls. The importance of research outside of high-income countries is accented by the fact that depression is a global phenomenon, affecting both developed and developing contexts (Lépine & Briley, 2011). Indeed, depression is predicted to become the leading cause of loss of disability adjusted life years globally in the coming decades (World Health Organization, 2004) with major impacts in developing countries (Murray & Lopez, 1997).

Despite the expected global burden of depression, few studies have focused on depression in countries in earlier stages of economic development (Guerra et al., 2016; Patel, Araya, & Bolton, 2004). This is an important distinction as factors which influence *both* depression and cognition may vary significantly across countries and economic context. Overall levels of education are often lower in developing countries, and a meta-analysis found low education to be consistently associated with depression in developing countries (Lima & Soares, 2008). A preponderance of evidence also shows education to be closely associated with cognitive ability (Fors, Lennartsson, & Lundberg, 2009; Jefferson et al., 2011; Lee, Kawachi, Berkman, & Grodstein, 2003; Singh-Manoux, Richards, & Marmot, 2005). Findings from Mexico indicate education is associated with both lower depression (García-

Peña et al., 2008; Slone et al., 2006) and better cognitive health (Al Hazzouri, Haan, Galea, & Aiello, 2011). Furthermore, mental health disorders in low- and middle-income countries are less likely to be detected (Lima & Soares, 2008) and treated (World Health Organization [WHO], 2018) which has been the case in Mexico (Guerra et al., 2009). Given the unique contexts of education and mental health in developing countries, more studies examining the association between late-life depression and cognitive ability are needed.

We build upon prior studies by evaluating individual cognitive domains to better elucidate the nuanced relationships between depression and cognition and estimate associations while accounting for confounding variables including demographic, health, and economic characteristics. Our results may guide the development of interventions aimed at ameliorating the effects of late-life depression on the risk of cognitive impairment and dementia, especially in the context of developing countries. Specifically, the aims of the current analysis are: 1) to estimate the association between depression and individual cognitive domains; and 2) to determine whether a respondent's history of depression is associated with cognitive function in the context of Mexico, a developing country experiencing rapid aging. Regarding our first aim, we hypothesize that depression will be associated with poorer cognitive function across cognitive domains. For our second aim, we hypothesize that respondents with a history of depression will have diminished cognitive function relative to their non-depressed counterparts without a history of depression.

Methods:

Data:

Data came from the 2012 and 2015 waves of the Mexican Health and Aging Study (MHAS) (MHAS, 2015). The MHAS is a large, nationally representative, sample of older adults (age 50+) and their spouses/partners. The first wave of the MHAS was collected in 2001 and the sample was followed-up in 2003. In 2012, a refresher cohort was added that was born between 1952 and 1962 to maintain representation of the Mexican population aged 50 and over. The original and refresher cohorts were followed up in 2015. The 2012 and 2015 waves were then the baseline and follow-up points for our analysis, respectively, as our analyses were only based on those interviewed 2012 and later (including both the original and refresher cohorts). The MHAS collects data across a variety of domains including demographics, chronic conditions, depression, cognitive function, income, and wealth, among others. The MHAS is highly comparable to the United States Health and Retirement Study (HRS) and has been described in greater detail elsewhere (Wong, Michaels-Obregon, & Palloni, 2017). The MHAS is partly sponsored by the National Institutes of Health/ National Institute on Aging (grant number NIH R01AG018016). Data files and documentation are public use and available at www.MHASweb.org. While the 2015 MHAS sample included 14,217 respondents age 50 and older, we omitted proxy interviews as they do not contain the cognitive measures we analyze (n=918), and also individuals missing information on: depression (n=132) all cognitive domains (n=72), and covariates included in the analysis (n=197) resulting in a sample size of 12,898 for our cross-sectional analyses.

Cognitive Function:

Cognitive function was measured using the Cross-Cultural Cognitive Examination (CCCE) (Glosser et al., 1993). The CCCE is useful among populations with limited literacy and mathematical ability (Wolfe et al., 1992). Several domains are captured in the CCCE including verbal learning (the respondent was read a list of eight words and asked to recall them, this was repeated two more times and the total number of words recalled across trials was summed, range 0–24), verbal recall (the eight word list was recalled after a delay, range 0–8), visual scanning (the respondent was asked to identify a visual stimulus in an array of visual stimuli, range 0–60), visuospatial ability (respondent was asked to draw a figure, range 0–6), and visual memory (respondent was asked to recall the figure they drew after a delay, range 0–6). We also analyzed verbal fluency (respondent identified as many animals as he/she was able in one minute, range 0–60), and orientation (respondent identified the day, month, and year, range 0–3). We standardized cognitive scores by calculating the respondent's z-score using sample means and standard deviations across cognitive tasks. Standardization was done by task due to the large differences in domain ranges so regression parameter estimates represented differences in cognition in terms of standard deviations for all domains. Higher scores indicated better cognitive functioning across domains. Standardized cognitive scores were constructed for both the 2012 and 2015 waves of the MHAS. We used the 2015 cognitive scores as outcome variables in our analyses and used the 2012 cognitive scores to adjust for past differences in cognitive function.

Depressive Symptoms:

Depressive symptoms were assessed in the MHAS using a modified nine-item version of the Center for Epidemiologic Studies – Depression (CES-D) scale (Radloff, 1977). Respondents were asked whether they experienced the following symptoms of depression in the previous week: 1) feeling depressed, 2) feeling that everything he/she did was an effort, 3) feeling that his/her sleep was restless, 4) feeling happy (reverse coded), 5) feeling lonely, 6) feeling that he/she enjoyed life (reverse coded), 7) feeling sad, 8) feeling tired, and 9) feeling that he/she had a lot of energy (reverse coded). These items were presented as binary outcomes (yes/no). Following previous research using the MHAS (Agudelo-Botero, Giraldo-Rodríguez, Murillo-González, Mino-León, & Cruz-Arenas, 2018), we classified participants who responded "yes" to five or more items as being depressed and participants who responded affirmatively to four or fewer items as non-depressed. The reliability of the modified CES-D instrument and the validity of this cut-point have been established in this population in prior work (Aguilar-Navarro, Fuentes-Cantú, Ávila-Funes, & García-Mayo, 2007). Respondents were classified as depressed or non-depressed in both the 2012 and 2015 waves of the MHAS. With these classifications, we constructed a four-level variable based on depression status in both 2012 and 2015. Categories included: stable non-depressed (non-depressed in 2012 or 2015), formerly depressed (depressed in 2012 but not in 2015), newly depressed (depressed in 2015 but not in 2012), or stable depressed (depressed in both 2012 and 2015).

Covariates:

We included several covariates in our analysis to capture the respondents' demographic, economic, and health characteristics. We included the respondent's age, sex, educational

attainment, marital status, and locality size as demographic covariates. Educational attainment was measured as years of formal education. Marital status was categorized as married/partnered, widowed, or other (divorced, separated, or never married). Locality size was categorized as 100,000+ residents, 15,000–99,999 residents, 2,500–14,999 residents, or fewer than 2,500 residents. We measured economic wellbeing through income and wealth. Income was measured at the individual level as the sum of income from various sources while wealth was assessed at the household level as the total value of assets including money in stocks and accounts, businesses, vehicles, real estate, and other assets. Missing values of both income and wealth were imputed by the MHAS (Wong, Orozco-Rocha, Zhang, Michaels-Obregon, & Gonzalez-Gonzalez, 2016). We categorized both income and wealth into deciles which were treated as continuous variables in our models. Parameter estimates then represented the change in cognition associated with increasing one decile of either income or wealth.

We also evaluated the respondents' health characteristics by including chronic conditions and health behaviors. Chronic conditions were measured using respondents' self-report of hypertension, diabetes, cancer, stroke, heart attack, and respiratory conditions. We then created a categorical variable representing whether the respondent reported no chronic conditions, one chronic condition, or two or more chronic conditions. Health behaviors included smoking (classified as current smoker, former smoker, or never smoker) and whether the respondent reported binge drinking (having four or more alcoholic beverages in a single occasion) in the past three months. All economic, demographic, and health covariates came from the 2015 wave of the MHAS.

Statistical Analysis:

We presented descriptive results of respondents in the 2015 wave of the MHAS stratified by elevated depressive symptomatology and conducted t-tests to test for differences in continuous variables by depression status and chi-square tests to test for differences in binary and categorical variables by depression status. In descriptive results, cognitive scores were presented before standardization to provide distributional information while regression results used standardized cognitive scores so that depression parameter estimates were in similar scales across cognitive tasks with differing ranges. We conducted two sets of regression analyses. First, we used ordinary least squares (OLS) regressions to model the cross-sectional associations between elevated depressive symptoms and cognitive domains, both determined in 2015. The purpose of our first set of analyses was to determine whether elevated depression and cognition were associated in similar ways across domains of cognitive function. In addition to elevated depressive symptoms, these models included respondents' age, sex, level of education, marital status, locality size, income decile, wealth decile, smoking behavior, binge drinking, and number of chronic conditions. We also tested interactions between sex and depression as prior studies have noted differences in the associations between depression and cognition by sex (Biringer et al., 2005; Forno et al., 2005; Paterniti, Dufouil, Bisserbe, & Alpérovitch, 1999). In our second set of analyses, we modeled cognitive domains in 2015 as a function of our four level variable combining depression status in 2012 and 2015 to understand how history of depression and current depressive status was related with cognition across domains. In this set of analyses, we

modeled cognition in 2015 with and without accounting for differences in cognition in 2012 to determine whether cognitive differences in 2015 were due to persistent cognitive differences over follow-up. All regression models were estimated using Stata SE version 14.2.

Results:

Descriptive Results:

We present our descriptive results for our analytic sample in 2015 (follow-up) by depression status in Table 1. Approximately 31% (3,972) of our sample was classified as depressed based on the count of depressive symptoms. The analytic sample was 57.8% female and had an average age of 66.5. Respondents with elevated depressive symptoms performed significantly worse on all cognitive tasks. Cohen's d statistics for each cognitive task by depression were 0.31, 0.22, 0.37, 0.34, 0.21, 0.18, and 0.27 for verbal learning, verbal recall, visual scanning, verbal fluency, visuospatial, visual memory, and orientation, respectively. The depressed and non-depressed groups in our sample showed several other significant differences in terms of their demographic, health and health behavior, and economic characteristics. Depressed respondents were more likely to be older, female, less educated, widowed, living in a more rural area, and in a lower decile of income and wealth. Depressed respondents also reported higher levels of never smoking, not binge drinking in the previous three months, and reported more chronic conditions.

Cross-Sectional Results:

Regression results are shown in Table 2. Depression was associated with poorer cognitive performance across all cognitive domains. Parameter estimates for depression indicated that, compared to the non-depressed, individuals with elevated depressive symptoms scored between 0.04 and 0.15 standard deviations worse on cognitive tasks. Parameter estimates for depression were: verbal learning ($\beta=-0.15$, $p<0.001$), verbal recall ($\beta=-0.10$, $p<0.001$), visual scanning ($\beta=-0.09$, $p<0.001$), verbal fluency ($\beta=-0.11$, $p<0.001$), visuospatial ability ($\beta=-0.06$, $p<0.01$), visual memory ($\beta=-0.04$, $p<0.05$), and orientation ($\beta=-0.12$, $p<0.001$). Being older, having fewer years of education, living in a more rural area, having less income, and being in a lower decile of wealth were associated with poorer cognitive function across all cognitive domains. Women performed significantly better on verbal learning, verbal recall, and visual scanning tasks, whereas men performed better on the visuospatial task. In ancillary analyses (results not shown, available upon request), we tested whether the association between depression and cognitive domains differed for older males and females by creating an interaction between sex and elevated depressive symptomatology. While the interaction between sex and depression did not reach statistical significance for any domain, the interaction was marginally significant for verbal learning ($p=0.0557$) suggesting the association between depression and cognition may be stronger among males than females. When we stratified the models by sex, the depression parameter estimates were ($\beta=-0.19$, $p<0.001$) and ($\beta=-0.09$, $p<0.001$) for males and females, respectively, indicating a stronger negative association between depression and verbal learning for males.

History of Depression & Current Depression:

We then present our regression results for history of depression in Table 3. As our analysis of history of depression inherently required that respondents be interviewed at baseline and follow-up, our sample size for the second set of analyses was reduced to 11,299 respondents. Based on our four-level variable on depression status at baseline and follow-up, approximately 55% of respondents were classified as stable non-depressed, 14% were classified as formerly depressed, 13% were classified as newly depressed, and 18% were classified as stable depressed. For each cognitive domain, we fit two models. Models in Panel A regressed cognition at follow-up as a function of depression operationalized as the four-level variable on depression status at baseline and follow-up and the control variables used in Table 2. Models in Panel B added standardized domain specific cognitive scores from baseline. While depression was contemporaneously associated with poorer cognition across domains in our cross-sectional results, several differences by domain emerged when considering a respondent's history of depression.

In Panel A, compared to stable non-depressed, formerly depressed respondents still exhibited poorer cognitive performance in verbal learning ($\beta=-0.06$, $p<0.05$), verbal recall ($\beta=-0.06$, $p<0.05$), visual scanning ($\beta=-0.07$, $p<0.01$), and verbal fluency ($\beta=-0.09$, $p<0.001$) at follow-up. No significant differences in cognition were noted for visuospatial ability, visual memory, or orientation between stable non-depressed and formerly depressed. When we adjusted for differences in baseline cognitive function in the models in Panel B, respondents who had elevated depressive symptoms at baseline and had recovered by follow-up only performed significantly worse on the verbal fluency task. This suggests that, rather than having greater cognitive decline between baseline and follow-up, respondents who recovered from elevated depressive symptoms had poorer cognitive function at baseline than the stable non-depressed, and this disparity persisted in several cognitive domains despite improvements in depression symptomatology. In sensitivity analyses (results not shown, available upon request), the associations between former depression and cognitive tasks did not differ significantly by sex.

Incident depression (having elevated depressive symptoms at follow-up but not at baseline) was associated with poorer cognitive outcomes compared to the stable non-depressed across all cognitive domains in Panel A with the exception of visual memory. The significant parameter estimates for onset in Panel A remained statistically significant even after accounting for baseline cognitive function in Panel B. Last, having stable depression (i.e. elevated depressive symptoms in both baseline and follow-up) was associated with poorer cognitive outcomes in all cognitive assessments, with the exceptions of visuospatial ability and visual memory in Panel A. After we adjusted for differences in baseline cognitive function in Panel B, the significant parameter estimates for stable depression in Panel A were reduced but remained statistically significant.

In sensitivity analyses, we changed the reference group to individuals who were newly depressed and found no significant differences in follow-up cognitive function between the newly depressed and the stable depressed group, with or without adjustment for cognitive function at baseline. We then changed the reference group to the formerly depressed and found that, regardless of adjustment for baseline cognitive function, respondents with new

depression performed significantly worse on verbal learning, visuospatial ability, and orientation tasks; whereas individuals with stable depression performed significantly worse on verbal learning, visual scanning, and orientation tasks (although the differences in visual scanning performance were no longer significant after adjusting for baseline visual scanning). Results of analyses with newly depressed respondents as the reference group are provided in Supplemental Table 1 and results with formerly depressed as the reference group are provided in Supplemental Table 2.

Conclusions:

Regarding our cross-sectional findings, we found support for our first hypothesis that elevated depressive symptomatology would be associated with poorer cognitive function. Our results were consistent with a large body of research demonstrating negative associations between depression and cognitive function (Diniz et al., 2013; González et al., 2008; Goveas et al., 2014; Mourao et al., 2016; Richard et al., 2013). Elevated depressive symptomatology was associated with poorer performance across all cognitive domains in our cross-sectional analyses. In our regression analyses, elevated depressive symptomatology exhibited the largest negative association with verbal learning performance. However, it should be noted that there was significant overlap in the confidence intervals for depression parameters across cognitive domains. The associations between depression and cognitive domains appeared to be independent of demographic, health, and economic characteristics.

We found marginal evidence suggesting the association between elevated depressive symptomatology and poorer cognitive function differed by sex for the verbal learning task. The marginally significant interaction suggested a stronger association between depression and cognition for males than females, which is consistent with prior studies (Biringer et al., 2005; Forno et al., 2005; Paterniti et al., 1999). One study finding mild depressive symptoms to be associated with incident amnestic mild cognitive impairment among men, but not women (Sundermann, Katz, & Lipton, 2017) posited that sex differences may be due to greater depression related changes in medial frontal lobe volume among males (Taki et al., 2005). Sundermann et al. (2017) and Forno et al. (2005) also attributed their findings to gender based societal expectations which may lead men to be more reluctant to acknowledge depression symptoms due to gender roles of suppressing emotional expression. Thus, depressive symptoms reported by men have the potential to be more severe.

Regarding our findings combining depression status at baseline and follow-up, we also found support for our second hypothesis that the formerly depressed would continue to exhibit poorer cognitive function relative to their non-depressed counterparts without a history of depression, despite improvements in depressive symptomatology. Our results were consistent with previous work suggesting poorer cognitive function persisting among individuals with prior episodes of depression from which they have recovered (Bhalla et al., 2006; Hasselbalch et al., 2011; Neu et al., 2005; Reppermund et al., 2009; Richard et al., 2013; Rock et al., 2014). Although this was not observed for all cognitive tasks, respondents who had elevated depressive symptoms three years prior and recovered still had significantly lower verbal learning, verbal recall, visual scanning, and verbal fluency scores than those

who were not depressed three years prior and remained non-depressed. These differentials (with the exception of verbal fluency) were explained by differences in cognitive function three years prior. Our results did not generally suggest that the formerly depressed had steeper cognitive decline over follow up. Rather, it appeared that respondents who recovered from elevated depressive symptoms that were present at baseline had poorer cognitive function at baseline than the stable non-depressed, and this disparity persisted despite improvements in depression symptomatology.

Persistent differences in cognitive function, specifically on our memory tasks including verbal learning and verbal recall performance, despite recovery from depression may be explained by atrophy of the hippocampus during past periods of elevated depressive symptomatology. While some research has shown hippocampal volume recovery following depression remission (Arnone et al., 2013), others have found smaller hippocampal volumes relative to non-depressed controls (Neumeister et al., 2005) even long after depression has remitted (Sheline et al., 1996). In the case of our analysis, the relatively short period between baseline and follow-up may not have given the formerly depressed ample opportunity to recover. We suggest the hippocampus as an area for future work. These results suggest that, in addition to current mental health status, health professionals should also consider a patient's history of depression when assessing cognitive functioning among older adults (Jorm, 2001; Panza et al., 2010; Potter & Steffens, 2007).

While considering the respondent's history of depression provided valuable information among non-depressed respondents, a history of depression did not appear to modify associations between current depression and cognition. Among those with elevated depressive symptoms at follow-up, we found no significant differences in cognitive outcomes according to baseline depressive status. The lack of an additive effect is somewhat surprising given that the formerly depressed did not seem to fully recover cognitively after becoming non-depressed. Further, it is somewhat surprising that the stable depressed group did not have significantly worse cognitive function than respondents with an onset of depression as previous work has found number of depressive episodes to be positively related to dementia diagnosis among individuals with depressive disorder (Kessing & Andersen, 2004). Both greater durations of major depression (McKinnon, Yucel, Nazarov, & MacQueen, 2009; Sheline et al., 1996) as well as greater lengths of time with untreated depression (Sheline, Gado, & Kraemer, 2003) are associated with decreased hippocampal volume. Our results are consistent with Richard et al., (2013) who found similar hazard ratios for dementia incidence whether comparing those with persistent depression or an onset of depression to those were stable non-depressed.

Our analysis comes with several limitations. First, while we consider the respondents' history of depression, our analysis is based on two waves of data which greatly limits our ability to conduct longitudinal analyses of cognitive decline. Future work should consider how trajectories of depressive symptoms are associated with trajectories of cognitive decline across longer follow-up periods. Second, while the CES-D is widely used in studies of depression, the CES-D provides merely a snapshot of the respondent's level of depression as the items refer to the "last week." This is an important limitation as prior literature has suggested that depression which has an onset in early versus late life may be associated

differently with cognitive health (Herrmann, Goodwin, & Ebmeier, 2007; Sachs-Ericsson et al., 2013). Studies of depression and cognition in developing countries would be enriched by conducting detailed life-histories including questions about prior episodes of depression. Last, many of our variables are based on self-reported data which may result in biased responses.

Despite these limitations, our analyses come with several strengths. First, the MHAS data is rich, consisting of a large sample size with detailed information on a respondent's cognitive health using tasks representing a variety of cognitive domains. This affords us the opportunity to evaluate the associations between depression and cognition, across time, in the context of a developing country. Second, our analyses were adjusted for a broad array of confounding variables which allowed us to estimate associations between depression and cognitive domains that were independent of demographic, health, and economic confounders.

Depression remains a prevalent issue among older adults in Mexico (García-Peña et al. 2008). However, mental health disorders are infrequently treated in low- and middle-income settings where an estimated 76% to 85% of individuals with mental health problems do not receive treatment (WHO, 2018). In Mexico in particular, between 87% (in urban areas) and 96% (in rural areas) of individuals with a depressive episode do not report having received treatment (Guerra et al., 2009). This clearly points to the need to improve both screening and treatment of depressive disorders in the context of Mexico and other developing countries. Dementia is also costly as it represents the largest contributor to disability in Mexico (Sousa et al., 2009) and had an estimated worldwide cost of US $604 billion in 2010 (WHO & Alzheimer's Disease International [ADI], 2012) with substantial informal care costs in Latin America (Custodio, Wheelock, Thumala, & Slachevsky, 2017; WHO & ADI, 2012). Given population aging in Mexico, it is becoming increasingly important to understand the nuanced associations between depression and cognition to develop targeted interventions to promote cognitive health among the currently depressed as well as individuals with a history of depression. Successful interventions may aid in reducing burdens on healthcare systems and family care-givers in Mexico.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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TABLE 1.

Sociodemographic, Cognitive, Health, and Economic Characteristics of Older (Age 50+) Mexican Adults by Depression Status in 2015

	Non-Depressed (n=8,926)		Depressed (n=3,972)		
	Mean	**SD**	**Mean**	**SD**	**Sig**
Cognitive Function					
Verbal Learning	14.6	3.7	13.4	3.8	***
Verbal Recall	4.3	2.1	3.8	2.2	***
Visual Scanning	30.6	15.8	24.8	14.8	***
Verbal Fluency	16.0	5.3	14.2	5.0	***
Visuospatial	5.6	0.9	5.4	1.2	***
Visual Memory	4.9	1.6	4.6	1.8	***
Orientation	2.5	0.8	2.3	1.0	***
Age	65.9	9.2	67.8	9.9	***
Years of Education	6.4	4.9	4.4	4.0	***
Sex					
Male (n, %)	4,211	47.2	1,237	31.1	***
Female (n, %)	4,715	52.8	2,735	68.9	
Marital Status					
Married/Partnered (n, %)	6,249	70.0	2,356	59.3	
Widowed (n, %)	1,431	16.0	994	25.0	***
Other (n, %)	1,246	14.0	622	15.7	
Locality Size					
100,000+ (n, %)	5,360	60.0	2,092	52.7	
15,000–99,999 (n, %)	1,151	12.9	551	13.9	***
2,500–14,999 (n, %)	789	8.8	435	11.0	
<2,500 (n, %)	1,626	18.2	894	22.5	
Economic Well-being (Continuous)					
Income Decile	4.6	3.0	4.1	2.7	***
Wealth Decile	4.7	2.8	4.2	2.8	***
Smoking					
Never (n, %)	5,152	57.7	2,544	64.0	
Former (n, %)	2,661	29.8	1,026	25.8	***
Current (n, %)	1,113	12.5	402	10.1	
Binge Drinking (Last 3 Months)					
No (n, %)	8,085	90.6	3,749	94.4	***
Yes (n, %)	841	9.4	223	5.6	
Chronic Conditions					
0 (n, %)	3,082	34.5	772	19.4	***
1 (n %)	3,400	38.1	1,512	38.1	
2+ (n, %)	2,444	27.4	1,688	42.5	

Source: Author's own calculations using data from the 2015 wave of the Mexican Health and Aging Study. Depression status is determined cross-sectionally using scores from the Center for Epidemiologic Studies - Depression scale. n=12,898.

*indicates p<0.05

**indicates p<0.01

***indicates p<0.001.

Descriptive results are presented as means and standard deviations for continuous variables as indicated by the column headings. Descriptive results for binary/categorical variables are presented as sample size (n) and %. This is indicated in the category labels for each categorical variable. All percentages are column percentages. Sample size used for calculations of mean scores for verbal learning, verbal recall, visual scanning, verbal fluency, visuospatial, visual memory, and orientation tasks were 12,854, 12,834, 12,027, 12,865, 12,048, 11,928, and 12,898 respectively. Descriptive results for all independent variables were based on the full analytic sample (n=12,898).

TABLE 2.

Ordinary Least Squares Regression of Cognitive Scores by Domain among Older (Age 50+) Mexican Adults

	Verbal Learning		Verbal Recall		Visual Scanning		Verbal Fluency		Visuospatial		Visual Memory		Orientation	
Depression	β	SE	β	SE	β	SE	β	SE	β	SE	β	SE	β	SE
Depressed	−0.15***	(0.017)	−0.10***	(0.017)	−0.09***	(0.015)	−0.11***	(0.017)	−0.06**	(0.019)	−0.04*	(0.019)	−0.12***	(0.018)
Demographics														
Age	−0.03***	(0.001)	−0.03***	(0.001)	−0.03***	(0.001)	−0.02***	(0.001)	−0.02***	(0.001)	−0.03***	(0.001)	−0.02***	(0.001)
Female	0.34***	(0.018)	0.33***	(0.019)	0.08***	(0.016)	0.00	(0.018)	−0.05**	(0.021)	−0.04	(0.021)	0.02	(0.020)
Years of Education	0.06***	(0.002)	0.05***	(0.002)	0.09***	(0.002)	0.07***	(0.002)	0.05***	(0.002)	0.04***	(0.002)	0.05***	(0.002)
Marital Status (Ref: Married)														
Widowed	−0.03	(0.022)	−0.00	(0.023)	−0.10***	(0.020)	−0.04	(0.022)	−0.13***	(0.025)	−0.06*	(0.025)	−0.12***	(0.024)
Other	−0.05*	(0.022)	−0.04	(0.023)	−0.08***	(0.020)	−0.08***	(0.023)	−0.02	(0.026)	−0.06*	(0.025)	−0.05	(0.024)
Locality Size (Ref: 100,000+)														
15,000–99,999	−0.03	(0.023)	−0.03	(0.024)	−0.08***	(0.020)	−0.03	(0.023)	−0.01	(0.026)	−0.03	(0.026)	−0.06*	(0.025)
2,500–14,999	−0.13***	(0.026)	−0.06*	(0.028)	−0.22***	(0.024)	−0.12***	(0.027)	−0.04	(0.031)	−0.02	(0.030)	−0.10***	(0.029)
<2,500	−0.19***	(0.021)	−0.10***	(0.022)	−0.30***	(0.019)	−0.15***	(0.021)	−0.14***	(0.024)	−0.11***	(0.024)	−0.22***	(0.023)
Economic Well-being														
Income Decile	0.02***	(0.003)	0.01*	(0.003)	0.02***	(0.002)	0.02***	(0.003)	0.01*	(0.003)	0.01	(0.003)	0.01***	(0.003)
Wealth Decile	0.01*	(0.003)	0.00	(0.003)	0.02***	(0.002)	0.01***	(0.003)	0.01***	(0.003)	0.01*	(0.003)	0.01**	(0.003)
Smoking (Ref: Never)														
Former	0.06**	(0.018)	0.03	(0.019)	0.13***	(0.016)	0.14***	(0.019)	0.06**	(0.021)	0.06**	(0.021)	0.03	(0.020)
Current	0.04	(0.025)	0.05*	(0.026)	0.13***	(0.022)	0.11***	(0.025)	0.05	(0.029)	0.05	(0.028)	−0.00	(0.027)
Binge Drinking (Last 3 Months)														
Yes	−0.02	(0.028)	−0.01	(0.030)	−0.02	(0.025)	−0.04	(0.029)	−0.05	(0.032)	−0.04	(0.032)	−0.03	(0.031)
Chronic Conditions (Ref: 0)														
1	0.03	(0.018)	0.02	(0.019)	−0.01	(0.016)	0.02	(0.019)	0.05*	(0.021)	0.04	(0.021)	0.07***	(0.020)
2+	0.01	(0.020)	−0.01	(0.021)	−0.11***	(0.018)	−0.03	(0.020)	0.02	(0.023)	0.02	(0.023)	0.04*	(0.022)
Sample Size:	12854		12834		12027		12865		12048		11928		12898	

Source: Authors' own calculation using data from the 2015 wave of the Mexican Health and Aging Study. Cognition and depression are determined contemporaneously in 2015.

*
indicates p<0.05

**
indicates p<0.01

***
indicates p<0.001.

TABLE 3.

Ordinary Least Squares Regression of Cognitive Scores by Domain among Older (Age 50+) Mexican Adults

PANEL A														
	Verbal Learning		**Verbal Recall**		**Visual Scanning**		**Verbal Fluency**		**Visuospatial**		**Visual Memory**		**Orientation**	
Depression (Ref: Stable Non-Depressed)	β	SE	β	SE	β	SE	β	SE	β	SE	β	SE	β	SE
Formerly Depressed	−0.06*	(0.024)	−0.06*	(0.026)	−0.07**	(0.022)	−0.09***	(0.025)	0.02	(0.027)	−0.03	(0.028)	−0.03	(0.027)
Newly Depressed	−0.16***	(0.024)	−0.10***	(0.026)	−0.07**	(0.023)	−0.13***	(0.025)	−0.06*	(0.028)	−0.03	(0.028)	−0.10***	(0.027)
Stable Depression	−0.17***	(0.022)	−0.12***	(0.024)	−0.12***	(0.021)	−0.12***	(0.023)	−0.03	(0.025)	−0.03	(0.026)	−0.13***	(0.025)
Sample Size	11,217		11,155		10,117		11,195		10,144		9,956		11,255	
PANEL B														
	Verbal Learning		Verbal Recall		Visual Scanning		Verbal Fluency		Visuospatial		Visual Memory		Orientation	
Depression (Ref: Stable Non-Depressed)	β	SE	β	SE	β	SE	β	SE	β	SE	β	SE	β	SE
Formerly Depressed	−0.02	(0.023)	−0.04	(0.024)	−0.03	(0.019)	−0.05*	(0.023)	0.01	(0.025)	−0.03	(0.027)	−0.02	(0.025)
Newly Depressed	−0.13***	(0.023)	−0.09***	(0.025)	−0.06**	(0.020)	−0.10***	(0.023)	−0.06*	(0.026)	−0.02	(0.027)	−0.09***	(0.025)
Stable Depression	−0.12***	(0.021)	−0.06**	(0.023)	−0.06**	(0.018)	−0.08***	(0.021)	−0.02	(0.024)	−0.01	(0.025)	−0.10***	(0.023)
Baseline Cognitive Function														
2012 Cognitive Score	0.35***	(0.009)	0.32***	(0.009)	0.47***	(0.008)	0.41***	(0.009)	0.34***	(0.009)	0.27***	(0.010)	0.36***	(0.009)
Sample Size	11,217		11,155		10,117		11,195		10,144		9,956		11,255	

Source: Authors' own calculation using data from the 2015 wave of the Mexican Health and Aging Study. Dependent cognition variables comes from 2015, baseline cognitive score comes from 2012. "Stable non-depressed" indicates not depressed in 2012 or 2015, "Formerly depressed" indicates respondent was depressed in 2012 but not depressed in 2015, "Newly depressed" indicates respondent was not depressed in 2012 but was depressed in 2015, "Stable depression" indicates respondent was depressed in both 2012 and 2015. Models are also adjusted for 2015 age, sex, education, marital status, locality size, income, wealth, smoking, binge drinking, and chronic conditions.

* indicates p<0.05

** indicates p<0.01

*** indicates p<0.001.