NEUROPSYCHOLOGICAL AND NEUROPSYCHIATRIC PREDICTION OF COGNITIVE FUNCTIONING AND COGNITIVE DECLINE: A CROSS-CUTURAL PERSPECTIVE

by

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A dissertation submitted to the Graduate Faculty in Neuropsychology in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York

2011

This manuscript has been read and accepted for the Graduate Faculty in Neuropsychology in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

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Abstract

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by

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The goal of this study was to examine whether seven neuropsychological tests and three depression measures were associated with cognitive functioning among Hispanic elderly, and to assess whether they operated differently for Hispanic and White ethnic groups. Participants were 89 community-dwelling elderly Hispanics and 89 Whites matched on clinical and demographic characteristics, all followed longitudinally at the NYU Alzheimer's Disease Center (NYUADC). Their cognitive functioning ranged from normal to moderate dementia. Although a large proportion of the measures evidenced an association with cognitive status, hierarchical regression analyses showed that the initial recall of the NYU-Paragraph Test and the Retardation measure (especially for Spanish-speaking Hispanics), as well as WAIS-Digit Symbol (especially for English-speaking Hispanics) were most strongly associated with cognitive status after controlling for demographic and other cognitive measures. Retardation (for the entire Hispanic group)

and the total score of the Hamilton Depression Rating Scale (HDRS; for the entire White group) differentiated between normal cognition and Mild Cognitive Impairment (MCI). For the full range of cognitive status, the combined predictive usefulness of the 10 measures differed significantly between Hispanics and Whites; this difference was especially driven by the Retardation measure. For nondemented participants, only the depression measures predicted differently between the two ethnic groups. When the analyses examined the primary language of the participants, the predictive usefulness of neuropsychological and depression measures differed between Spanish-speaking Hispanics and their matched Whites, but no differences were found between English-speaking Hispanics and their White counterparts. Subsequent analyses showed that, for Hispanics, the usefulness of the 21-item HDRS-total score reflected the contributions of Work and Activities and Retardation, but not the other 19 items. The WAIS-Digit Symbol lacked specificity for Spanish-speaking Hispanics. Preliminary longitudinal analysis showed that the delayed recall of the NYU-Paragraph Test predicted cognitive decline among Spanish-speaking Hispanics. These results suggest that the NYU-Paragraph Test and Retardation may improve diagnostic accuracy and prediction of decline among Spanish-speaking Hispanics.

ACKNOWLEDGMENTS

I would like to thank the members of my dissertation committee Drs. Kluger, Sailor, and Lizardi for their continued support, guidance, and recommendations. I was fortunate to have met Dr. Kluger, whose amazing undergraduate courses influenced my decision to pursue a career in neuropsychology. His support, encouragement, and trust in my abilities continued during my graduate years and led to this accomplishment. I thank the outside readers, Drs. Caro and Schnaider Beeri for their encouragement and suggestions. I would like to thank Dr. James Schmeidler with whom I worked closely on this dissertation. I learned much from him and commend him for his outstanding statistical work. I would like to acknowledge the significant contribution of the NYU Alzheimer's Disease Center for facilitating the data for this dissertation. I especially would like to thank Drs. Golomb, Ferris, and Reisberg.

I thank my friends and family, especially Dr. Ruby Phillips, my friend and mentor who planted the seed of my pursuing a doctoral degree; Snezana Stiefel and Richard Stiefel, for their invaluable friendship and support throughout the years. Richard was responsible for the editorial work of this dissertation. I take this opportunity to say thank you to Tricia Spoto who has been incredibly supportive in so many ways, and to my mother and grandmother for their unconditional love.

Above all, I dedicate this accomplishment to Shirley C. B. Boyle whose support and love for so many years helped shape the person that I am today.

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INTRODUCTION

With the development of new forms of treatment aimed at preventing or delaying the onset of dementia, identification of elderly individuals at increased risk of cognitive decline has become of utmost importance, leading to a myriad of investigations that have focused on the examination of possible predictive variables that could aid in the identification of these at-risk individuals. The elderly population, especially those aged 65 and over, is projected to increase in the next four decades, and ethnic/racial minority groups are expected to increase more than White Americans (US Census Bureau, 2000). In 2010, Whites represent 80% of the US population over 65 years of age, but this number is expected to decrease to 59% in 2050. However, over the same 40-year interval the percentage of the Hispanic elderly population in the US is projected to increase from 7% to 20% and for African Americans from 9% to 12% of the elderly older than 65 (Alzheimer's Association, 2010).

Some investigators have found a higher prevalence and incidence rate of dementia among African Americans and Hispanics as compared with non-Hispanic Whites (e.g., Gurland et al., 1999; Tang et al., 2001). For the following age groups, 65-74, 75-84, and 85 +, a study reported the prevalence of dementia, including Alzheimer's disease (AD), to be 7.5%, 27.9%, and 62.9% for Hispanics; 9.1%, 19.9%, and 58.6% for African Americans; and 2.9%, 10.9%, and 30.2% for Whites (Gurland et al.). However, it is important to note that, after age and education were controlled, differences in rate of dementia disappeared among these three ethnic-racial groups. Another study reported that among African-American men, the prevalence of dementia was twice that among Whites (20.9% vs. 11.6%, respectively), and similar cross-cultural differences have been

reported in prevalence rates of AD (i.e., African-American men = 14.4%, White men = 5.4% [Demirovic et al., 2003]). Compared to White elderly, Hispanic elderly are more likely to be diagnosed with dementia (Fitten, Ortiz, & Pontón, 2001) at more advanced stages of the disease, and when drug intervention may be less effective. Identification of at-risk Hispanic elderly represents a challenge in both clinical and research settings due to cultural barriers such as language, low educational attainment, and income (Borson, Scanlan, Watanabe, Tu, & Lessig, 2006; Fitten et al.), as well as a negative attitude about participation in research. Fitten and colleagues reported that 22% of Hispanic elderly with dementia were symptomatic for five years before receiving a diagnosis, and lower acculturation level and lower income were among the factors that influenced this delayed diagnosis. These factors, and others (e.g., education and test bias), can interfere with the ability of neuropsychological tests to correctly identify/differentiate normal and cognitively impaired Hispanic elderly. Neuropsychological tests are widely used as predictors of cognitive functioning/cognitive decline; however, their utility is better understood among White elderly as compared to Hispanic elderly. These tests are used to identify individuals at high risk of decline or dementia, such as those with Mild Cognitive Impairment (MCI). These individuals are good candidates for clinical trials (Grundman et al., 2004; Lu et al., 2009; Salloway et al., 2004) and may benefit from early treatment. Most MCI studies, with some noteworthy exceptions (e.g., Manly et al., 2005; Manly et al., 2008), have included mainly well-educated White participants. Currently, little is known about MCI in the Hispanic elderly population, which should be of major concern considering the high rates of dementia in this population. Although, not all MCI cases decline to dementia, they tend to perform more poorly on

neuropsychological tests and are at greater risk of developing dementia than normal elderly (Kluger, Ferris, Golomb, Mittelman, & Reisberg, 1999).

It is important to find accurate predictors of cognitive functioning/decline that do not rely (or that rely minimally) on the individual's intellectual ability and sociodemographic characteristics (e.g., education, language, and cultural experiences). Such measures could also aid in the prediction of cognitive decline among individuals with diverse linguistic and cultural background. The Digit Symbol subtest of the Wechsler Adult Intelligence Scale (WAIS), for instance, a test of psychomotor functioning, is relatively independent of memory and intellectual ability (Lezak, 1995). However, it is noteworthy that performance on this task may rely on intact attentional function, which has been recognized as one of the earliest changes observed in AD (see Foldi, Lobosco, & Schaefer, 2002). WAIS-Digit Symbol effectively differentiated individuals with normal cognitive function from those with MCI and from those with early AD (Kluger et al., 1997). Among patients with mild AD, this same test was important in distinguishing those who progressed to moderate or severe AD from those whose dementia remained unchanged (Berg et al., 1984); and it was useful in differentiating decliners from nondecliners to dementia or AD (Kluger et al., 1999; Masur, Sliwinski, Lipton, Blau, & Crystal, 1994).

Assessments of motor performance, including gait measures have been used to differentiate normal from MCI elderly (Kluger et al., 1997; Kluger et al., 2008). Biological markers can be of great usefulness when used with elderly of different ethnic/racial backgrounds. Ideally, these markers should not only be valid in their prediction of cognitive decline, but also relatively cost effective and noninvasive. One

such marker could be MRI scans of the hippocampus. Indeed, measures of hippocampal atrophy have been useful in predicting dementia in elderly with MCI and have been found to correlate with neurofibrillary tangles (Mortimer, Borenstein, Gosche, & Snowdon, 2005) and delayed recall performance (Golomb et al., 1994).

The evaluation of neuropsychiatric symptoms (e.g., depression) as predictors of cognitive functioning/dementia is cost effective, brief, and probably less dependent than neuropsychological tests on the intellectual or educational experience of the individual. Neuropsychiatric symptoms have been found to be associated with a higher prevalence of dementia, higher rate of progression to dementia at follow-up, more deficits in neuropsychological functioning (for a review, see Alexopoulos et al., 2002), and more AD neuropathology (Rapp et al., 2006). For instance, depression and apathy/lack of motivation have been found to be the most frequent neuropsychiatric symptoms in MCI and dementia (Lyketsos et al., 2002), and their predictive accuracy in identifying AD individuals at risk of greater cognitive decline has also been evaluated (Starkstein, Jorge, Mizrahi, & Robinson, 2006). Although the literature addressing the association between depression and cognitive functioning/dementia is expanding, with at least perhaps one exception (Perrino, Mason, Brown, Spokane, & Szapocznik, 2008), this relationship is poorly understood in Hispanic elderly.

Neuropsychological Testing

The use of neuropsychological tests in dementia research is unavoidable: it is common practice in the assessment of cognitive functioning; in the effort to identify at-risk individuals; in the differentiation of individuals with normal cognitive functioning

from those with MCI and from those with dementia; and in the evaluation of drug treatment in clinical trials.

In the Goteborg MCI study, Nordlund and colleagues (2005) examined the sensitivity of 21 neuropsychological tests in differentiating MCI ($N = 112$) from normal controls ($N = 35$). Findings revealed that 10 of the neuropsychological tests differentiated between the MCI and the control groups; and that these tests covered different areas of cognitive function: speed/attention, memory and learning, visuospatial function, language, and executive function. Using a cut-off score of 1.5 SD below the mean score of controls, a greater proportion of MCI individuals showed impairment in language and executive function (57.1% and 52.7%, respectively), followed by learning and memory (48.2%). Findings also revealed that only 2 participants (1.8%) were purely amnestic MCI; 64.2% were impaired in multiple cognitive domains; 17.0% were impaired in one nonmemory domain; and 17.0%, surprisingly, showed no deficit. This last group had higher educational attainment and greater cognitive capacity than a comparison control group. The authors suggested three factors that could have accounted for this finding: (1) this cognitively intact group probably had greater cognitive reserve capacity (as shown by their education and cognitive ability), and thus were more able to compensate for early cognitive deficits; (2) most of the tests were not sensitive enough to detect impairment in these individuals; and (3) their MCI status was probably due to deficits caused by psychosocial variables such as stress. Aside from demonstrating the sensitivity of neuropsychological tests in differentiating MCI from normal cognitive function, this study also supports the notion that MCI is a heterogeneous condition that affects not only memory, but also other areas of cognitive function, as well. Other

studies have confirmed this heterogeneity. Kluger et al. (1997), for instance, found that elderly with MCI have impairments in multiple cognitive domains (i.e., memory, language, and fine and complex motor function).

In general, cognitive deficits, particularly in memory, language, and psychomotor function, are probably the earliest changes observed in preclinical dementia, especially of the AD type. Poor performance on tests of episodic memory (e.g., delayed recall) and language (e.g., verbal fluency) have been useful in identifying early AD (Salmon et al., 2002). Tasks of delayed verbal recall have considerable validity in predicting future decline to AD (Chodosh, Reuben, Albert, & Seeman, 2002; Flicker, Ferris, & Reisberg, 1991; Kluger et al., 1999; Lange et al., 2002). For example, Lange and colleagues, using the Logical Memory Subtest of the Wechsler Memory Scale-Revised (WMS-R; Wechsler, 1987) and the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987), found a decline in verbal memory 1 to 2 years prior to the development of AD. Baseline performance on a Paragraph Delayed Recall Test, administered to nondemented elderly, was the single best predictor in differentiating decliners from nondecliners to dementia or AD (Kluger et al.).

Issues in Cross-Cultural Neuropsychological Testing

The lack of sensitivity of neuropsychological tests when used with individuals of different ethnic/cultural backgrounds has spurred interest in cross-cultural neuropsychology, especially in the last two decades (e.g., Byrd, Touradji, Tang, & Manly, 2004; Jacobs et al., 1997; Manly et al., 1998). Differences in neuropsychological test performance have been attributed to test bias, which can be referred to as a diagnostic misclassification affecting especially one group over others. This misclassification can

be the result of poor psychometric properties of the test itself when used with a particular racial/ethnic group or the result of inherent or achieved characteristics that define an individual (age, education, or cultural influences; see Pontón & Ardila, 1999). A recent study aimed at examining neuropsychological performance among nondemented oldest-old (90–98 years) Hispanics residing in Puerto Rico found that education was the strongest predictor of performance (Carrión-Baralt, Meléndez-Cabrero, Schnaider Beeri, Sano, & Silverman, 2009). Other studies have found that performance on one of the most widely used screening tests for dementia, the Mini-Mental State Exam (MMSE; Folstein, Folstein, & McHugh, 1975) correlates with educational attainment (Crum, Anthony, Bassett, & Folstein, 1993; Monsch, Foldi, Ermini-Funfschilling, et al., 1995). Black et al. (1999) used the MMSE in Mexican-Americans and found that the test was influenced not only by education and literacy, but also by immigrant status (U.S.-born vs. foreign-born) and language used (English vs. Spanish). Indeed, some of the MMSE items rely on cultural experience, such as those asking for the "season' and the "county." This test may be especially inappropriate when used with immigrants who have not lived long enough in the US to become acclimated.

Cross-cultural differences in test performance have been found across the spectrum of cognitive function, from normal to mildly through moderately cognitively impaired individuals. One study, for instance, examined differences in neuropsychological test performance among Spanish-speaking (Cuban Americans) and English-speaking women with mild and moderate AD. Participants were matched in age and levels of cognitive impairment (using the Fuld Object Memory Evaluation [FOME]; Fuld, 1977). The neuropsychological battery included the MMSE; WMS-Logical

Memory and Visual Reproduction subtests; WAIS-R Block Design, Object Assembly, Similarities, Comprehension, and Digit Span Subtests; the Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 1983); and the FAS Controlled Word Association Test (Benton & Hamsher, 1977). After controlling for the effect of education, findings revealed significant differences, favoring White non-Hispanics, in WAIS-R Comprehension, Digit Span, Block Design, and Object Assembly subtests; and FAS in the moderately impaired AD group. In the mildly impaired AD group, also favoring White non-Hispanics, differences were found in one test only, the WAIS-R Digit Span subtest (Loewenstein, Arguelles, Barker, & Duara, 1993). The investigators suggested possible cultural/linguistic issues that could influence test performance: First, because patients with moderate AD performed more poorly in a greater number of tests than patients with mild AD, it is possible that cultural bias becomes more salient in advanced stages of AD. Second, using American norms for the verbal fluency task, the FAS may not be appropriate, since these letters occur with less frequency in the Spanish language. Third, the poor performance in the Digit Span subtest may be due to cultural differences in strategies used to chunk information. Because there are more syllables in single-digit numbers in Spanish as compared to English, syllable length has also been suggested to interfere with performance in Digit Span among Hispanics. However, Loewenstein et al., after controlling for syllable length, did not find support for this explanation.

Similarly to Hispanics, African-Americans also performed more poorly on cognitive tests than Whites. For example, Manly and colleagues (1998) found that cognitively intact African Americans performed significantly lower on tests of verbal learning and memory, figure memory, abstract reasoning, word fluency, and visuospatial

ability than their White counterparts, after controlling for educational attainment. It is important to note that controlling only, and not matching, may not be sufficient to equate groups in a given variable (e.g., education). In other words, when two ethnic groups are matched on important demographic variables, differences in neuropsychological scores may significantly decrease. Manly et al. found that differences in performance in the Selective Reminding Test (SRT; Buschke & Fuld, 1974) were attenuated after matching a subgroup of African Americans and Whites on educational attainment. But once groups are matched, the question remains: why does bias exist in some neuropsychological tests but not others? This question is of special interest when group matching fails to resolve differences in tests that have been suggested to be "culture free." Some of the tests used in the above-cited study, those assessing visuospatial ability, showed group differences in performance despite the matching procedure. A possible explanation relates to the fact that years of education, one of the matched variables, was used to define educational experience. However, studies have found that quality of education is a more appropriate way of measuring educational experience than years of formal education (Consentino, Manly, & Mungas, 2007**;** Manly, Byrd, Touradji, & Stern, 2004)**.** Examining quality of education may be especially important when comparing cognitive test scores of individuals from different socio-economic and cultural backgrounds.

Cross-cultural differences in test performance could also be the result of the stereotype threat. When this threat is elicited in the testing environment, minority groups (such as African Americans and Hispanics) have lower scores than Whites. The stereotype threat appears to work by triggering thoughts that one's performance may confirm the negative stereotype of one's racial/ethnic group. This perception may in turn

create test anxiety, decrease motivation, and interfere with the cognitive processes required to perform well on a cognitive task (Hollis-Sawyer & Sawyer, 2008; Kit, Tuokko, & Mateer, 2008; Steele & Aronson, 1995).

Issues with test translations and norms. One could infer that the cultural bias of some neuropsychological tests can be solved with the use of culturally appropriate translations and norms, which have already been implemented in some tests and represent a major contribution to the field of neuropsychology. For example, normative data was provided for the SRT (Stricks, Pittman, Jacobs, Sano, & Stern 1998); their sample mainly comprised persons of Caribbean descent. Another study developed and provided normative data (English and Spanish versions) for the Spanish English Verbal Learning Test (SEVLT; González, Mungas, & Haan, 2002; González, Mungas, Reed, Marshall, & Haan, 2001) with a sample of Mexican-American elderly. Although, some agree that ethnic group norms would serve well in increasing the sensitivity and specificity of cognitive tests in detecting cognitive dysfunction (Ardila, 1995; Manly, 2005), the use of norms and translations has been criticized for various reasons. First, the Spanish language and Hispanic culture is rather diverse across different Spanish-speaking countries. Thus, tests that have been translated/developed for specific Hispanic groups (e.g., Mexicans) may not be valid when used with other groups (e.g., Puerto Ricans and Dominicans). Second, some suggest that the use of group norms and demographic adjustments can interfere with the findings of real ethnic group differences that can be attributed to brain injury or pathology (Brandt, 2007), and could impede the identification of sociodemographic factors (e.g., culture and education) that can be mediating the effects of ethnicity on cognitive test scores (Manly & Echemendia, 2007). A recent MRI

study examined the validity of adjusted and unadjusted test scores in a demographically diverse sample of elderly individuals with different levels of cognitive functioning. Findings revealed that adjusting for education increased the relationships of neuropsychological test scores with brain structure in the combined sample and among Hispanic elderly, but made no difference among Whites and decreased some of the relationships among African-Americans. Adjusting for the effect of ethnicity increased the associations with MRI measures (Mungas, Reed, Tomaszewski, & Decarli, 2009). Although there appear to be good reasons against and in favor of adjustments of test scores, it is probably more important to consider the context in which the interpretation of scores is being made, and whether researchers and clinicians have to adhere to a single method.

The effects of bilingualism in test performance. The effects of bilingualism have been addressed in the literature. Most studies have found a significant effect for the language in which bilingual individuals are tested. For example, when tested in the English language, fully fluent bilingual Hispanics and those who report English as their primary language outperform their Spanish-dominant bilingual counterparts. Findings from a recent study revealed that people who spoke English as a second language performed more poorly on Digit Span, BNT, and FAS than those who were fully bilingual or who spoke English as a first language (Boone, Victor, Wen, Razani, & Pontón, 2007). Razani and colleagues examined differences in test performance among two healthy groups (age ranged from 20 – 72 years and education ranged from 10 – 16 years). One group was an ethnically diverse, fluent English-speaking group, and the other was a native English-speaking group. They found that the native English speakers

outperformed the ethnically diverse group on Trail Making Test Part B (TMT; Reltan, 1958), Stroop (Stroop, 1935), and Auditory Consonant Trigrams (Brown, 1958; Peterson & Peterson, 1959). The number of years of educational attainment outside the U.S., the amount of English spoken when growing up, and scores obtained in an acculturation scale were all related to test performance (Razani, Burciaga, Madore, & Wong, 2007). Another study (Harris, Cullum, & Puente, 1995) addressed the effects of bilingualism by developing a verbal memory and learning test to compare the performance of three groups (ages 21 to 50) with intact cognitive functioning and who were matched on important demographic variables (age, education, and gender). These groups were (1) bilingual Mexican-Americans (whose expressive language was fully fluent in both English and Spanish), (2) bilingual Mexican-Americans (whose expressive language was more fluent in Spanish than English), and (3) monolingual Whites (whose spoken language was only English). Findings revealed that the Spanish-dominant bilingual group recalled fewer words than the other two groups when they were tested in English (nondominant language); the fully bilingual group showed no difference in performance when they were tested in either language; and all three groups performed similarly when they were tested in their dominant languages (i.e., Spanish for the two Hispanic groups and English for the monolingual group). It is noteworthy that the generalizability of some of these studies is limited by the small sample size, and exclusion of elderly and cognitively impaired individuals. Moreover, findings regarding test performance in the Hispanic population have been based mainly on one Hispanic group, Mexican-Americans (e.g., Harris), thus limiting generalization to other groups such as Puerto Ricans, Dominicans, and Cubans.

How is educational experience best assessed in cross-cultural research?

The effects of education on neuropsychological testing have become an area of increasing interest in cross-cultural research. As mentioned earlier, tests as brief and easy to administer as the MMSE can correlate with educational attainment (Monsch et al., 1995). The main question to date is: how should one measure education? There are those who argue that formal education alone may not be sufficient to account for differences in test scores among diverse ethnic/cultural groups, since quality of education (e.g., reading ability) may differ across culture/ethnic groups. Manly and colleagues used the reading recognition subtest from the Wide Range Achievement Test – Version 3 (WRAT-3; Wilkinson, 1993) to examine the association between quality of education (or reading level as measured by the WRAT-3) and neuropsychological performance among nondemented African Americans. They found that reading level was strongly associated with performance (accounting for 3% to 40% of the variance in test scores), especially on measures of verbal abstraction, naming, and phonemic fluency. This association was independent of age, sex, years of education, and acculturation level. Reading ability was a stronger predictor of test performance than was educational attainment in this sample (Manly et al., 2004). A more recent study compared single word reading scores among White, African American, and Hispanic English-speaking elderly with equivalent years of formal education. Findings revealed that, at a given grade level that was equivalent across the ethnic groups, Whites obtained higher reading scores (Consentino et al., 2007). Overall, these studies suggest that controlling for formal education alone may not resolve test bias that is accounted for by educational experience in cross-cultural research.

Can nonverbal neuropsychological tests address cross-cultural differences in test performance? The use of nonverbal neuropsychological measures has been recommended with nonnative Americans because of the assumption of their relatively culture-free properties. However, findings from many studies have refuted this assumption (e.g., Coffey, Marmol, Schock, & Adams, 2005; Jacobs et al., 1997, Loewenstein et al., 1993). For instance, cultural differences have been found in nonverbal tasks such as the Wisconsin Card Sorting Test (WCST; Heaton, Chelune, Talley, Kay, & Curtiss, 1993), a nonverbal test of executive function; TMT; and nonverbal measures of the WAIS (e.g., Block Design and Object Assembly subtests). Coffey and colleagues found that Whites performed better on the WCST than Hispanics, and that higher levels of acculturation among Hispanics improved performance on this test. Cross-cultural differences were found in the performance of the WAIS Block Design and Object Assembly subtests in patients with moderate AD (Loewenstein et al., 1993). The performance of nondemented Spanish-speaking elderly (mainly immigrants from the Caribbean) was compared to that of English-speaking elderly (mainly U.S. and European-born). Participants were matched for age, years of education, and gender distribution. The Spanish-speaking group had lower scores than the English-speaking group on verbal and nonverbal measures (Jacobs et al., 1997). Furthermore, nonverbal tests are generally timed, making good performance rely on effective speed. Hispanic immigrants are at a disadvantage because when they perform a cognitive task the emphasis/motivation appears to be placed on the accuracy of responses and not on speed. Indeed, a recent study aimed at examining the longitudinal assessment and the psychometric properties of established and newly developed outcome measures in

clinical trials among Spanish-speaking AD patients found that a Maze test speed score failed to differentiate the Hispanic AD patient from the Hispanic control group due to the slow performance of the latter group (Sano et al., 2006). There are cognitive and situational factors that can impair test performance such as the belief that one's performance will confirm the stereotype of one's group (the stereotype threat), as well as situational conditions such as being evaluated by an examiner whose race/ethnicity is different from that of the examinee (Hollis-Sawyer & Sawyer, 2008; Kit, Tuokko, & Mateer, 2008; Marx & Goff, 2005; Steele & Aronson, 1995). Thus, interpretation of performance, even on nonverbal measures, should not exclude the possibility of cultural bias.

Identification of At-Risk Individuals of Cognitive Decline/Dementia

Much research has been aimed at identifying elderly persons presenting with MCI and at investigating the rate of decline to dementia in this group. Individuals with MCI present with a level of cognitive functioning that is intermediate between normal aging and dementia. Clinically, MCI is defined as impairment in one or more cognitive domains, typically in memory (amnestic MCI); however, the degree of the deficit is insufficient to interfere with the individual's social and occupational functioning. Despite the existence of MCI cross-cultural differences, there is a lack of research addressing MCI progression to dementia among ethnic minority groups (Rose, 2005). For example, after a 3-year follow-up, Xu and colleagues (2004) found that Chinese were more likely than American elderly with MCI to progress to dementia of the vascular type (VaD) than to dementia of the Alzheimer's type (DAT). Among minimally impaired nondemented Mexican-Americans, MRI and PET studies have failed to detect

hippocampal atrophy and hypometabolsim in the posterior cingulate cortex (Jagust et al., 2002; Wu et al., 2002).

Interest in mild cognitive impairment dates back to the 1960s, when Kral introduced the construct benign senescent forgetfulness (BSF; Kral, 1962). BSF was the first attempt to differentiate between memory loss as part of the normal aging process and memory loss due to brain pathology (i.e., dementia). Approximately 20 years later, Crook introduced the term age-associated memory impairment (AAMI; Crook et al., 1986), which also describes memory loss occurring in healthy individuals. Elderly individuals with AAMI must present with memory complaints and neuropsychological test performance of at least 1 standard deviation (SD) below the mean scores of young adults. In addressing some of the criticisms of AAMI, another term was introduced, aging-associated cognitive decline (AACD; Levy, 1994). AACD criteria includes decline, as defined by 1 SD below the mean scores of age and education-matched normal controls, in at least one cognitive domain (e.g., memory, language, and visuospatial functioning). Other terms have been introduced by diagnostic manuals. The DSM-IV uses the term age-related cognitive decline (ARCD) when there is objective evidence of cognitive decline that is related to the aging process. For instance, the person may present with problems remembering names and medical appointments. The ICD-10 uses the term mild cognitive disorder (MCD) to describe individuals presenting with cognitive impairment caused by medical or psychiatric conditions (for a review, see Bischkopf, Busse, & Angermeyer, 2002).

The term MCI is a relatively recent construct that has been widely used in several research centers (e.g., NYU and the Mayo clinic). Research criteria for MCI include:

memory complaint, preferably corroborated by an informant; objective memory impairment; normal general cognitive function; intact activities of daily living; and absence of dementia (Petersen et al., 1999). Although not all MCI cases decline to dementia, the rate of decline in MCI cases is greater than in elderly with age-appropriate cognitive function. For instance, in the clinical setting, one study that used the Paragraph Recall Test found that 67.2% (n = 59/87) of the MCI cases declined to dementia, compared to only 11.9% (n = 15/126) of the normal cases, after a follow-up period of about 4 years (Kluger et al., 1999). Another longitudinal study (Flicker et al., 1991), using a verbal list learning test, found that 72% of MCI cases declined to dementia after a follow-up interval of 2.2 years.

Two of the most widely used clinical rating scales to stage global and cognitive capacity have been useful in identifying individuals with MCI. These scales are the Global Deterioration Scale (GDS; Reisberg, Ferris, de Leon, & Crook, 1982) and the Clinical Dementia Rating Scale (CDR) scale (Hughes, Berg, Danziger, Coben, & Martin, 1982). The GDS is a 7-point scale that assesses global cognitive functioning based on well-defined criteria. Individuals with a GDS rating of 1 and 2 are cognitively and functionally unimpaired; however, those with a GDS rating of 2 present with subjective memory complaints that are not objectively supported by their performance on neuropsychological tests. Individuals with a GDS rating of 3 present with subjective memory complaints that are corroborated by their poor performance on cognitive tests. These elderly comprise those with MCI. Finally, individuals with a GDS rating of 4 or higher have severe enough cognitive deficits to receive a diagnosis of dementia, with

higher scores indicating greater impairment (GDS = 4, mild; GDS = 5, moderate; GDS = 6, moderately severe; and GDS = 7, severe).

The CDR is a 5-point scale that examines six areas of cognitive function: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. The five levels of impairment are none (CDR = 0); questionable (CDR = 0.5), which has also been equated as MCI; mild (CDR = 1); moderate (CDR = 2); and severe (CDR = 3).

Depressive Symptoms

The association between depression and cognitive decline or dementia has been extensively addressed in clinical research. For instance, researchers have successfully used depression rating scales such as the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977) and the Hamilton Depression Rating Scale (HDRS; Hamilton, 1960) to identify elderly persons at risk of cognitive decline (Devanand et al., 1996; Wilson, Mendes de Leon, Bennett, Bienias, & Evans, 2004). Devanand et al. found that a single item of the HDRS-17 (item 1: mood), as well as the total HDRS item score, predicted cognitive decline. Another study (Berger, Fratiglioni, Forsell, Winblad, & Backman, 1999) found motivation-related depressive symptoms (lack of interest, psychomotor change, loss of energy, and concentration difficulties) to be associated with cognitive decline. Nevertheless, the predictive utility of depression scales or depression assessment remains a controversial issue. While some studies have found an association between depression and cognitive decline that is independent of preexisting cognitive deficits, age, gender, race, or educational attainment (Wilson et al., 2004), others have found either negative results (Dufouil, Fuhrer, Dartigues, & Alperovitch, 1996) or an

association that interacts with other factors such as gender (Cervilla, Prince, Joels, & Mann, 2000), educational attainment (Geerlings, Schmand, Braam, & Jonker, 2000), age of depression onset (van Reekum, Simard, Clarke, & Binns, 1999), and preexisting cognitive deficits (Alexopoulos, Meyers, Young, & Mattis, 1993). Depression appears to increase decline in cognitive status both from normal to MCI and from MCI to AD. One study found depression at baseline to increase the risk of incident MCI (Geda et al., 2006). Another study found that 85% of depressed elderly with MCI developed dementia in comparison with 32% of the nondepressed MCI elderly after a mean follow-up of 3 years (Modrego & Ferrandez, 2004). Similarly, in a controlled follow-up study, other investigators found that many of the depressed elderly with great cognitive impairment developed dementia (Alexopoulos et al., 1993).

Other longitudinal studies provide support for an association between depressive symptoms and dementia (e.g., Paterniti, Verdier-Taillefer, Dufouil, & Alpérovitch, 2002; Wilson et al., 2002). Wilson and colleagues found that depressive symptoms predict dementia and cognitive decline after controlling for age, sex, education, cognitive function, major depression (to examine only depressive symptoms, excluding major depression, as predictors), memory complaint, and a number of medical conditions at baseline, as well as for the presence of one or more APOE-ε4 alleles. Some of the strengths of this study include postmortem neuropathological confirmation of AD in more than 85% of the clinically diagnosed AD cases, and the use of a comprehensive neuropsychological evaluation assessing episodic memory, semantic memory, working memory, visuospatial ability, and perceptual speed.

However, in contrast to these findings, a recent longitudinal study aimed at examining the relationships between cognitive functioning and depression across three years found that poorer cognitive functioning predicted higher depressive symptoms, but depressive symptoms did not predict poorer cognitive functioning (Perrino et al., 2008). One important difference between this study and the previously mentioned studies is that Perrino et al. followed a minority group (Hispanic elderly). As suggested by the investigators, the lack of an association between depression and cognitive functioning could have been explained by the low educational level of participants and the absence of chronic, clinically diagnosed depression. One of the limitations of this study was the use of a self-reported measure of depressive symptoms, the CES-D. Hispanic elderly may underreport depressive symptoms due to stigma toward psychiatric illnesses or misperception about depression. Minority elderly may think that depression is a normal process of aging or part of life's burden that they have to endure (Steffens, Artigues, Ornstein, & Krishnan, 1997).

Age of Depression Onset

Lifetime history of depression has also been related to decline to dementia. Some have investigated whether late-onset vs. early-onset depression can differentially predict further cognitive decline. One study (van Reekum et al., 1999) found that individuals with late-onset depression showed more cognitive deficit than those with early-onset depression, as measured by total Mattis Dementia Rating Scale (MDRS; Mattis, 1976) and MMSE scores. When the individual subscales of these tests were examined, the MDRS subscale that significantly differentiated between the two groups, after adjusting for multiple comparisons using the Bonferroni procedure, was conceptualization; and

there was a trend for the memory subscale. For the MMSE, orientation differentiated greatly between the two groups, and language approached significance. It is important to note that these between-group differences were nonsignificant when age and education were controlled. However, results from logistic regression analyses found that age of depression onset was a predictor of cognitive status (as defined by MDRS scores greater than or less than 123) independently of the effects of age and education. The number of participants scoring below the cutoff score for dementia (MDRS < 123) was greater for the late-onset depression group than for the early-onset depression group (47.5% vs. 31.5%). Moreover, because the cognitive deficit of those with late-onset depression did not change significantly (as assessed by the MDRS) after depression had subsided (HDRS < 17), researchers concluded that late-onset depression associated with cognitive impairment might represent an early sign of AD.

Specific Depressive Symptoms

Using a prospective, longitudinal design, Devanand et al. (1996) examined the association between depressed mood at baseline and the risk of decline to dementia after a follow-up period of 1 to 5 years. Participants were community-dwelling elderly comprising various ethnic backgrounds (non-Hispanic Whites, Hispanics, and African-Americans). Baseline findings revealed that greater cognitive impairment was associated with age, education, and language of assessment (some participants were tested in Spanish). There was a positive association among the HDRS depressed mood item, HDRS total score, and cognitive impairment. Of the 478 participants who were evaluated for at least one of the follow-up periods, 61 became demented. They comprised 36 (21%) of the 173 depressed, and 25 (9%) of the 283 nondepressed elderly

at baseline. Participants with depressed mood at baseline were at increased risk of developing dementia, especially AD.

It still remains questionable as to the identification of those symptoms that have the highest predictive validity of cognitive decline. For instance, in a prospective study for a follow-up period of 3 years, baseline motivation-related symptoms (lack of interest, loss of energy, and concentration difficulties) were significantly associated with subsequent decline to AD (Berger et al., 1999).

Depression, Educational Attainment, and Gender

One of the potential uses of assessing depressive symptoms as predictors of cognitive decline is that they could aid in the identification of highly educated elderly who may be less likely to be identified as at-risk individuals by neuropsychological testing. For example, Geerlings et al. (2000) examined whether depressive symptoms were associated with dementia or cognitive decline among individuals with normal cognitive function at baseline. The study included two independent samples of community-residing elderly selected from the community-based Amsterdam study of the elderly (AMSTEL) and the Longitudinal Aging Study Amsterdam (LASA). In the AMSTEL sample, diagnoses of AD were made following DSM-IV criteria; and in the LASA sample, cognitive decline was defined by a change in MMSE score > 1SD (a drop of 3 or more points) at follow-up. Findings from both the AMSTEL and LASA samples revealed that depressed elderly, after a follow-up period of 3.2 years, were at risk of developing AD or becoming cognitively impaired. However, depression was associated with dementia/cognitive decline only among those with more than 8 years of education. The authors suggested that baseline depression symptoms may represent early symptoms

of a dementia process in highly educated individuals. Although, baseline inclusion criteria included normal cognitive function, it is important to note that assessment of cognitive function did not include a comprehensive neuropsychological battery, which would likely have detected cognitive impairment in some of the participants at baseline. Indeed, with some exceptions (e.g., Wilson et al., 2002), many studies addressing the relationship between depression and dementia define cognitive impairment/decline using screening measures such as the MMSE.

Epidemiological studies have commonly reported that males are at reduced risk of dementia as compared with females. However, at least one study found depression to be a better predictor of cognitive decline only among men. In a longitudinal study, Cervilla et al. (2000) followed 1083 elderly (aged 65-74) for a period of 9 to 12 years to investigate the association between baseline depression and cognitive function. Baseline depression was measured using the Self-CARE-D (Bird, MacDonald, Mann, & Philpot, 1987), a 12-item self-rating questionnaire derived from the Comprehensive Assessment and Referral Evaluation (CARE; Gurland et al., 1977) instrument; and baseline cognitive function was assessed using three neuropsychological tests: the Paired Associate Learning Test (PALT; Inglis, 1959), the TMT part A, and Raven's Progressive Matrices (RPM; Raven, Court, & Raven, 1976). The investigators estimated premorbid intelligence using the New Adult Reading Test (NART; Nelson & O'Conell, 1978). At follow-up, the only cognitive measure used was the MMSE. Baseline findings revealed that depression was related to poorer cognitive performance. In contrast, the longitudinal analysis (n = 374) revealed that those who were depressed at baseline did not show overall poorer MMSE performance than those who were not depressed (after controlling

for baseline cognitive function, premorbid intelligence, education level, smoking status, age, and gender). However, among men, depression did in fact predict cognitive decline over a period of 9 to 12 years, and this association was independent of baseline cognitive function and age, and premorbid intelligence.

Although cross-cultural differences in depression symptomatology can largely be explained by sociodemographic variables such as education and income (Romero, Ortiz, Finley, Wayne, & Lindeman, 2005), some studies have found ethnoracial differences after controlling for sociodemographic variables and health risk factors (Falcon & Tucker, 2000; Sachs-Ericsson, Plant, & Blazer, 2005; Skarupski et al., 2005). These studies have generally found higher depressive symptoms among Hispanics and African-Americans, but at least one study reported higher rates among Whites (Sachs-Ericsson, et al., 2005). Levels of acculturation among Hispanic elderly have been negatively associated with depression symptoms, with less acculturated individuals being at higher risk of these symptoms (Falcon & Tucker; Swenson, Baxter, Shetterly, Scarbro, & Hamman, 2000).

Aside from its usefulness as a predictor, there are many other reasons to examine depression and its individual symptoms: First, depression and AD share common symptoms, such as concentration problems, lack of interest, fatigue, psychomotor retardation, weight loss, and insomnia, which can mislead diagnosis of either condition (for a review see Starkstein, Mizrahi, & Power, 2008; Teri & Wagner, 1992). Second, depression is underreported in the elderly population, one reason being that depressed elderly tend to complain more of somatic symptoms such as sleep changes, appetite problems, and body pains (Krach, DeVaney, DeTurk, & Zink, 1996) rather than

expressing their feelings of sadness or depression. Finally, depression has often been undetected by health care professionals, especially in minority individuals (see Alexopoulos et al., 2002; Borson et al., 2006; Lichtenberg, 1997).

Neurobiological Findings

Associations of verbal memory tests with neuropathological and neuroimaging findings

At the neurobiological level, tasks of delayed verbal recall have been correlated with neurofibrillary tangle density (NFT; one of the neuropathological hallmarks of AD) and hippocampal volume. One longitudinal postmortem study found that performance on the CERAD word list was significantly associated with NFT density in the temporal lobe, and participants with MCI showed a higher NFT density than those with normal cognition (Guillozet, Weintraub, Mash, & Mesulam, 2003). Another longitudinal postmortem study also found NFT density and especially left hippocampal volume to be associated with performance on tasks of delayed verbal recall (Mortimer, Gosche, Riley, Markesbery, & Snowdon, 2004). Two Golomb et al. studies showed that hippocampal atrophy correlated with poor delayed recall performance in normal elderly (Golomb et al., 1993; Golomb et al., 1994).

Relationships among depression, cognitive functioning, and neurobiological findings

The nature of the relationship between depression and dementia is unclear. Depression could be either a reaction to cognitive deficits, a risk factor, or a prodrome of dementia. From a neurobiological perspective, much work needs to be done to clarify the basis of this association. Depression could affect brain mechanisms important for normal cognitive function, it could be one of the first clinical presentations of an already

compromised brain, or the two conditions could be the final consequences of another factor such as vascular disease. Indeed, late-life depression is associated with white and gray matter hyperintensities, which are also associated with cognitive deficits and dementia (Alexopoulos et al., 2002; Kramer-Ginsberg et al., 1999).

Lavretsky and colleagues (2008), using MRI, examined the brain correlates of depressed mood, anhedonia, apathy, and anergia in elderly persons with a range of cognitive statuses. Univariate logistic regression analyses found that these symptoms were all associated with higher total volume of lacunes, and greater volume of lacunes in white matter and putamen. Anhedonia, anergia, and apathy were also associated with smaller white matter volume; anergia and apathy were further associated with reduced cortical gray matter volume; depressed mood was associated with larger lacunar volume in the thalamus; anergia and anhedonia were associated with greater volume of WMH; apathy was associated with reduced hippocampal volume. They found that all these psychiatric symptoms were prevalent in dementia and in nondemented cognitively impaired individuals. Education and African-American ethnicity were both related with the presence of apathy. However, it is noteworthy that the minority groups (African-Americans, Hispanics, and Asians) comprised a small portion of the study sample compared to Whites. The findings from the univariate logistic regression analysis did not hold when multivariate analyses were used adjusting for cognitive status, age, gender, and education. Only greater lacunar volume in white matter was significantly associated with all four psychiatric symptoms. Having dementia was associated with all the symptoms, except depressed mood. Thus, these findings suggest an association between cerebrovascular disease and mood and motivation-related symptoms. These results are

also consitent with those of Jonsson et al., who found that apathy and mental slowness predicted white matter changes in dementia (Jonsson et al., 2010), but inconsistent with those of Lind et al. However, it is important to note that Lind et al. did not include motivation-related symptoms in their study (Lind et al., 2006).

Some investigators have proposed that the association between depression and cognitive decline may be linked through the glucocorticoid cascade (Jorm, 2001). It is well established that prolonged and repeated exposure to both external and internal stressful stimuli can cause dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis (Dhabhar, 2009; Leonard, 2001; Sapolsky, Krey, & McEwen, 1986). This HPA alteration involves a cascade of events, which starts with the hypothalamic release of corticotropin-releasing factor (CRF). This hormone then activates the pituitary gland, which releases the adrenocorticotropic hormone (ACTH); the ACTH activates the adrenal gland, which releases glucocorticoids (or cortisol in humans). A malfunctioning HPA axis leads to overproduction of glucocorticoids, which can cause damage to the hippocampus, one of the main brain structures involved in learning and memory (Martinez & Kesner, 1998). Atrophy of the hippocampus can lead to memory deficits and AD (McEwen, 1997, 2004). One follow-up study (Steffens et al., 2002) examined baseline hippocampal volume in a group of nondemented elderly (n = 115) suffering from depression. Participants underwent MRI scans at baseline. They were also administered a neuropsychological test battery at baseline and at each follow-up (at least every three months). Findings revealed that small left hippocampal volume at baseline was associated with a higher risk of developing dementia, especially AD and vascular dementia.

The neuroendocrine system (e.g., the HPA axis) can activate the immune system (Leonard, 2001), and neuroinflammation has also been involved in the pathogenesis of AD (Mrak, & Griffin, 2001). Although depression can cause a decrease in immune responses, thus leading to illness, it can also increase the proinflammatory response of the immune system through high concentrations of glucocorticoid release. One can speculate that another biological mechanism that may link depression and dementia is through the immune system. Under normal conditions, one of the functions of glucocorticoids is to inhibit the inflammatory response of the immune system, which helps in preventing inflammatory conditions (e.g., allergy, autoimmune, and cardiovascular diseases). However, hypersecretion of glucocorticoids can cause downregulation of glucocorticoid receptors in the cells of the immune system, which in turn can make these cells less sensitive to the inhibitory signal of glucocorticoids. Miller and colleagues, for instance, found that chronic stress impaired the inhibitory signals of a synthetic glucocorticoid hormone, dexamethasone, to suppress the immune system's inflammatory activity. Dexamethasone's ability to suppress interleukin-6 (IL-6) was significantly reduced in parents of cancer patients as compared to parents of medically healthy children (Miller, Cohen, & Ritchey, 2002).

Moreover, decreased levels of norepinephrine (NE) are found in the cortex of both depressed and demented patients. Postmortem studies have found decreased levels of NE in demented patients with depression (Zubenko, Moossy, & Kopp, 1990). However, because noradrenergic neuronal loss is seen mostly in the later stages of dementia, it is difficult to link the NE abnormality of depression to later decline to dementia (Jorm, 2001).

Cross-cultural neurobiological differences

Recent studies have addressed biological differences across different ethnic/racial groups. For example, a recent study examined the association between clinical diagnoses and MRI measures in a cognitively and ethnically diverse elderly sample.
Results were consistent with previous findings of mainly White participants, cognitively impaired individuals, especially with dementia, have reduced cerebral brain and hippocampus volume and greater white matter hyperintensities (WMH). However, some ethnic differences were found: Hispanic elderly had larger mean brain volume than White and African American elderly; cognitively normal and demented Hispanics and African Americans had a smaller hippocampus than Whites; however, Hispanics with MCI (and also African Americans) had a larger hippocampal volume than Whites. To clarify the difference in brain volume, further analyses showed that absolute brain matter volume did not show differences across the three ethnic groups, but intracranial volume (head size) was smaller among Hispanics; thus, normalized brain matter was larger among Hispanics than the other groups (DeCarli et al., 2008). The investigators suggested that early life experience, such as environmental and nutritional factors, may account for the difference in intracranial volume. Of note, these ethnic differences in brain structures were evident even after correcting for demographic variables and vascular risk factors, and taking into account cognitive status. Also, to further clarify the associations among ethnicity, brain structure, and cognitive function, the investigators examined the relationship between the hippocampus and episodic memory performance. They found a positive association, which was independent of ethnicity. Overall, these findings suggest

that although there might be ethnic differences in brain structures, ethnicity does not appear to affect the relationship between the brain and cognitive functioning**.**

Similar to the above-mentioned results, a study of normal aging found that, compared to White elderly, Hispanic and African-American elderly had larger (2.8% and 1.6%, respectively) relative brain volume, smaller relative ventricular volume, and increased WMH (Brickman et al., 2008). However, inconsistent with the findings of DeCarli et al., this group did not find ethnic/racial differences in hippocampal volume.

A population-based study, the Sacramento Area Latino Study on Aging (SALSA) project, was aimed at investigating the associations between cognitive function and brain structure among cognitively normal and cognitively impaired (nondemented and demented) Mexican American elderly. The study included four groups: Normal, Memory Impaired (MI; of note, some of the MI cases also had impairment in other cognitive domains, but were functionally normal), Cognitively Impaired but not Demented (CIND), and Demented. Consistent with other studies with mainly White participants (Jonsson et al., 2010; Mortimer et al., 2004), there was a reduction in hippocampal volume and an increase in WMH in individuals with dementia. Hippocampal volume, but not WMH, was reduced in the CIND group. Contrary to other studies with mainly White participants (Convit et al., 1997; Jacobs et al., 2010) no changes were found in hippocampal volume and WMH in the MI group. Although this null result for the MI group differed from other studies including mainly White elderly with MCI, it is important to note that MI and MCI might represent different conditions. The investigators clarified that MI generally did not present with memory complaints (which is one of the features of MCI). The investigators indicated that lack of changes in

the hippocampus and WMH in the MI group may be associated with the absence of subjective complaint, as well as the presentation of minimal memory deficit, thus preventing the findings of any measurable brain abnormality. Thus this level of impairment may not be measurable at the level of brain function. The study also examined the relationship between structural brain changes and presence of dementia (i.e., nondemented, which included the normal, MI, and CIND groups vs. demented). Findings revealed that hippocampal atrophy and WMH increased the risk of dementia. The combined presence of these two structural changes more than tripled the development of dementia, for which the investigators suggested the possibility of two comorbid conditions, AD and cerebrovascular disease (Wu et al., 2002).

Moreover, PET findings from the SALSA sample showed that reduced glucose metabolism in the posterior cingulate cortex was evident in the CIND and dementia groups (consistent with the literature on White elderly), but not in the MI group. Inconsistent with the literature on Whites, the temporoparietal cortices were not as hypometabolic as the posterior cingulate cortex. The authors argue that this discrepancy may be related to the small sample size, low educational attainment, and high prevalence of cerebrovascular diseases among these Hispanic elderly. Findings also revealed that decreased glucose metabolism in the cingulate cortex increased the risk of dementia independently of the effects of hippocampal volume and WMH (Jagust et al., 2002).

Conclusions

The association between poor performance in some neuropsychological tests (e.g., delayed recall and psychomotor tasks) and cognitive functioning or cognitive decline/dementia has been validated in many research studies. However, this association

is less understood in the Hispanic elderly population. The few existing cross-cultural studies have mainly compared differences in test performance, but have not addressed the accuracy of validated neuropsychological predictors of dementia in the Hispanic population (e.g., the Paragraph Recall Test and WAIS-Digit Symbol). The Paragraph Recall Test, for instance, is a widely used test in dementia research and studies of clinical trials (Lu et al., 2009; Salloway et al., 2004), but little is known about its usefulness among Hispanic elderly. The WAIS-Digit Symbol subtest has been found to be an accurate predictor of cognitive decline/dementia among Whites, but its predictive accuracy among Hispanic elderly is still to be determined. Similarly, the literature addressing the relationship between depression and cognitive decline has included mainly White elderly. The recent study by Perrino and colleagues (2008) is one of the few exceptions; but their sample consisted mainly of Hispanics with low educational level, they used a self-report measure of depression, and they excluded a White comparison group. Thus, the current study adds to the existing literature by examining the predictive accuracy of both validated neuropsychological tests and depressive symptoms among relatively highly educated Hispanic elderly, with different levels of cognitive functioning, and including a comparison White elderly group.

This research addresses three questions. *Question 1*: Do any of seven baseline neuropsychological tests predict cognitive functioning of Hispanic elderly? *Question 2*: In this population, do any of three baseline depression measures predict cognitive functioning? and *Question 3*: Does the combined usefulness of neuropsychological tests and depression measures differ between Hispanic and White elderly?

METHOD

Participants

Participants were community-dwelling elderly from a longitudinal database (N = 4,334) of the NYU Alzheimer's Disease Center (NYUADC). The demographic characteristics of all participants comprising the entire database were as follows: they were predominately White (86.8%) and female (63.3%), with a mean age of 68.41 years (SD = 13.87) and education 14.61 years (SD = 4.60). They signed a consent form and received comprehensive medical, psychiatric, neurologic, laboratory, and neuroimaging (computed tomographic [CT] or magnetic imaging [MRI]) evaluations at baseline. The exclusionary criteria were: stroke; movement and motor system disorders; malignancy; significant cardiovascular, rheumatologic, endocrinologic, hematologic, pulmonary, gastrointestinal, or psychiatric illness (including clinical depression); a history of alcohol or drug abuse.

All participants received diagnoses that were made at a clinical consensus meeting. The diagnosis of AD was based on well-established diagnostic and research criteria (i.e., the Diagnostic and Statistical Manual of Mental Disorders [DSM-IV; American Psychiatric Association, 1994] and the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders [NINCDS/ADRDA; McKhann, Drachman, Folstein, & Katzman, 1984]). The normal (NL) and MCI diagnoses were based on GDS rating and medical data. Criteria for the diagnosis of MCI were memory complaint, as reported by the patient/informant; GDS rating = 3; mild cognitive deficits (especially memory); intact general cognitive function; normal activities of daily living; and absence of dementia (De Santi et al., 2008).

Two ethnic/language groups were selected for analyses, called "Hispanics" and "Whites." Participants were eligible for the Hispanic group if they identified themselves as Hispanic and their primary language was either Spanish or English. However, the exception was one participant who was born in Guatemala and reported Spanish as primary language, but did not report any information regarding ethnicity or race. Participants were eligible for the White group if they identified themselves as White, but not as Hispanic, and their primary language was English. The majority of the Hispanics identified themselves as White (n = 43, 48.3 %) or chose not to report their race (n = 28, 31.4 %), with a minority identifying as Black (n = 10, 11.2 %) or Hispanic (n = 8, 9.0 %).

For all cases, the baseline visit was the first visit to the NYU-ADRC. Inclusion criteria were: normal to moderately impaired cognitive functioning (GDS rating up to 5), MMSE score at least 10, age at least 50, and at least three visits for Whites.

Since there were many more White (n = 2047) than Hispanic (n = 177) participants, for each Hispanic participant, we sought a White participant with complete cognitive and depression data who was clinically and demographically similar. Matching criteria were: the same values of GDS, gender, and clinical diagnosis [NL, MCI, AD, Possible Normal (PN), Possible MCI (PM), Possible AD (PA), Depression (DP), Vascular Normal (VN)**,** or Other (OT)]. When a clinical diagnosis is referred to as "Possible," as in the case of PM, it means that there are other contributing factors affecting such a diagnosis (e.g., depression). Additional matching criteria were similarity of age (typically within two years); education (typically within two years); and follow-up interval (typically within one year, if the Hispanic was followed up).

Few Hispanics had more than three follow-up interviews. For Hispanics who were followed, follow-up was the third visit if there was one. The longer interval was better because it provided more opportunity to observe decline than the second visit, and increased stability of changes. Nonetheless, if there was only one follow-up for a Hispanic participant, that follow-up was included in the analyses. For Whites, follow-up was always the better third visit, even if a Hispanic had only a second visit. Regardless of the number of visits for the Hispanic, a White was selected with a follow-up interval similar to that of the Hispanic.

The matched sample consisted of 112 pairs of Hispanic and White participants. There was complete neuropsychological and depression data for 89 Hispanics and 38 of them had follow-up GDS. These 89 pairs were used for the cross-sectional analyses, and these 38 pairs were used for the longitudinal analysis. A flow chart (Figure 1) summarizes the selection process.

The diagnoses of MCI, PM, AD, and PA refer to conditions that are often associated with AD, while the diagnoses of DP, VN**,** and OT refer to other conditions; NL and PN participants are within the limits of normal cognition. Secondary analysis was performed excluding the DP, VN, and OT diagnoses to limit consideration to participants who were NL or with only AD-related conditions. The exclusion created 84 pairs for cross-sectional analyses. None of the participants who were part of the longitudinal analyses had DP, VN, or OT diagnoses.

Outcome Measures

The primary outcome measure was the GDS, a 7-point scale that assesses global cognitive functioning based on well-defined criteria. Individuals with a GDS rating of 1

and 2 are functionally and cognitively unimpaired; however, those with a GDS rating of 2 present with subjective memory complaints that are not objectively supported by their performance on neuropsychological tests. Individuals with a GDS rating of 3 present with subjective memory complaints that are corroborated by their poor performance on cognitive tests. These elders comprise those with MCI. Finally, individuals with a GDS rating of 4 or higher have severe enough cognitive deficits to receive a diagnosis of dementia, with higher scores indicating greater impairment (GDS = 4, mild; GDS = 5, moderate; GDS = 6, moderately severe; and GDS = 7, severe). The GDS was found to be strongly correlated with behavioral, neuropsychological, and neuroimaging assessments (Reisberg et al., 1988).

Cognitive decline, as measured by the GDS, was the main outcome at follow-up. Cognitive decline was operationally defined by change in cognitive functioning at follow-up (e.g., change from GDS rating 2 to GDS rating ≥ 3; change from GDS rating 3 to GDS rating ≥ 4). Conversely, "Nondecline" was defined as having unchanged or improved GDS ratings at follow-up. The GDS rating was assigned independent of the neuropsychological data, and clinicians providing the GDS rating were blind to the neuropsychological test results.

The MMSE was employed as an alternative outcome measure to assess the generalizability of the cross-sectional results. Although its validity when used with individuals who are foreign-born and Spanish-speaking has been questioned (Black et al., 1999), it is one of the most widely used screening instruments for dementia and is available in Spanish.

Neuropsychological and Depression Measures

There were seven neuropsychological measures, of which some were included because of their consistent sensitivity in their prediction of cognitive functioning/decline. These measures were the immediate and delayed recall scores of the Paragraph Recall subtest (also known as the NYU Paragraph Test) of the Guild Memory Test (Crook, Gilbert, & Ferris, 1980; Gilbert, Levee, & Catalano, 1968) and the Digit Symbol Substitution Subtest of the WAIS (Wechsler, 1955). Four additional neuropsychological measures were immediate and delayed scores from the Paired Associates subtest of the Guild Memory Test, the Memory for Designs subtest of the Guild Memory Test, and the WAIS Vocabulary subtest. These seven neuropsychological measures have been previously described (Ferris, Crook, & Flicker, 1986; Reisberg et al., 1988). Spanish language translations for all seven neuropsychological tests were used. To our knowledge, for Spanish-speaking Hispanics, normative data and psychometric properties are available only for the WAIS subtests (Escala de Inteligencia Wechsler para Adultos [EIWA], Wechsler, 1968; Renteria, Tinsley, & Pliskin, 2008; TEA Ediciones, 2001).

The three depression measures were the total score of the 21-item HDRS and two of its items, Work and Activities and Retardation. Successful administration of this scale relies on the prowess and sensitivity of the interviewer who asks culturally relevant questions corresponding to the questionnaire item. Although, the HDRS has been used with the Hispanic population (Lewis-Fernandez et al., 2006; Williams, Kerber, Mulrow, Medina, & Aguilar, 1995), to our knowledge, its psychometric properties have not been evaluated with this population.

The Paragraph Recall Subtest. This subtest of the Guild Memory Test requires immediate recall of two stories (paragraphs). Both stories are read to the participant, who is required to recall the stories verbatim immediately (immediate recall; Paragraph-I) and after a period of 5-10 minutes (delayed recall, Paragraph-D) in which the participant is asked to complete an interference task. This subtest yields two scores, immediate recall and delayed recall.

Digit Symbol Substitution Subtest. For this subtest of the WAIS, the participant is presented with a test key that contains digits ranging from 1 to 9 paired with a geometrical symbol. After a short practice, the test session begins, and the participant is required to enter the symbol that corresponds to each digit as quickly as possible. The task is timed for 90 seconds. It is important to note that because one can refer to the test key, memory is not required to perform well on this task.

Paired Associates Recall Subtest. This subtest of the Guild Memory Test requires the ability to remember associated pairs of familiar words. This task consists of the verbal presentation of a list of 10 pairs of words. At the end of the presentation, the participant is provided with the first word and required to provide the second word of the pair (immediate recall; Paired Associates-I). After an incorrect response, or if no response is given, the examiner provides the two words (the pair). After a 5-minute delay, in which the participant is asked to complete an interference task, he/she is re-tested (delayed recall; Paired Associates-D). The total score is the sum of correct responses of immediate and delayed recall.

Memory for Designs Subtest. This subtest of the Guild Memory Test is a task of nonverbal-verbal associative memory. Ten simple designs are presented one at a time,

and each of them is paired with a number. In the test trial, each design (without the number) is presented again, and the participant has to provide the number that is matched with each design. The total score is the number of correct responses.

WAIS-Vocabulary Subtest. This subtest of the WAIS assesses language and vocabulary ability. The participant is required to define 40 words, with each response scored 2 points for a complete definition and 1 for a partial definition. The total score is the sum of the points earned for the 40 words.

Hamilton Depression Rating Scale. The 21-item version of the HDRS is a clinician-administered depression inventory with items ranging from 0 to 2 through 0 to 4. The advantages of the HDRS include its administration compared to self-administered questionnaires and validity when used with patients with moderate dementia (Katz, 1998). In addition to the total HDRS score, two items, Work and Activities and Retardation, were selected a priori to represent motivation-related/apathy symptoms, which consistently predict cognitive decline/dementia (Berger et al., 1999; Starkstein et al., 2006)**.** (see **Appendix D** for the HDRS). Since the HDRS-total score includes Work and Activities and Retardation as two of its constituents, an alternative 19-item sum (HDRS-19), excluding these two items, was similarly analyzed for comparison.

Retardation was not normally distributed, primarily due to a floor effect. Examination of the distribution of scores on this variable indicated that about two thirds of the participants were rated as “normal” (0). For the vast majority of participants showing some degree of retardation, most were rated as “slight” (1) rather than “obvious” (2). Only one participant was categorized as “interview difficult” (3). Parallel analysis was performed employing the square root transformation. Use of the transformation

reduced the two-way interaction for Retardation reported in Table 3 from p = .005 to p = .026, and eliminated the significance of the p = .029 three-way interaction. Nonetheless, the untransformed retardation results are presented throughout. A square root transformation would make the difference in scores between "slight" (1.0) and "obvious" (1.4) less than half the difference in scores between "normal" (0.0) and "slight" (1.0). Thus, this transformation would reduce the most valuable distinctions in this important measure. Transformation would also make the reported results inconsistent with all other Retardation analyses in the literature.

The only other variable with apparent non-normality was the WAIS-Vocabulary subtest for Whites. The mean was 62.09, the *SD* was 16.02, and the minimum value was 0, an outlier almost 4 *SD*s below the mean. This variable was also not transformed since such a transformation is not usually found in the literature.

Overall, selection of the outcome measure (i.e., the GDS), the neuropsychological tests, and the HDRS was dictated by theoretical and practical reasons. Most participants had complete data on these measures. The neuropsychological tests cover different cognitive domains (e.g., memory, language, and attention/psychomotor functioning), which have been found to be sensitive to the prediction of dementia (e.g., Kluger et al., 1997; Kluger et al., 1999; Masur et al., 1994).

Analytic Methods

Since the Hispanic and the White groups were not perfectly matched on age, education, and follow-up interval, paired sample t-tests were performed to compare the matched samples on these variables. Since primary language of the Hispanic participants was critical in subsequent analyses, similar analyses were performed separately for the

pairs with a Spanish-speaking Hispanic or an English-speaking Hispanic. For descriptive purposes, independent sample t-tests were used to compare the Spanish-speaking Hispanics with English-speaking Hispanics, and to compare their respective matched White participants. Pearson's chi-square was employed to compare Spanish- and English-speaking Hispanics on the categorical variables of gender, GDS, and clinical diagnosis.

Multiple Tests of Significance. Questions 1 and 2 ask whether any of seven neuropsychological or three depression measures predict cognitive functioning. This introduces the problem of multiple tests of significance; if seven or three measures are each tested at the .05 level of significance, the probability that one or more true null hypotheses will be rejected by chance may be larger than .05. A common solution to this problem is to use the Bonferroni inequality. If each of k measures is tested at the .05/k level of significance, the probability of rejecting one or more true null hypotheses by chance is less than or equal to .05. This is true regardless of the number of true null hypotheses or the interrelationships among the tests of significance.

The Holm procedure is a refinement of the multiple comparisons procedure using the **Bonferroni inequality** that improves power for all the tests of significance except the most significant one, without any additional assumptions. It tests the p-values in order, from the most significant to the least significant, with successively less challenging criteria for significance. The criterion for the most significant result is .05/k, which is prescribed by the Bonferroni inequality for all tests. If it is not significant, testing stops. If it is significant, the criterion for the next most significant result is .05/(k - 1). This is repeated until—if all results except the least significant are significant by their respective

criteria—the criterion for the least significant result is .05/[k - (k - 1)] = .05/1 = .05 (Holm, 1979). Thus, for Question 1, which is comprised of seven neuropsychological tests, the most significant result must achieve a p-value < 05/7 = .00714; for Question 2, with three depression measures, .05/3 = .01667. Question 3 is tested by a single overall test of significance for all 10 neuropsychological and depression measures; therefore, no adjustment for multiple comparisons is needed.

For the cross-sectional analyses, results that are statistically significant at the .05 level by the conservative Holm criteria are called "strongly significant." A result with $p < .05$ is referred to as "approaching significance." This replaces the relaxed standard of $.05 < p < .10$ for "approaching significance" in the context of the conventional requirement of $p < .05$ for "significance."

For the longitudinal analyses, which were only preliminary, there was no adjustment for multiple comparisons. Thus, the conventional standards of $p < .05$ for "significance," and $.05 < p < .10$ for "approaching significance" were used.

Cross-sectional analyses. In order to provide descriptive information for each neuropsychological and depression measure separately, a preliminary analysis was performed using repeated measures analysis of covariance (ANCOVA). This analysis evaluated the interaction of GDS with group (i.e., were the differences in a neuropsychological or depression measure associated with GDS discrepant between matched Hispanic and White participants?). The neuropsychological or depression measure was the dependent variable. GDS rating, evaluated as a categorical variable, was the between-pairs factor; examining the GDS as a categorical variable also indicated the extent to which the neuropsychological and depression measures were linearly

correlated with GDS status (Questions 1 and 2). Group (Hispanic vs. White) was the "repeated measures variable" within the matched pair. The control variables were age, gender, and education. (Unlike Questions 1 and 2, for which the sets of neuropsychological and depression measures were considered separately, the Holm procedure for these ANCOVAs included all 10 measures. Thus, the most significant result must achieve a p-value < .05/10 = .005.)

Since low levels of acculturation can adversely affect test performance, the primary language of the Hispanic participant was taken into account in the analyses. Similar to the inclusion of Group as a moderating variable influencing the association of GDS with the neuropsychological or depression measures, primary language was included as an additional moderating variable. Since GDS was a between-pairs factor and Group was a within-pairs factor, three-way repeated measures ANCOVAs included the primary language (Spanish or English) of the Hispanic participant of the matched pair as a second between-pairs factor. This examined the three-way interaction of primary language with GDS and group (i.e., does the discrepancy between Hispanic and White matched participants in the two-way interaction differ according to primary language of the Hispanic participant?). If such a three-way interaction is significant, this implies that the overall two-way interaction does not apply equally to the distinct primary language subgroups. Thus, interpretation of the two-way analysis as a generality—not taking account of primary language—is problematical.

For the ANCOVAs, since there were few participants with GDS 1 (6 pairs), they were included with those with GDS 2. This co-grouping of GDS 1 and 2 participants is common practice (Kluger et al., 1997; Kluger et al., 1999). Participants with GDS 5 were

excluded since none of the English-speaking Hispanics had such a rating, and their inclusion would have been inappropriate for the three-way ANCOVAs.

Hierarchical regression analyses were performed to answer Question 1 (Do any of seven baseline neuropsychological tests predict cognitive functioning of Hispanic elderly?) The regression analysis entered two sets of predictors, demographics (age, gender, years of education) and seven neuropsychological measures (the Paragraph Recall subtest immediate and delayed recall, WAIS-R Digit Symbol and Vocabulary subtests, Paired Associates immediate and delayed recall, and Memory for Designs). GDS rating was the dependent variable. Since the regression analyses examined the linear relationship of the predictors with GDS, GDS rating was treated as a continuous variable with equally spaced categories

To answer Question 2 (In Hispanic elderly, do any of three baseline depression measures predict cognitive functioning?) the set of three depression measures, Work and Activities, Retardation, and HDRS-total score were added onto the regression analysis answering Question 1. As mentioned earlier, since the HDRS-total score includes Work and Activities and Retardation, the HDRS-19, (which excludes these two items) was similarly analyzed for comparison.

In Question 1, the significance of the partial correlation of each neuropsychological measure with GDS was evaluated primarily by controlling for demographics and other neuropsychological measures. Correspondingly, for Question 2, the significance for the partial correlation of each depression measure with GDS was evaluated primarily by controlling for demographics, the seven neuropsychological tests, and the other depression measures. Secondarily, each neuropsychological measure was

evaluated controlling only for demographics, and each depression measure controlling only for demographics and neuropsychological measures. For comparison, parallel analyses were performed also for White participants. To compare partial correlations in different samples, Fisher's z transformation was employed. In view of the significant three-way interactions in the ANCOVAs for some measures, Questions 1 and 2 were also analyzed separately by primary language of the Hispanic participant.

When the sample was limited to nondemented participants, and GDS was characterized as objectively intact cognition (GDS 1 or 2) vs. mild cognitive impairment (GDS 3), there were only two categories derived from the original GDS scale. Therefore, Questions 1 and 2 were examined using hierarchical logistic regression analysis with the same independent and control variables as for the hierarchical regression analysis.

Different hierarchical regression analyses, to compare the usefulness of larger sets of variables, were performed to answer Question 3 (Does the combined usefulness of neuropsychological tests and depression measures differ between Hispanic and White elderly?). This question was interpreted as referring to differences in how the measures were predictive for Hispanic and White participants, rather than a difference in the overall extent of usefulness (regardless of which measures were involved). The difference in the predictive usefulness of a neuropsychological or depression measure by the Hispanic and White participants was represented by a predictor referring to an interaction. Each interaction predictor was calculated as the product of the predictor and the dichotomous variable distinguishing Hispanics from Whites.

Hierarchical regression analysis was performed with the following sets of predictors: the difference between Hispanics and Whites; the three demographic variables

(age, gender, and education); their interactions with the difference between Hispanics and Whites; the 10 neuropsychological and depression measures; and their interactions with the difference between Hispanics and Whites. The Hispanic and White participants were perfectly matched on GDS and gender, and—by using the average of the pair—on the demographic control variables, age and education. If the Hispanic and White participants had not been matched, the analysis would unquestionably have controlled for demographic variables (group, age, gender, and education). Due to matching, the first and third steps of the regression analysis did not account for any variation. Nonetheless, they were still included in the analysis to remove from the model the degrees of freedom referring to the variables on which there was exact matching. If these steps had not been included in the analysis, the residual sum of squares (not accounted for in the model) would have been the same, but the degrees of freedom would have been inappropriately larger.

Question 1 and Question 2 distinguished between the neuropsychological test and the depression measures. In order to make a similar distinction between their contributions to Question 3, in subsidiary analyses, the interactions involving neuropsychological and depression measures were entered in separate steps. For nondemented participants, the corresponding hierarchical logistic regression analyses were performed to distinguish between cognitively intact (GDS 1 and 2) and mildly impaired (GDS 3) participants.

Longitudinal analyses. In view of the matched samples, McNemar's test was used to assess whether there was a difference between Hispanics and Whites in whether or not they declined. This procedure tests whether the number of pairs with only the

Hispanic declining differs from the number of pairs with only the White declining. Pairs for which there was no difference in decline are excluded from the analysis. Additional analyses examined the associations of demographic variables with decline for Hispanics and Whites separately.

Despite the small sample size, preliminary analyses of decline were performed. To answer Questions 1 and 2, for each ethnic group separately, hierarchical logistic regression analyses controlled first for baseline age, gender, education, GDS, and follow-up interval. For Question 1, analysis was performed for the seven neuropsychological tests. For Question 2, the three depression measures were the next step. These analyses could be performed only for neuropsychological tests for Hispanics, due to the small sample size and the strong intercorrelations among the neuropsychological tests. Therefore, hierarchical regression analyses were performed for longitudinal decliners vs. non-decliners, as was done for baseline GDS.

For Question 3, on the discrepancy between Hispanics and Whites of usefulness of sets of predictors for predicting cognitive decline, hierarchical logistic regression was similarly not feasible. Therefore, hierarchical regression analyses used the following sets of predictors: group, five variables used for matching (baseline GDS, length of follow-up, age, gender, and education), interaction of group with these five matching variables, seven neuropsychological tests and three depression measures, and interaction of group with these ten predictors. Similar to the cross-sectional analysis, the average of the highly correlated variables used for matching (i.e., age, education, and length of follow-up) was employed as a predictor for both participants in each matched pair.

RESULTS

Demographic Characteristics

The final study sample consisted of 178 (89 Hispanic and 89 White matched elderly) participants with complete neuropsychological and depression data. The Hispanic group was mainly from the U.S. (*n* = 33, 37.1 %), Puerto Rico (*n* = 17, 19.1 %), as well as Cuba (*n* = 12, 13.5 %), Dominican Republic (*n* = 6, 6.7 %), Ecuador (*n* = 5, 5.6 %), Colombia (*n* = 4, 4.5 %), and others (*n* = 12, 13.3 %). Most reported that Spanish was their primary language (*n* = 56, 62.9 %), rather than English (*n* = 33, 37.1 %). Participants were interviewed and tested in their language of preference (Spanish or English). The White group was from the U. S. (*n* = 81, 91.0 %), Europe (*n* = 4, 4.4 %), and others (*n* = 4, 4.4 %). All of them had English as their primary language, which was one of the inclusion criteria.

Table 1A describes both Hispanics and Whites on perfectly matched variables. There were 142 (79.9%) female participants. Over a half (52.8%) of the sample had GDS = 1 or 2 (*n* = 94), almost a quarter (23.6%) had GDS = 3 (*n* = 42), and almost a quarter (23.6%) had GDS ≥ 4 (*n* = 42). Similarly, approximately half of the sample (50.6%) had clinical diagnoses of Normal or Possible Normal (*n* = 90), 23.6% had MCI or Possible MCI (*n* = 42), 20.2% had AD or Possible AD (*n* = 36), and 5.6% had other various diagnoses (*n* = 10).

For the entire sample, the average age was 67.0 years (SD = 10.4, range: 50 – 91 years), and the average education was 13.9 years (SD = 3.5, range: 4 – 20 years). For the Hispanics with a follow-up GDS and their matched Whites, the average of follow-up interval was 2.2 years (SD = .6, range: 1.4 – 5.0). Although the samples were

approximately matched on age and education, matched sample t-tests for differences in age, education, and follow-up interval are shown in **Table 1B**, and the differences on the matching variables are presented in **Table 1C**. Of these variables, only education was significantly different between the two ethnic groups. Hispanics, on the average, were less educated (*Mean* = 13.5, *SD* = 3.6) than Whites (*Mean* = 14.3, S*D* = 3.4, $t = 5.064$, $p < .0005$). None of the differences between matched Hispanics and Whites on any of the neuropsychological or depression variables were significantly correlated with the difference in education. Therefore, this difference in education was not used as an additional control variable in the comparisons of Hispanics and Whites.

For Spanish- and English-speaking Hispanics separately, corresponding matched sample t-tests comparing them with their matched Whites are presented in **Table 1D.** In both language subgroups, Hispanics were less educated than their matched Whites (Spanish-speaking: $t = 4.359$, $p < .0005$; English-speaking: $t = 2.602$, $p = .014$). None of the differences between Spanish-speaking Hispanics and their matches Whites or between English-speaking Hispanics and their matched Whites on any of the neuropsychological or depression variables were significantly correlated with the difference in education. Therefore, this difference in education was not used as an additional control variable in the comparisons of Hispanics and Whites by primary language. None of the other differences in demographic characteristics reached statistical significance.

Distinction between Spanish- and English-speaking Hispanics on matching variables. Since the Hispanic group comprised two distinct subgroups differing in their report of primary language (Spanish or English), demographic and clinical characteristics

were compared. **Table 2A** presents the results of independent sample t-tests for differences in age, education, and follow-up interval between the Spanish- and English-speaking Hispanics. None of these differences on the continuous matching variables were statistically significant. Distributions of gender, GDS, and clinical diagnosis for these two subgroups are presented in **Table 2B**. To avoid categories with very low frequencies in chi-square tests of significance, GDS = 1 was combined with GDS = 2 and GDS = 5 was combined with GDS = 4. Possible diagnoses were combined with the corresponding diagnoses (e.g., PN with NL), and the other three infrequent diagnoses (DP, VN, and OT) were excluded. After this exclusion, the three grouped diagnoses corresponded perfectly with the grouped GDS categories. None of these differences between the primary language subgroups on the categorical matching variables were statistically significant.

Preliminary ANCOVAs

The originally planned two-way repeated measures ANCOVAs compared Hispanics and Whites on their associations of GDS with neuropsychological and depression measures. However, additional ANCOVAs demonstrated that there were some substantial three-way interactions with the primary language of the Hispanic member of the pair. Thus, the two-way interactions for those measures must be interpreted with caution.

The tests of both two-way and three-way interactions from the three-way ANCOVAs are presented in **Table 3**. Of the ten neuropsychological and depression measures, only WAIS-Digit Symbol and Retardation approached statistical significance

for either interaction. Retardation approached significance for both two-way (p = .0052) and three-way (p = .029) interactions.

WAIS-Digit Symbol (*p* = .015) approached a significant three-way interaction. These significant three-way interactions indicate that the discrepancy between matched Hispanics and Whites in the association of GDS with the seven measures (e.g., WAIS-Digit Symbol) differed according to the primary language of the Hispanic participant.

Therefore, results of the three-way ANCOVAs, rather than the two-way ANCOVAs, are presented in detail (**see Appendix C**). For the two neuropsychological or depression measures for which the interaction was strongest, **Tables 4A** and **4B** present the means by GDS rating (1 or 2, 3, 4) separately by the subgroups of Hispanics and Whites according to the primary language of the Hispanic participant. These results showed main effects that performance on WAIS-Digit Symbol declined and Retardation symptom increased as GDS increased, indicating increased impairment. Significant interactions showing differences among the subgroups can be described by identifying how a subgroup differs from the GDS main effect.

On WAIS-Digit Symbol (**Table 4A**), Spanish-speaking Hispanics did not show decline in performance from GDS 1-2 to GDS 3. However, these WAIS-Digit Symbol scores were substantially lower than those of the other three subgroups. Whites matched to the English-speaking Hispanics also did not decline from GDS 1-2 to GDS 3 (unlike the two remaining subgroups). Overall, differences in performance among the four subgroups were less apparent for GDS 4 than the other GDS categories. (**Figure 2** illustrates these findings).

On Retardation (**Table 4B**), Whites matched to Spanish-speaking Hispanics changed substantially from GDS = 1-2 to GDS 3, but not from GDS 3 to GDS 4. In contrast, for the other three subgroups, the increase between GDS 3 and GDS 4 was substantially larger than the increase between GDS 1-2 and GDS 3. Finally, Whites who were matched to English-speaking Hispanics did not show so much increasing impairment on Retardation as the other two subgroups. (see **Figure 3**).

ANCOVAs limited to normal participants or with AD-related conditions. When the ANCOVAs were limited to participants who were normal or had only AD-related conditions (excluding the ten participants with DP, VN, and OT diagnoses), results corresponding to **Table 3** tended to be less significant, consistent with the reduced sample size. An exception was Paragraph-D, the Group by GDS interaction [F (2, 70) = 3.135, p = .050] now approached statistical significance. All three results that approached significance in **Table 3** still approached significance: for WAIS-Digit Symbol, the Group by GDS by Primary Language interaction [F (2, 70) = 2.999, p = .016], for Retardation, the Group by GDS interaction [F (2, 70) = 4.219, p = .019] and the Group by GDS by Primary Language interaction [F (2, 70) = 3.189, p = .047].

Tables 4C present the means by GDS rating (1 or 2, 3, 4) separately by the two ethnic groups, since the two-way ANCOVA approached significance, but the three-way ANCOVA did not [F (2, 70) = 1.214, p = .303]. Although Paragraph-D performance declined as GDS increased, the decline for Hispanics from GDS 3 to GDS 4 was much smaller than for Whites (**Figure 4**).

Questions 1 and 2: Prediction of Cognitive Functioning/Status by Baseline Cognitive and Depression Characteristics

Prediction among Hispanics and Whites (*n* = 89 matched pairs). The first and second questions were whether neuropsychological tests (Question 1) and depression measures (Question 2) are useful in Hispanic elderly for prediction of cognitive functioning/status, as measured by GDS rating. Hierarchical regression analyses were used, with neuropsychological and depression measures as the independent variables and GDS rating as the dependent variable, controlling for baseline age, gender, and education. For the primary analyses, the analysis for the neuropsychological measures controlled for the other neuropsychological measures, and the analysis for the depression measures, controlled for all the neuropsychological measures and the other depression measures. As presented in **Table 5**, for Question 1, only the NYU-Paragraph-I (partial r = -.284, $p = .011$) and the WAIS-Digit Symbol approached significance (partial r = -.238, $p = .034$) in their association with baseline cognitive functioning. For Question 2, Retardation (partial r = .513, $p < .0005$) was strongly associated with cognitive functioning.

Results of the regression analysis for the White participants (n = 89) are also presented in **Table 5**. WAIS-Digit Symbol (partial r = -.340, $p = .002$) was strongly associated with cognitive status, and Paragraph-D (partial r = -.254, $p = .023$) approached significance; but no depression measures approached significance. When the partial correlations for Hispanics and Whites were compared using Fisher's z transformation, the partial correlations for Retardation ($p < .0005$) were strongly different from each other, and for Paragraph-D almost approached significance ($p = .0501$).

Questions 1 and 2: Prediction according to primary language. The hierarchical regression analyses were repeated for subgroups to examine whether the predictive value of neuropsychological and depression measures (Questions 1 and 2) differs according to the primary language of the Hispanic participant. As shown in **Table 6**, among Spanish-speaking Hispanics (n = 56), both Paragraph-I (partial r = -.400, p = .005) and Retardation (partial r = -.578, p <.0005) strongly predicted cognitive status. Predictors were different for their corresponding Whites, for whom Paragraph-D (partial r = -.560, p < .0005) and WAIS-Digit Symbol (partial r = -.464, p = .001) were both strongly significant. When the regression analysis was limited to English-speaking Hispanics (n = 33), WAIS-Digit Symbol (partial r = -.544, p = .006) was strongly significant. In contrast, for their corresponding Whites, no neuropsychological or depression measures approached significance

Comparisons between correlations for Spanish-speaking Hispanics (n = 56) and their matched Whites showed a strong significant difference for Paragraph-D (p < .0005), with Paragraph-I (p = .038) and Retardation (p = .042) approaching significance, but WAIS-Digit Symbol (p = .065) did not. Similar comparisons between the smaller (n = 33) subgroups of English-speaking Hispanics and their matched Whites did not show any differences approaching significance, including Retardation (p = .060). Differences between correlations between the two Hispanic subgroups approached statistical significance for WAIS-Vocabulary (p = .045). For the two White subgroups, differences between correlations approached significance for Paragraph-D (p = .009).

Similar to the ANCOVAs, the regression analyses were performed limited to participants who were normal or had only AD-related conditions. The results did not

differ from those in Table 6 in their status of statistical significance, with the exception of the HDRS-total score (partial r = .502, p = .029) that now approached significance for Whites matched with English-speaking Hispanics.

To summarize the above results from the primary hierarchical regression analyses, it is important to note that the interpretation of the results for Hispanics can be clarified by making an additional distinction according to their primary language. WAIS-Digit Symbol was associated with cognitive status among English-speaking Hispanics and among Whites who were matched with Spanish-speaking Hispanics. While Paragraph-I was associated with cognitive status among Spanish-speaking Hispanics, Paragraph-D was useful among their corresponding Whites. Among the three depression measures, Retardation was the only useful measure, but only among Spanish-speaking Hispanics.

Alternative analyses: HDRS-19. An alternative HDRS summary (HDRS-19) excluded Work and Activities and Retardation items from the total, but included the other 19 items. The HDRS-19 was almost perfectly correlated with the original 21-item HDRS-total score among all four subgroups. Among Spanish-speaking Hispanics and their corresponding matched Whites (r = .935 and r = .950, respectively); among English-speaking Hispanics and their corresponding matched Whites (r = .966 and r = .940, respectively). When the hierarchical regression analysis was repeated using the HDRS-19, the Question 2 results in **Table 6** were substantially unchanged, with strong significance only for Retardation among the Spanish-speaking Hispanic subgroup (partial r = .586, $p < .0005$).

Alternative analyses: MMSE as the measure of cognitive status. As an alternative to the GDS, the MMSE was used as the dependent variable in regression analyses to answer Questions 1 and 2. Compared with the results in Table 6, among Spanish-speaking Hispanics, the association of cognitive status (baseline MMSE) with the cognitive and depression measures was unchanged for Retardation (partial r = -.543, $p < .0005$), disappeared for Paragraph-I, and now approached significance for WAIS-Digit Symbol (partial r = .357, $p = .014$). For their corresponding Whites, results were stronger for WAIS-Digit Symbol (partial r = .678, $p < .0005$ vs. partial r = -.464, p = .001), less significant for Paragraph-D (partial r = .356, $p < .014$ vs. partial r = -.560, p <.0005), and an additional measure, WAIS-Vocabulary (partial r = .432, $p = .002$), became strongly significant. Among English-speaking Hispanics, WAIS-Digit Symbol (partial r = .516, $p = .010$) still approached significance, and for their corresponding Whites, WAIS-Digit Symbol (partial r = .539, $p = .007$) now approached significance.

Questions 1 and 2: Secondary analyses not controlling for other measures in the same step. The predictive value of each measure was evaluated by itself, not controlling for other measures in the same step (for the analyses of neuropsychological tests, controlling only for demographics; and for the analyses of depression measures, controlling only for demographics and neuropsychological tests). As shown in **Appendix A**, for all neuropsychological and depression measures for both ethnic groups, associations with cognitive status (i.e., GDS) had partial $r \geq .347$ and $p \leq .002$, except for Retardation among Whites (partial r = .226, $p = .045$).

Appendix B presents partial correlations, corresponding to Appendix A, by primary language. Among Spanish-speaking Hispanics, all seven neuropsychological

tests (partial r = -.342 to -.574, $p \leq .012$) and all three depression measures (partial r = .321 to .675, $p \leq .030$) were strongly associated with cognitive status. Among their matched Whites, all seven neuropsychological tests (partial r = -.611 to -.834, $p < .0005$) were strongly associated with cognitive status, but no depression measures (partial r = .109 to .269, $p \geq .071$) approached significance. Among English-speaking Hispanics, Paragraph-I, Paragraph-D, and WAIS-Digit Symbol (partial r = -.531 to -.670; $p \leq .003$) were strongly significant, with Paired Associates-D (partial r = -.425, p = .019) approaching statistical significance. All depression measures (partial r - .456 to .575, $p \leq .029$) were also strongly significant. However, among their corresponding Whites, none of the neuropsychological or depression measures achieved strong statistical significance; only Paragraph-D, Paired Associates-D, and WAIS-Digit Symbol (partial r = -.366 to -.464, $p \leq .047$), and HDRS-total score (partial r = .490, p = .018) approached significance.

(When the three depression measures were controlled for demographic variables, but not for the seven neuropsychological tests or the other two depression measures, for both ethnic groups all associations were strongly significant, with partial $r \geq .438$ and $p \leq .0005$. When the analysis was performed by primary language, all associations had partial $r \geq .440$ and $p \leq .007$, except for Work and Activities (partial r = .348, p = .060) and Retardation (partial r = .258, p = .168) for Whites who were matched to English-speaking Hispanics and HDRS-total score (partial r = .327, $p = .017$) for Spanish-speaking Hispanics.)

Of note, when the above analyses were repeated using the HDRS-total score that excluded Work and Activities, and Retardation (HDRS-19), the Question 2 results for the

Spanish-speaking Hispanics showed that HDRS-19 did not approach significance. For their matched Whites, it also did not approach significance. For English-speaking Hispanics, HDRS-19 did not approach significance. For their matched Whites, only HDRS-19 (partial r = .493, p = .017) approached significance. Overall, these results suggest that, among Spanish- or English-speaking Hispanics, the usefulness of the HDRS-21 reflects the contributions of Work and Activities and Retardation rather than the other 19 items comprising the HDRS-19. On the contrary, among both White subgroups, results suggest that neither Work and Activities nor Retardation contribute substantially to the usefulness of the HDRS-21, which was comparable in significance to the HDRS-19.

Results for nondemented participants. Hierarchical logistic regression analysis was employed to answer Questions 1 and 2, distinguishing between GDS 1-2 vs. GDS 3, for nondemented participants (n = 68 matched pairs). For Question 1, for each ethnic group separately, the control variables of age, gender, and education were initially forced into the equation. After controlling for the other six neuropsychological tests, none of the neuropsychological tests were identified as useful predictors. When the analysis was limited to primary language; among Spanish-speaking Hispanics, WAIS-Vocabulary approached significance (p = .045). Analyses were not possible for English-speaking Hispanics due to the small sample size and the strong intercorrelations among the variables. Among the Whites who were matched to the two Hispanic subgroups, none of the neuropsychological tests were identified in the model.

For Question 2, after initially forcing into the equation the control variables of age, gender, and education and the seven neuropsychological tests; and after controlling

for the other two depression measures, for the entire Hispanic group, none of the depression measures were identified as useful predictors, including Retardation (p = .054). For the entire White group, the model identified the HDRS-total score (p = .001) as strongly significant. When the alternative HDRS-19 was used, among Hispanics, the procedure identified Retardation (p = .049). Among Whites, the model again identified only HDRS-19 (p = .001). These results are consistent with those of the regression analysis for the entire range of the GDS, 19 items of the HDRS excluding Work and Activities and Retardation relevant for Whites, but not for Hispanics, for whom Retardation had some relevance. It was not feasible to perform these hierarchical logistic regression analyses separately by primary language due to the small sample sizes.

Question 3: Prediction of baseline cognitive functioning, GDS 1- 5 (*n* = 89 matched pairs)

To examine the third question, how the combined usefulness of neuropsychological tests and depressive measures differed between Hispanic and White elderly, a hierarchical regression analysis included all 10 neuropsychological and depression measures as predictors, and the GDS rating as the dependent variable. The interaction of group with all 10 neuropsychological and depression measures was significant, [F (10, 150) = 2.402, p = .011]. In a subsidiary analysis, corresponding to the distinction between Question 1 and Question 2, the neuropsychological measures were not significant, [F (7, 153) = 1.062, p = .391], but the depression measures were, [F (3, 150) = 5.319, p = .002]. The distinctions between the associations of Hispanics and Whites for the specific neuropsychological and depression measures have already been discussed (**Table 5**). To interpret these interactions, it was helpful to examine the

proportions of explained variance attributable to the seven neuropsychological tests and to the three depression measures, for Hispanics and Whites. For Hispanics, the seven neuropsychological tests made a strong contribution [F (7, 78) = 7.256, p < .0005], accounting for 33.9% of the variance. The three depression measures also made a strong contribution [F (3, 75) = 17.810, p < .0005], accounting for 21.6% of the variance in predicting GDS status. For Whites, the seven neuropsychological tests made an even stronger contribution than for Hispanics [F (7, 78) = 14.900, p < .0005], accounting for 48.0% of the variance, but the three depression measures made a weaker contribution [F = 5.119 (3, 75), p = .003] to the prediction of cognitive status, accounting for 6.1% of the variance

Question 3: Prediction according to primary language. The hierarchical regression analyses were repeated to examine Question 3 according to the primary language of the Hispanic participant. For Spanish-speaking Hispanics and their matched Whites, the interaction of group with all 10 neuropsychological and depression measures was significant, [F (10, 84) = 3.109, p = .002]. The subsidiary analysis showed that both the neuropsychological [F (7, 87) = 2.216, p = .04] and depression measures [F (3, 84) = 4.558, p = .005] significantly contributed to the interaction. For the Spanish-speaking Hispanics, both the neuropsychological tests [F (7, 45) = 4.813, p < .0005, 33.5%] and the depression measures [F (3, 42) = 12.165, p < .0005, 20.8%] made a strong contribution to the prediction of GDS status. For their matched Whites, the neuropsychological tests made an even stronger contribution [F (7, 45) = 24.886, p < .0005, 60.1%], but the depression measures did not contribute [F (3, 42) = 1.114, p = .354, 1.1%).

For English-speaking Hispanics and their matched Whites, the interaction of group with all 10 neuropsychological and depression measures was not significant [F (10, 38) = .758, p = .667], nor were neuropsychological tests, [F (7, 41) = .503, p = .827] or depression measures, [F (3, 38) = 1.325, p = .280]. The lack of significance reflects a lack of relationship as well as the smaller sample of English-speaking Hispanics. For English-speaking Hispanics, the neuropsychological tests made a strong contribution [F (7, 22) = 3.751, p < .0008, 49.7%], but the depression measures made a weaker contribution [F (3, 19) = 3.822, p < .027, 15.7%]. For their matched Whites, neither the neuropsychological tests [F (7, 22) = 1.425, p = .245, 28.7%] nor the depression measures [F (3, 19) = 2.317, p = .108, 16.9%] were significant. The lack of significance of interaction despite the better prediction by neuropsychological tests among Hispanics compared with Whites may be attributed to the WAIS-Digit Symbol being by far the strongest predictor for each group (see **Table 6**), so the measures were used similarly for prediction in the Hispanic and White subgroups.

In summary, while the proportion of explained variance accounted for by the neuropsychological tests was greater for the White subgroup than for the Spanish-speaking subgroup, only for the Spanish-speaking subgroup did the addition of the depression measures add significantly to the model. For English-speaking Hispanics, while the depression measures added significantly to the model and to the change in R^2 beyond the contribution of the neuropsychological measures, neither set of measures was significant for their matched Whites. Altogether, these results suggest that, particularly for Hispanics, motivation-related depressive symptoms can add substantially to the prediction of cognitive status.

Results for nondemented participants. When Question 3 was examined limited to nondemented participants, the hierarchical logistic regression analysis yielded significant results [χ^2 (10) = 25.623, p = .004] for how the usefulness of neuropsychological tests and depressive measures differed between Hispanic and White elderly. When the neuropsychological and depression measures were distinguished, the neuropsychological tests were not significant [χ^2 (7) = 4.444, p = .727], but the depression measures were significant [χ^2 (3) = 13.674, p = .003].

Prediction of Cognitive Decline in the Longitudinal Sample

Baseline characteristics of the longitudinal sample (*n* = 76). The longitudinal sample consisted of 38 Hispanics with follow-up GDS ratings who were matched with Whites on baseline characteristics and follow-up interval. **Table 7A** presents the results on perfectly matched baseline variables, corresponding to Table 1A. Seventy-six percent were females (n = 29). Fifty percent of the sample had baseline GDS = 1 or 2, 26% had GDS = 3, and 24% had GDS ≥ 4. Correspondingly, half of the sample had clinical diagnoses of Normal or Possible Normal, 26% had MCI or Possible MCI, and 24% had AD. For the entire sample, the average age was 67.3 years (SD = 10.0, range: 50 - 91 years), and the average education was 14.5 years (SD = 2.9, range: 6 - 19 years). Matched sample t-tests for differences between the two ethnic groups in age, education, and follow-up interval are shown in **Table 7B**, and the differences on the matching variables are presented in **Table 7C**. Of these variables, only education was significantly different between the two ethnic groups. Hispanics, on the average, were less educated (*Mean* = 14.1 years, *SD* = 2.9) than Whites (*Mean* = 14.8 years, *SD* = 3.0, t (37) = -3.189, p = .003). None of the differences between matched Hispanics and Whites on any of the

neuropsychological or depression variables were significantly correlated with the difference in education. Therefore, this difference in education was not used as an additional control variable in the comparisons of Hispanics and Whites.

McNemar's test of difference between Hispanics and Whites in decline. Among the 38 matched pairs in the longitudinal analysis, 18 had no decline, 6 had declined by only the Hispanic, 8 had declined by only the White, and 6 had declined by both participants. McNemar's test of the discrepancy between 6 and 8 declines for the respective ethnic groups was not significant ($p = .791$ by the binomial distribution). Thus, decline was not primarily among only one ethnic group.

Although there was no overall difference between Hispanics and Whites in the proportion of decliners, additional preliminary analyses examined the associations of demographic variables with decline for Hispanics and Whites separately. **Tables 8A** (for Hispanics) **and 8B** (for Whites) compare the demographic and follow-up characteristics of decliners and nondecliners. None of these differences achieved statistical significance ($p < .05$). **Table 9** compares decliners and nondecliners by baseline GDS, separately for Hispanics and Whites. Although the sample sizes are very small, the proportion of decliners are higher in Hispanics for low baseline GDS and higher in Whites for high baseline GDS.

Preliminary longitudinal analyses for Questions 1 and 2. Although there were only 38 matched pairs of Hispanic and White participants with follow-up information, results for each group are presented as preliminary findings. To examine whether neuropsychological or depression measures are useful for prediction of cognitive decline, hierarchical logistic regression analyses were performed, forcing in baseline age,

education, gender, GDS, and follow-up interval; neuropsychological measures (for Question 1); and then three depression measures (for Question 2). However, it was not possible to evaluate the depression measures for either the Hispanic or White groups due to the strong intercorrelations among the variables. Among Hispanics, poor performance on Paragraph-D (p = .055) was the only predictor of cognitive decline that approached significance. Among Whites, the analysis of neuropsychological variables could not be computed since the measures were more strongly correlated than for Hispanics.

Since logistic regression was not substantially feasible, hierarchical regression analysis was performed for longitudinal decliners vs. non-decliners, as was done for baseline GDS. Results for both groups are presented in **Table 10**. Among Hispanics, none of the neuropsychological tests predicted cognitive decline after controlling for baseline GDS, demographics, follow-up interval, and the other six neuropsychological tests. Similarly, none of the depression measures were significantly associated with cognitive decline after controlling for baseline GDS, demographics, follow-up interval, the seven neuropsychological tests and the other two depression measures. Among Whites, only poor performance on WAIS-Digit Symbol (partial r = -.468, p = .014) significantly predicted cognitive decline, but good performance on Paired Associates-I, poor performance on Paired Associates-D, and good performance on WAIS-Vocabulary approached significance. No depression measures approached significance for predicting cognitive decline.

Secondarily, each measure was evaluated not controlling for other measures in the set (for the analyses of neuropsychological tests, controlling only for demographics; for the analyses of depression measures, controlling only for demographics and

neuropsychological tests). Among Hispanics, the only measures associated with decline were Paragraph-D (partial r = -.534, p = .001, significant even by the Holm criteria), Paragraph-I (partial r = -.411, p = .017*);* WAIS-Digit Symbol (partial r = -.373, p = .032); and Paired Associates-D (partial r = -.369, p = .035). Among Whites, the only cognitive test associated with decline were WAIS-Digit Symbol (partial r = -.552, p = .001, significant even by the Holm criteria), and Paired Associates-D (partial r = -.410, p = .018).

Table 11 presents the results for Questions 1 and 2 for Spanish-speaking Hispanics (n = 24) and for their matched Whites. [Due to the small sample size, regression analyses for Hispanics (n = 14) whose primary language was English and for their matched Whites were not possible.] Among Spanish-speaking Hispanics, the only significant predictor was Paragraph-D (partial r = -.588, p = .034). No depression measure was significantly associated with cognitive decline. In contrast, for their matched Whites one depression measure, Work and Activities (partial r = .715, p = .020), but no neuropsychological test, was significantly associated with cognitive decline. The difference between these two subgroups on the association of Paragraph-D with cognitive decline approached significance (p = .054).

Secondarily, when not controlling for other measures in the set, the same neuropsychological and depression measures, Paragraph-D (partial r = -.560, p = .013) for the Spanish-speaking subgroup, and Work and Activities (partial r = .646, p = .023) for their matched Whites, were significantly associated with cognitive decline.

Preliminary longitudinal analyses for Question 3. Analysis of the difference between Hispanic and White elderly in the combined usefulness of neuropsychological

and depression measures was not feasible by hierarchical logistic regression analyses. Thus, we examined this question using hierarchical regression analysis (as was done for baseline GDS). The combined usefulness of the ten measures was not significant, [F (10, 44) = 1.156, p = .345]; when the neuropsychological measures and depression measures were distinguished, neither set was significant. Since the usefulness of the combined predictors did not differ significantly between the groups, the entire sample of Hispanic and White participants was analyzed together. The combination of all 10 measures was significantly associated with cognitive decline [F (10, 60) = 3.901, p < .0005], with the neuropsychological measures contributing strongly [F (7, 63) = 3.953, p = .001] and the depression measures [F (3, 60) = 2.932, p = .041] making an additional contribution.

Baseline demographic variables and GDS were controlled for in the analysis for Question 3 of longitudinal decline. Baseline GDS had a significant interaction with group, t (5, 64) = 2.967, p = .004. This discrepancy reflected a negative association with relatively less decline in Hispanics at higher baseline GDS, partial r = -.313, p = .067, controlling for baseline age, gender, and education. In contrast, for Whites, the relationship was in the opposite direction, partial r = .262, p = .128. **Table 9** presents the decliners and nondecliners for Hispanics and Whites at different baseline GDS levels.

DISCUSSION

Cross-Sectional Findings

Despite the increased risk of both depression and dementia in the Hispanic elderly population (Gurland et al., 1999; Tang et al., 2001, Falcon & Tucker, 2000), research addressing the accuracy with which validated neuropsychological tests and depression symptoms may predict cognitive functioning/decline in this population is limited. The longitudinal study by Perrino and colleagues (2008) represents one of the few efforts. The specific aims of the present study add to the longitudinal findings of Perrino et al. in several ways by: (1) using a more comprehensive neuropsychological test battery to predict cognitive functioning; (2) examining the unique contributions of the neuropsychological and depression measures to the prediction of cognitive functioning/decline among Hispanic elderly; (3) contrasting the results for Hispanics with those of Whites; and (4) distinguishing between Spanish- and English-speaking Hispanics, with matched White participants.

The current study examined the data of two distinct Hispanic groups, different in their report of primary language (Spanish vs. English), but with similar educational attainment. Although the educational difference was not statistically significant, Spanish-speaking Hispanics were, on the average, less educated than English-speaking Hispanics (13 years vs. 14 years, respectively). After controlling for demographics and six neuropsychological tests, for the entire Hispanic group (Spanish- and English-speaking), the initial recall of the NYU-Paragraph Test and the WAIS-Digit Symbol were the only neuropsychological tests associated with baseline cognitive status. However, these results did not hold when the data were reanalyzed taking into account the primary

language of the Hispanic participant. While the initial recall of the NYU-Paragraph Test was the only neuropsychological test strongly associated with baseline cognitive status among Spanish-speaking Hispanics, for English-speaking Hispanics, WAIS-Digit Symbol was the only test significantly associated with cognitive status. For the entire White group, WAIS-Digit Symbol was associated with cognitive status, and the delayed recall of the NYU-Paragraph Test, specifically for Whites matched with Spanish-speaking participants.

None of the neuropsychological or depression measures were associated with cognitive status among Whites matched with the English-speaking Hispanics. This result is inconsistent with previous research that included mainly White participants from the longitudinal database of the NYUADC (Flicker et al., 1991; Kluger et al., 1999). For instance, Kluger et al., in a longitudinal study, found that both delayed recall of the Paragraph Test and the WAIS-Digit Symbol were among the best neuropsychological predictors of cognitive decline. However, differences in research methodology could account for this discrepancy. For example, the White subgroup is considerably smaller (n = 33) than the number of participants in the study by Kluger et al., and the current result is based on cross-sectional findings. The matching approach in this study forced this White subgroup to be matched with relatively highly educated Hispanics (the English-speakers), which is not a common practice in the literature. Additionally, in this study, their adjusted mean scores for some of the neuropsychological measures were quite similar for the cognitively normal and the MCI, thus decreasing the likelihood of a significant association of these neuropsychological tests with cognitive status (as measured by the GDS). It is important to note that when the MMSE was used to define

cognitive status in the regression analysis, among Whites who were matched with English-speaking Hispanics, WAIS-Digit Symbol approached significance after adjusting the *p*-value for multiple comparisons (partial r = .539, *p* = .007).

Regarding the associations of depression with cognitive status, Retardation was strongly significant, after controlling for demographic variables, seven neuropsychological, and two other depression measures among Hispanics, but specifically only among Spanish-speaking Hispanics. This result remained unchanged when the analysis excluded conditions such as depression and vascular normal, as well as when the alternative criterion measure, the MMSE, was used.

Other analyses that controlled only for the demographics and the seven neuropsychological tests showed that Retardation and Work and Activities, but not the total of the other 19 items of the HDRS, were significantly associated with cognitive status in the two Hispanic subgroups. Results were in the opposite direction for the Whites who were matched with the English-speaking Hispanics; after excluding Retardation and Work and Activities, the significance of the HDRS-total score remained unchanged. Results also indicated that the HDRS-total score for Whites, and possibly Retardation, for Hispanics, may be helpful in differentiating normal from MCI cases. Overall, these results suggest that Hispanics differ from Whites in the contribution of Retardation and Work and Activities to the association between depression (as measured by the HDRS-total score) and cognitive status.

Moreover, both the neuropsychological and depression measures contributed to the distinction of their predictive usefulness among Spanish-speaking Hispanics from their matched Whites. When the analysis was limited to nondemented participants, only

the depression measures predicted differently. For English-speaking Hispanics and their matched Whites, there was no difference in the combined or separate predictive usefulness of these measures.

These findings suggest that among Hispanics, examining only the total score from a depression scale might not be sufficient to achieve diagnostic accuracy, or to accurately identify individuals at risk of cognitive decline. The emerging literature suggests an association between neuropsychiatric symptoms and cognitive function, providing support for the assessment of specific symptoms (Berger et al., 1999; Starkstein et al., 2006). Identification of specific symptoms may also shed some light on the neurobiological basis underlying their association or the association of depression with dementia. For example, apathy and mental slowness predicted white matter changes in dementia (Jonsson et al., 2010). Another study found that dementia was associated with anhedonia, apathy, and anergia (Lavretsky et al., 2008). These symptoms were in turn associated with greater lacunar volume in white matter, after adjusting for cognitive status, age, gender, and education. Similarly, frontostriatal dysfunction has been associated with changes in various cognitive abilities and behavioral changes including impairment in information processing speed, visuospatial ability, executive functioning, impaired insight, psychomotor retardation, and reduced interest in activities/apathy (Alexopoulos, 2003; Butters et al., 2004).

The above findings are consistent with the clinical data of this study. Retardation was substantially increased among mildly impaired Whites (GDS 3), compared to Whites with normal cognitive function, and remained relatively unchanged among Whites with dementia (GDS 4). Among Hispanics, although retardation was increased at the level of

mild impairment, it became more apparent at the level of dementia. Similarly, a recent study performed in Japan found that psychomotor retardation was significantly higher in AD patients with Major Depressive Episodes than in nondemented patients with Major Depressive Disorder. Psychomotor retardation was among the symptoms that improved with treatment (Mizukami, Hatanaka, Tanaka, Sato, & Asada, 2009). The current study showed that retardation, as a symptom of subclinical depression, is prevalent not only in dementia, but also among mildly impaired individuals.

Results from the preliminary ANCOVAs aimed at examining possible group differences in neuropsychological test performance for different cognitive categories (NL, MCI and AD) by primary language (i.e., Spanish vs. English), showed that WAIS-Digit Symbol lacked specificity in the Spanish-speaking subgroup. Cognitively normal Spanish-speaking Hispanics had considerably lower scores on WAIS-Digit Symbol than the other three Hispanic and White subgroups**.** In fact, if one were to interpret their scores using normative data for Whites, the WAIS-Digit Symbol scores of Spanish-speaking Hispanics would be suggestive of cognitive impairment. Remarkably, cognitively normal (GDS 1-2) Spanish-speaking Hispanics had a mean score on WAIS-Digit Symbol that was similar to that obtained by those with mild cognitive impairment (35.3 vs. 36.3, respectively). This result is inconsistent with previous findings, using data mainly from White participants, reporting that WAIS-Digit Symbol successfully differentiated individuals with normal cognitive functioning from those with MCI and from those with early AD (Kluger et al, 1997). However, this result is consistent with those of Sano et al., who found that a Maze Test speed score was so low among cognitively normal Hispanics that they could not be differentiated from Hispanics with

AD (Sano et al., 2006). Similarly, Byrd et al. found that cognitively normal Hispanics had slower performance than Whites on tasks of letter and shape cancellation (Byrd et al., 2004).

It has been argued that the difference in test performance among individuals from different racial/ethnic backgrounds may reflect differences in cognitive style, which can be attributed to cultural factors (Byrd et al., 2004). The findings from the ANCOVAs highlight the importance of investigating not only demographic characteristics (e.g., age and education), but also aspects of a culture (e.g., language) that can account for possible test bias in some neuropsychological tests (e.g., WAIS-Digit Symbol). These findings demonstrated that report of primary language is an important variable, which should be included in research addressing cross-cultural differences in test performance. Primary language as a proxy of acculturation adds to the body of literature showing that low levels of acculturation can adversely affect test performance (Black et al., 1999; Coffey et al., 2005; Loewenstein et al., 1993; Pontón & Ardila, 1999). One study examined English fluency as a proxy of acculturation and found that Spanish-speaking Hispanics who were tested in Spanish and reported speaking little English or no English at all had worse performance on cognitive tests than English-speaking participants. On the contrary, Hispanics who also were tested in Spanish but reported being fluent in English performed similarly to English-speaking participants (Jacobs et al., 1997). The current findings are consistent with those of Jacobs and colleagues.

Although it would be reasonable to think that group differences on tasks of psychomotor ability might be explained by biological or health factors such as white matter changes and visual impairment (Salthouse, Hancock, Meinz, & Hambrick, 1996),

experience and cultural values could also explain differences in task performance. It is important to note that good performance on WAIS-Digit Symbol depends on both accuracy and speed, which can be perceived or valued differently from culture to culture. Whites may perceive being fast as demonstrating better intellectual performance, whereas other ethnic/racial groups (e.g., Hispanics) may place a higher value on being accurate at the expense of being fast (Helms, 1992; Llabre, 1991). Thus, the differential results of the WAIS-Digit Symbol compared with the other untimed neuropsychological tests suggest that Hispanics favored accuracy over speed on the WAIS-Digit Symbol more than Whites. Additionally, it is also possible that imposition of a time limit, independent of accuracy considerations, can affect performance on timed tasks. Moreover, the WAIS-Digit Symbol may be less familiar to Spanish-speaking Hispanics than the verbal neuropsychological tasks.

Since Retardation measures "slowness," it can affect performance on WAIS-Digit Symbol, which is a timed test. Separate partial correlations of Retardation with WAIS-Digit Symbol controlling for age, gender, and education in the four non-demented subgroups indicated a positive association approaching significance for Spanish-speaking Hispanics (partial $r = .319$, $p = .058$), but a significant negative association (partial $r = -.332$, $p = .048$) for their matched Whites. In the other two subgroups, the associations were negative and non-significant. This anomalous positive association that occurred only among Spanish-speaking Hispanics may suggest a strategy that specifically emphasizes accuracy at the cost of speed, presenting the appearance of retardation. On the contrary, for the other subgroups, the negative associations validate that being slow on the Retardation measure is associated with being slow on WAIS-Digit Symbol.

Because the WAIS-Digit Symbol is more a nonverbal than a verbal task, these results are in agreement with other findings reporting poor performance on nonverbal tests among Hispanics (Byrd et al., 2004; Coffey et al., 2005; Jacobs et al., 1997; Loewenstein et al., 1993). Indeed, there were no significant group differences on tests that require intact verbal ability, which is also consistent with other studies that matched ethnic/racial groups on important demographic characteristics (e.g., Jacobs et al.; Manly et al., 1998). For instance, Jacobs et al. found that Spanish-speaking Hispanics and Whites had similar performance on most verbal tasks, including the immediate and delayed recall of the SRT. Similarly, Manly et al. found that difference in performance on this test was attenuated after African Americans and Whites were matched on education. However, group differences were still evident on tests of visuospatial ability.

These results are consistent with the literature finding an association of decline in processing speed with increasing aging, as shown by decreased performance on psychomotor or perceptual tasks requiring speed (Salthouse, 2000). However, after controlling for education, this study showed that this association (as measured by the WAIS-Digit Symbol) was weaker for Spanish-speaking Hispanics (partial r = -.313) than for their English-speaking counterparts (partial r = -.417 to -.646).

This study showed that the neuropsychological profile of cognitively normal English-speaking Hispanics was similar to that of Whites, but different from that of Spanish-speaking Hispanics. The latter has implications for cross-cultural neuropsychological research and clinical practice. It raises an important question regarding which norm is most appropriate to use when a Hispanic participant reports English as his/her primary language.

Research should be aimed at understanding the cognitive processes that may affect performance on speed tasks among cognitively normal minority elderly. For instance, such studies could examine the associations among performance on pure motor tasks (e.g., using the Purdue Pegboard Test; Reddon, Gill, Gauk, & Maerz, 1988; Tiffin & Asher, 1948), psychomotor tasks (e.g., using WAIS-Digit Symbol or a cancellation task), and tasks that require other cognitive abilities (e.g., attention or executive functioning). In this regard, the optional tasks of the WAIS-Digit Symbol subtest (WAIS-III; Wechsler, 1997), Digit Symbol-Incidental Learning, and Digit Symbol-Copy could help to clarify which ability (e.g., attention/memory, perceptual, or graphomotor ability) might affect performance. In addition, future research can be aimed at investigating socio-cultural factors that can influence performance on speed tasks. These factors can be examined through the development/use of a comprehensive acculturation scale that includes items regarding education (e.g., number of years and where education was completed), language (e.g., spoken language and proficiency), US-born vs. foreign-born /number of years residing in the US, and how *speed and accuracy are* valued or perceived by the individual. The effects of bilingualism on neuropsychological test performance and specifically on tasks of psychomotor functioning should also be explored.

Preliminary Longitudinal Findings

Overall, the preliminary longitudinal findings suggest that the usefulness of delayed recall as a predictor of cognitive decline may generalize to Spanish-speaking Hispanics, consistent with findings for Whites (Chodosh, Reuben, Albert, & Seeman, 2002; Flicker et al., 1991; Kluger et al., 1999; Lange et al., 2002). For the entire White

group, WAIS-Digit Symbol was associated with cognitive decline (as analyzed by hierarchical regression analysis). However, WAIS-Digit Symbol was not a significant predictor among Whites matched with the Spanish-speaking group, but Work and Activities was. The fact that none of the depression measures predicted cognitive decline among Hispanics was inconsistent with the cross-sectional findings. Nevertheless, definite conclusions can only be drawn with a larger sample than the one presented in this preliminary longitudinal analyses.

The longitudinal analyses also showed group differences in GDS change at different levels of GDS rating at baseline. Hispanics were more likely than Whites to decline to higher GDS levels if they were cognitively normal at baseline (e.g., from GDS 2 to GDS 3). In contrast, among those with dementia at baseline, there was a lower rate of decline among Hispanics compared to Whites (33% vs. 89%, respectively; $p = .0498$ by Fisher's exact test). Specifically, only 1 of 5 Hispanics who had moderate dementia (GDS 5) at baseline declined to more severe levels of dementia, while all 5 Whites with moderate dementia showed cognitive decline with no difference in follow-up period.

Differences in rate of decline in the sample with dementia may reflect either a high baseline GDS rating (overestimation of dementia) or a low follow-up GDS rating (underestimation of dementia) among Hispanics. It is important to note that for the White group the third visit to the clinic was used as their follow-up longitudinal GDS, which could have resulted in a more accurate GDS rating compared to Hispanics, for whom 22 of 38 (58%) had only a second visit. Alternatively, other possible explanations unrelated to the GDS may include biological mechanisms and environmental factors such

as social support (Seeman, Albert, Lusignolo, & Berkman, 2001) or aspects of caregiving, which could impact cognitive functioning.

Rate of conversion of subsequent decline to dementia in MCI varies with reports ranging from 5% to 25% per year (Kluger et al., 1999; Manly et al., 2008; Petersen et al., 2001). These reported differences in rate of decline probably have a number of causes: different methodological criteria used to define MCI, different clinical rating scales used (CDR vs. GDS), diverse tests used to assess cognitive function, and differences in sample demographic characteristics. In this study, including both ethnic groups, the conversion rates were 10% in the MCI group (GDS 3) compared to 5% of the normal group (GDS 1-2), with a follow-up period averaging 2.2 years. Thus, the rates of the current study fall well within the ranges that have been previously reported. However, our conversion rate of approximately 5% per person year for the MCI group was different from the 15% reported by Kluger and colleagues. This inconsistency is associated with differences in methodological approaches. In their study, the baseline was not necessarily represented by the first clinic visit, but rather the most recent assessment period in which participants were nondemented (i.e., GDS = 1, 2, or 3) and had a subsequent follow-up assessment after that baseline. Also, participants were followed-up for a period of approximately four years. Thus, their selection strategy and follow-up period could have increased the number of cases that progressed to dementia.

Some of the strengths of this study include the perfectly matched baseline characteristics of the two ethnic groups (i.e., gender, GDS rating, and clinical diagnosis). An attempt was made to closely match and control for other variables that could affect neuropsychological performance and cognitive functioning/decline (i.e., age, education,

and length of follow-up). Group differences in education did not disappear with approximate matching. However, even when perfect matching is achieved, the literature suggests that group differences in test scores may still remain due to differences in quality of education. For example, reading ability was found to be a stronger predictor of test performance than years of education (Manly et al., 2004). Another study compared single word reading scores in three different ethnic/racial groups with the same level of educational attainment. Findings revealed that White elderly performed better than Hispanic and African American elderly (Consentino et al., 2007). Moreover, although in this study the Hispanic participants differed significantly from the matched Whites in education, none of the differences between matched Hispanics and Whites on any of the neuropsychological or depression variables were significantly correlated with the difference in education.

Although the matching procedure was one of the strengths of this study, it also created some limitations. For example, the attempt to match the groups on educational attainment produced a sample of relatively highly educated Hispanics who might not be representative of the Hispanic population residing in the U.S. For example, Gurland et al. found that more than 40% of their participants, Hispanics residing in the area of northern Manhattan in New York City, did not complete more than five years of formal education (Gurland et al., 1999). However, the current finding was consistent with that of Perrino and colleagues (2008), who did not find an association between depression and cognitive decline in less-educated Hispanics. Thus, the lack of an association between depression and cognitive decline in relatively highly educated Hispanics extends the findings of Perrino et al.

Moreover, the language (English or Spanish) in which the Hispanic participants were tested was unknown, so the interpretation of these findings is limited to the knowledge of reported primary language. Although speculative, it would be reasonable to think that participants were tested in their dominant language. Hispanics are quite a heterogeneous population, who can differ in important characteristics such as country of origin, cultural values, and language or dialect. It was clear in this study that cognitively normal Hispanics who reported Spanish as their primary language had impaired performance on WAIS-Digit Symbol. Their performance was also poorer on other neuropsychological tests (although statistical significance was not reached) than their English-speaking counterparts. The Hispanic participants in this study were mainly from the U.S. and the Caribbean; thus results may not generalize to other Hispanic groups or to Hispanics residing outside the U.S.

Due to the small sample size of the longitudinal sample, research aimed at investigating the association of neuropsychological and depression measures with cognitive decline among Hispanic elderly, as well as ethnic/racial differences in rate of decline, are warranted.

Overall, findings from the cross-sectional and the preliminary longitudinal analyses suggest that the NYU-Paragraph Test (initial and delayed recall) and motivation-related symptoms (e.g., Retardation and Work and Activities) can be useful in improving diagnostic accuracy and predicting cognitive decline among Hispanics. These results have implications for clinical trials enrolling Spanish-speaking Hispanics. Moreover, medication targeted at treating depression, and especially motivation-related

symptoms, may prove to be effective in ameliorating the cognitive deficits that can accompany both depression and dementia.

Table 1A

Baseline Exact Matching Characteristics for the Two Ethnic Groups

	N	%
Exact Matches	178	100.0
Female	142	79.9
GDS		
1	12	6.7
2	82	46.1
3	42	23.6
4	32	18.0
5	10	5.6
Diagnosis		
Normal	86	48.3
Possible Normal	4	2.2
MCI	34	19.1
Possible MCI	8	4.5
AD	34	19.1
Possible AD	2	1.1
Depression	4	2.2
Vascular Normal	2	1.1
Other	4	2.2

Table 1B

Baseline Approximate Matching Characteristics for the Two Ethnic Groups

	Hispanics		Whites			
	n	Mean (*SD*)	*n*	Mean (*SD*)	*t*	*p*
Age	89	66.9 (10.1)	89	67.2 (10.6)	.799	.218
Education	89	13.5 (3.6)	89	14.3 (3.4)	5.064	**<.0005**
Follow-up interval	38	2.3 (.75)	38	2.1 (.39)	.606	.117

Table 1C

Differences between Hispanics and Whites in Approximate Matching Characteristics

	Age		Education		Follow-Up Interval	
	n	(%)	*n*	(%)	*n*	(%)
Years [a]						
- 5	1	(1.1)				
- 4	2	(2.2)				
- 3	5	(5.6)				
- 2	4	(4.5)	5	(5.6)	2	(5.3)
- 1	6	(6.7)	4	(4.5)	5	(13.2)
0	43	(48.3)	40	(44.9)	29	(76.3)
1	9	(10.1)	6	(6.7)	2	(5.3)
2	10	(11.2)	31	(34.8)		
3	4	(4.5)				
4	2	(2.2)				
5	3	(3.4)	1	(1.1)		
6			2	(2.2)		

Note: This table presents paired Hispanics and Whites who differed on a characteristic by a specific number of years

[a] Years < 0 indicates that the Hispanic participant had a larger value than the White participant.

Table 1D

Baseline Approximate Matching Characteristics for Spanish and English-Speaking Hispanics and their Matched Whites

	Hispanics		Whites			
	n	Mean (*SD*)	*n*	Mean (*SD*)	*t*	*p*
		Spanish Match				
Age	56	66.3 (9.7)	56	66.8 (10.2)	1.780	.081
Education	56	13.2 (3.8)	56	14.1 (3.6)	4.359	**<.0005**
Follow-up interval	24	2.2 (.63)	24	2.1 (.42)	.594	.558
		English Match				
Age	33	67.9 (11.2)	33	67.7 (10.2)	.564	.577
Education	33	14.0 (3.0)	33	14.6 (3.0)	2.602	**.014**
Follow-up interval	14	2.4 (.94)	14	2.1 (.33)	1.727	.108

Table 2A

Baseline Demographic Characteristics for the Spanish and English-Speaking Hispanic Subgroups

	Hispanics				
	Spanish (n = 56)	English (n = 33)			
	Mean (*SD*)	Mean (*SD*)	*t*	*df*	*p*
Age (year)	66.3 (9.7)	67.9 (11.2)	.694	87	.490
Education – M (SD)	13.2 (3.8)	14.0 (3.2)	1.009	87	.316
Follow-up interval (year)	2.2 (.59) (*n* = 27)	2.4 (.91) (*n* = 15)	.665	40	.510

Table 2B

Gender, GDS, and Clinical Diagnosis Distribution for the Spanish and English-Speaking Hispanic Subgroups

	Hispanics						
	Spanish (*n* = 56)		English (*n* = 33)				
	n	(%)	*n*	(%)	χ^2	*df*	*p*
Gender(female)	46	(82.1)	25	(75.8)	.525	1	.469
GDS *					4.100	2	.129
1	4	(7.1)	2	(6.1)			
2	22	(39.3)	19	(57.6)			
3	13	(23.2)	8	(24.2)			
4	12	(21.4)	4	(12.1)			
5	5	(8.9)	0	--			
Diagnosis *					4.278	2	.118
Normal	24	(42.9)	19	(57.6)			
Possible Normal	1	(1.8)	1	(3.0)			
MCI	11	(19.6)	6	(18.2)			
Possible MCI	2	(3.6)	2	(6.1)			
AD	14	(25.0)	3	(9.1)			
Possible AD	1	(1.8)	0	--			
Depression	2	(3.6)	0	--			
Vascular Normal	0	--	1	(3.0)			
Other	1	(1.8)	1	(3.0)			

* To avoid small sample sizes for χ^2 analyses, GDS 1 and 2 and GDS 4 and 5 were combined. Similarly, clinical diagnoses were combined: Normal with PM, MCI with Possible MCI, AD with PA; Depression, Vascular Normal, and Other were excluded.

Table 3

Results of Three-Way ANCOVA Tests of Interactions

	Two-way Interaction (Group x GDS)		Three-way Interaction (Group x GDS x Primary Language)	
	F (*df* = 2, 75)	*p*	*F* (*df* = 2, 75)	*p*
Paragraph-Initial	.063	.939	1.594	.210
Paragraph-Delayed	1. 060	.352	2.342	.103
WAIS-Digit Symbol	1.559	.217	4.417	**.015**
Paired Associates-Initial	.684	.508	1.183	.312
Paired Associates-Delayed	1.465	.238	1.001	.372
WAIS-Vocabulary	1.234	.297	.331	.719
Memory for Designs	1.854	.164	.587	.559
Work and Activities	2.108	.129	2.758	.070
Retardation	5.643	**.005**	3.726	**.029**
HDRS-total score	2.559	.084	2.540	.086

Table 4A

Estimated *Mean* (*SEM*) Baseline Performance on WAIS-Digit Symbol among Hispanics and Their Corresponding Whites, according to the Primary Language of the Hispanic Participant

	Spanish (*n* = 51 pairs)			English (*n* = 33 pairs)		
	n	Hispanics	Whites	*n*	Hispanics	Whites
GDS 1-2	26	35.3 (2.3)	54.5 (2.1)	21	50.1 (2.4)	50.6 (2.2)
GDS 3	13	36.3 (3.2)	46.2 (2.9)	8	37.1 (4.0)	51.0 (3.7)
GDS 4	12	28.5 (3.4)	30.9 (3.1)	4	22.8 (5.7)	24.9 (5.3)

Note: *Mean* (*SEM*) based on analysis of covariance controlling for age, sex, and education.

Table 4B

Mean (*SEM*) Baseline Performance on Retardation among Hispanics and Their Corresponding Whites, according to the Primary Language of the Hispanic Participant

	Spanish (*n* = 51 pairs)			English (*n* = 33 pairs)		
	n	Hispanics	Whites	*n*	Hispanics	Whites
GDS 1-2	26	.02 (.09)	.17 (.13)	21	.00 (.10)	.24 (.14)
GDS 3	13	.29 (.13)	1.06 (.18)	8	.21 (.16)	.33 (.23)
GDS 4	12	1.00 (.13)	1.08 (.19)	4	1.81 (.23)	.80 (.33)

Note: *Mean* (*SEM*) based on analysis of covariance controlling for age, sex, and education.

Table 4C

**Mean* (*SEM*) Baseline Performance on Paragraph-D among Hispanics and Their Corresponding Whites, according to the Primary Language of the Hispanic Participant

	Spanish (n = 48 pairs)			English (n = 31 pairs)		
	n	Hispanics	Whites	*n*	Hispanics	Whites
GDS 1-2	25	4.9 (.52)	7.9 (.52)	20	7.5 (.54)	8.2 (.54)
GDS 3	13	4.3 (.69)	6.1 (.69)	8	4.6 (.87)	7.0 (.87)
GDS 4	10	2.2 (.82)	2.0 (.81)	3	3.1 (1.43)	1.2 (1.43)

Note: *Mean* (*SEM*) based on analysis of covariance controlling for age, sex, and education.
*These ANCOVAs excluded 5 pairs with the following diagnoses: Depression, Vascular Normal and Others.

Table 5

Association between Baseline Predictors and Baseline GDS 1 -5 among Hispanics and Their Matched Whites

	Hispanics (n = 89)		Whites (n = 89)	
Predictor	Partial r	p	Partial r	p
A. Neuropsychological Tests [a]				
Paragraph-I	**-.284**	.011	-.045	.695
Paragraph-D	.056	.624	**-.254**	.023
Digit Symbol	**-.238**	.034	-.**340***	.002
Paired Associates-I	-.009	.939	-.033	.772
Paired Associates-D	.002	.984	-.024	.833
Vocabulary	-.023	.838	-.040	.726
Memory for Designs	-.122	.283	- .041	.720
B. Depression [b]				
Work and Activities	.028	.810	.172	.134
Retardation	.**513***	<.0005	-.024	.836
HDRS-total score	.098	.398	.172	.135

[a] Controlling for age, sex, education, and 6 other cognitive tests.
[b] Controlling for age, sex, education, 7 cognitive tests, and two other depression measures.
*Significant at .05 by Holm multiple comparison procedure.
Note: I = Initial, D = Delayed, HDRS = Hamilton Depression Rating Scale.

Table 6
Association Between Baseline Predictors and Baseline GDS (1 -5) among Hispanics and Their Corresponding Whites

	Spanish Language Match (n = 56)				English Language Match (n = 33)			
	Hispanics		Whites		Hispanics		Whites	
Predictor	Partial *r*	*p*	Partial *r*	*p*	Partial *r*	*p*	Partial *r*	
A. Neuropsychological Tests [a]								
Paragraph-I	**-.400***	.005	.018	.903	-.179	.402	-.163	.448
Paragraph-D	.148	.322	**-.560***	<.0005	-.085	.693	.059	.785
Digit Symbol	-.109	.467	**-.464***	.001	**-.544***	.006	-.358	.086
Paired Associates-I	-.134	.370	.097	.519	.116	.590	-.064	.765
Paired Associates-D	.064	.669	-.011	.940	-.069	.750	-.180	.401
Vocabulary	-.206	.165	-.007	.964	.311	.139	.078	.717
Memory for Designs	-.208	.161	-.133	.374	.144	.502	.156	.468
B. Depression [b]								
Work and Activities	.012	.936	.035	.819	.043	.852	-.037	.873
Retardation	**.578***	<.0005	.208	.176	.407	.067	-.192	.405
HDRS-total score	.112	.470	-.026	.865	.179	.438	.409	.066

[a] Controlling for age, sex, education, and 6 other cognitive tests.
[b] Controlling for age, sex, education, 7 cognitive tests, and 2 other depression measures.
*Significant at .05 by Holm multiple comparison procedure.
Note: I = Initial, D = Delayed, HDRS = Hamilton Depression Rating Scale.

Table 7A

Baseline Exact Matching Characteristics for the Entire Longitudinal Sample

	n	%
Exact Matches	76	100.0
Female	58	76.3
GDS		
1	4	5.3
2	34	44.7
3	20	26.3
4	10	13.2
5	8	10.5
Diagnosis		
Normal	36	47.4
Possible Normal	2	2.6
MCI	16	21.1
Possible MCI	4	5.3
AD	18	23.7
Primary Language of Hispanics		
Spanish	24	63.2
English	14	36.8

Table 7B

Baseline Approximate Matching Characteristics for the Longitudinal Sample

	Hispanics		Whites			
	n	*Mean* (*SD*)	*n*	*Mean* (*SD*)	*t*	*p*
Age	38	67.1 (9.8)	38	67.5 (10.2)	-1.452	.155
Education	38	14.1 (2.9)	38	14.8 (3.0)	-3.189	.003
Follow-up interval	38	2.3 (.75)	38	2.1 (.39)	1.606	.117

Table 7C

Baseline Differences between Hispanics and Whites in Approximate Matching Characteristics for the Longitudinal Sample

	Age		Education		Follow-Up Interval	
	n	(%)	*n*	(%)	*n*	(%)
Years [a]						
- 4	1	(2.6)				
- 3	2	(5.3)				
- 2	3	(7.9)	4	(10.5)	2	(5.3)
- 1	2	(5.3)	2	(5.3)	5	(13.2)
0	13	(34.2)	12	(31.6)	29	(76.3)
1	6	(15.8)	3	(7.9)	2	(5.3)
2	7	(18.4)	17	(44.7)		
3	2	(5.3)				
4	1	(2.6)				
5	1	(2.6)				

Note: This table presents paired Hispanics and Whites who differed on a characteristic by a specific number of years

[a] Years < 0 indicates that the Hispanic participant had a larger value than the White participant.

Table 8A

Baseline Characteristics of Decliners vs. Nondecliners for the entire Hispanic Group

	Decliners (n = 12)	Nondecliners (n = 26)			
	Mean (*SD*)	*Mean* (*SD*)	*t or* χ^2 test	*df*	*p*
Age (years)	69.7 (11.2)	65.9 (9.1)	-1.109	36	.275
Gender (%)					
Female	7.0 (24.1)	22.0 (75.9)	3.138	1	.076
Male	5.0 (55.6)	4.0 (44.4)			
Education	14.4 (2.5)	14.0 (3.1)	-.410	36	.684
Follow-up interval (years)	2.3 (.90)	2.3 (.69)	.084	36	.933
Primary Language of Hispanics (%)					
Spanish	7.0 (29.2)	17.0 (70.8)	.175	1	.675
English	5.0 (35.7)	9.0 (64.3)			

Table 8B

Baseline Characteristics of Decliners vs. Nondecliners for the Entire White Group

	Decliners (n = 14)	Nondecliners (n = 24)			
	Mean (*SD*)	Mean (*SD*)	*t* or χ^2 test	*df*	*p*
Age (years)	70.6 (11.4)	66.1 (9.6)	-1.260	36	.216
Gender (%)					
Female	9.0 (31.0)	20.0 (69.0)	1.775	1	.183
Male	5.0 (55.6)	4.0 (44.4)			
Education	14.9 (2.1)	14.8 (3.3)	-.104	36	.918
Follow-up interval (years)	2.1 (.34)	2.1 (.41)	.374	36	.711
Primary Language of Hispanics					
Spanish	8.0 (33.3)	16.0 (66.7)	.345	1	.557
English	6.0 (42.9)	8.0 (57.1)			

Table 9

Number (*%*) of Decliners and Nondecliners by Ethnicity and Baseline GDS

		Hispanics				Whites			
		Decliners (*n* = 12)		Nondecliners (*n* = 26)		Decliners (*n* = 14)		Nondecliners (*n* = 24)	
Baseline GDS	*n*	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*
1	**2**	2	100.0	0	0.0	1	50.0	1	50.0
2	**17**	6	35.3	11	64.7	4	23.5	13	76.5
3	**10**	1	10.0	9	90.0	1	10.0	9	90.0
4	**5**	2	40.0	3	60.0	4	80.0	1	20.0
5	**4**	1	25.0	3	75.0	4	100.0	0	0.0
***n* total**	**38**	12	31.6	26	68.4	14	36.8	24	63.2

Table 10

Association Between Baseline Predictors and Cognitive Decline among Hispanics and Their Matched Whites

Predictor	Hispanics (n = 38) Partial r	p	Whites (n = 38) Partial r	p
A. Neuropsychological Tests [a]				
Paragraph-I	-.117	.560	-.126	.531
Paragraph-D	-.269	.175	.044	.826
Digit Symbol	-.030	.883	**-.468***	.014
Paired Associates-I	.168	.403	.361	.065
Paired Associates-D	-.153	.447	-.357	.067
Vocabulary	.052	.798	.376	.053
Memory for Designs	-.118	.557	-.135	.501
B. Depression [b]				
Work and Activities	.065	.763	.326	.120
Retardation	.305	.147	.083	.700
HDRS-total score	-.193	.365	-.327	.118

[a] Controlling for baseline GDS, follow-up interval, age, sex, education, and 6 other cognitive tests.
[b] Controlling for age, sex, education, 7 cognitive tests, and 2 other depression measures.
*p <.05 with no correction for multiple comparisons.
Note: I = Initial, D = Delayed, HDRS = Hamilton Depression Rating Scale.

Table 11

Association between Baseline Predictors and Cognitive Decline among Hispanics Whose Primary Language Is Spanish and Their Matched Whites

	Hispanics (n = 24)		Whites (n = 24)	
Predictor	Partial r	p	Partial r	p
A. Neuropsychological Tests [a]				
Paragraph-Initial	.380	.201	-.298	.323
Paragraph-D	**-.588**	.034	.185	.545
Digit Symbol	.061	.842	.031	.919
Paired Associates-I	.404	.171	.307	.307
Paired Associates-D	-.042	.890	-.519	.069
Vocabulary	-.125	.684	.106	.731
Memory for Designs	-.211	.488	.421	.152
B. Depression [b]				
Work and Activities	.200	.580	**.715**	.020
Retardation	.292	.413	-.477	.163
HDRS-total score	.025	.945	.135	.711

[a] Controlling for baseline GDS, follow-up interval, age, sex, education, and 6 other cognitive tests.
[b] Controlling for age, sex, education, 7 cognitive tests, and 2 other depression measures.
*p <.05 with no correction for multiple comparisons.
Note: I = Initial, D = Delayed, HDRS = Hamilton Depression Rating Scale.

Figure 1

Selection of Study Participants.

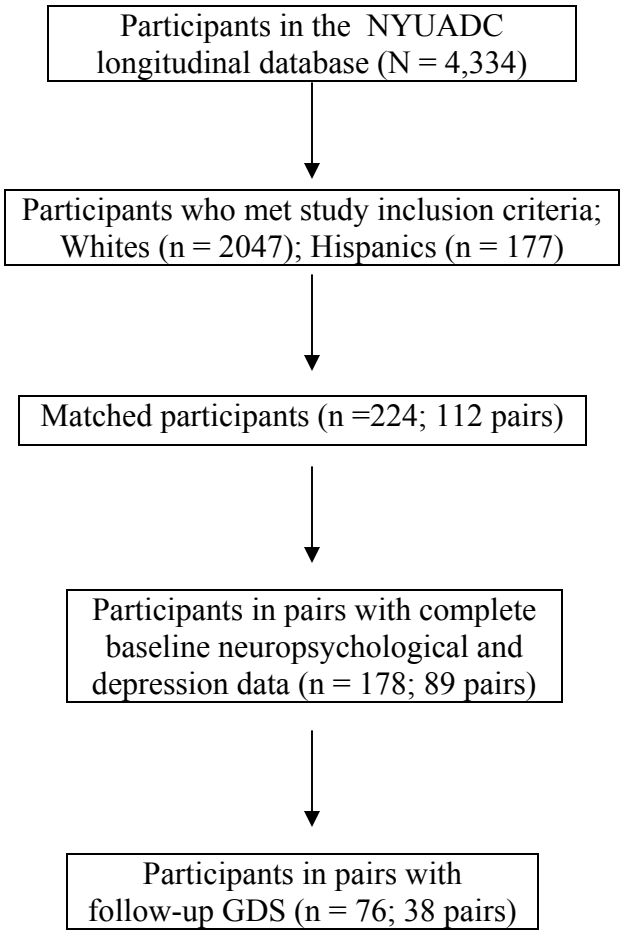


Figure 2. Adjusted mean (±SEM) scores for WAIS-Digit Symbol by primary language and GDS rating.

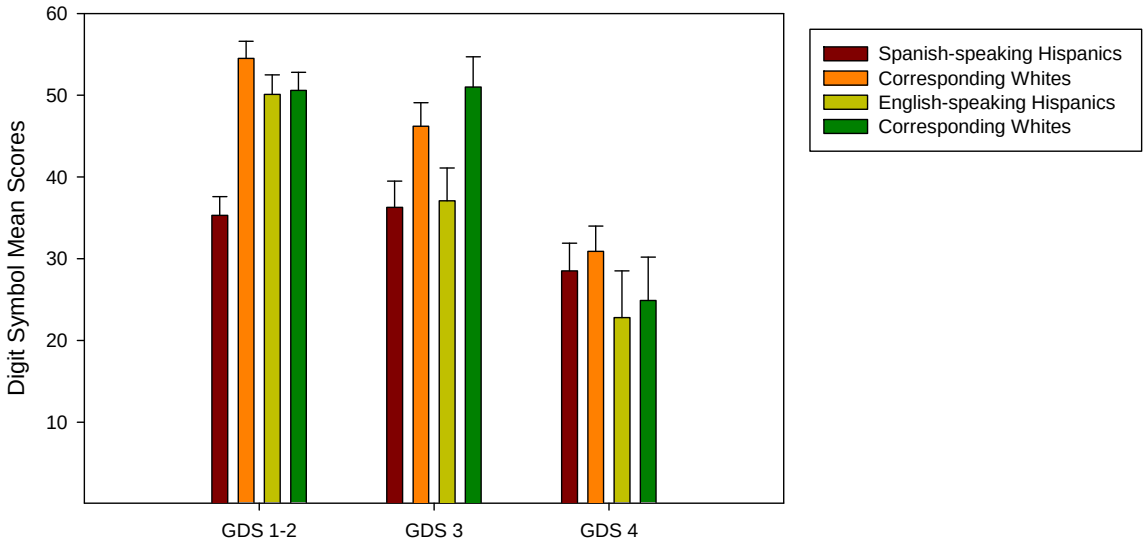


Figure 3. Adjusted mean (±SEM) scores for Retardation by primary language and GDS rating.

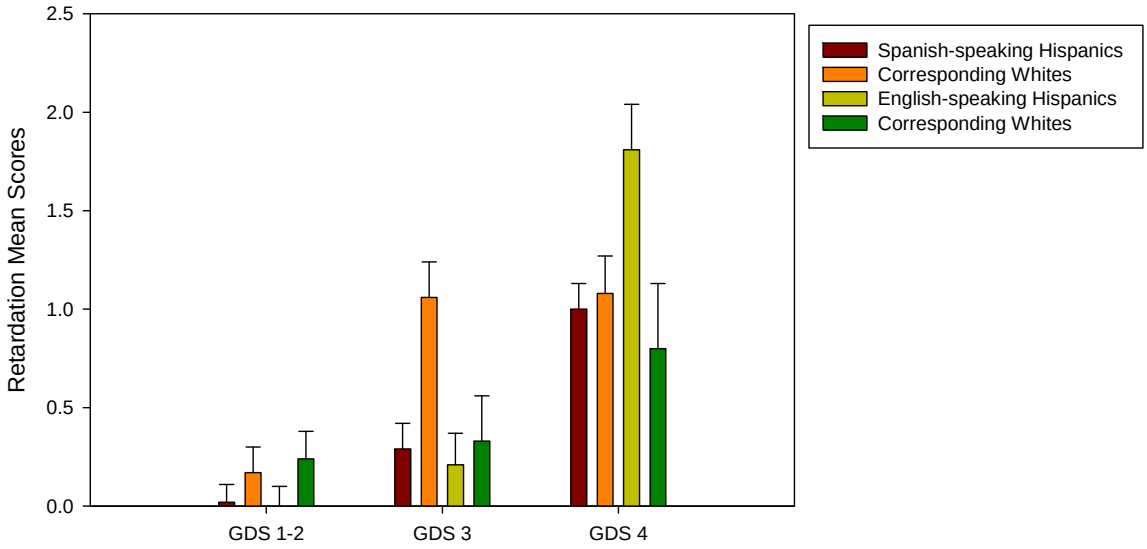
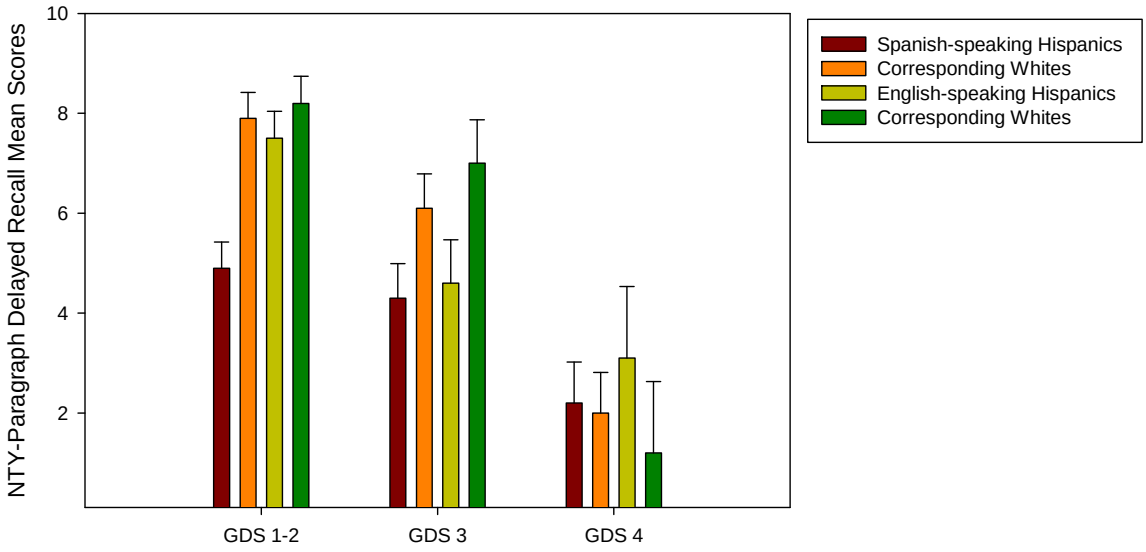


Figure 4. Adjusted mean (±SEM) scores for the NYU-Paragraph delayed recall by primary language and GDS rating.



Appendix A

Association between Baseline Predictors and Baseline GDS 1 -5 among Hispanics and Their Matched Whites

	Hispanics (n = 89)		Whites (n = 89)	
Predictor	Partial r	p	Partial r	p
A. Neuropsychological Tests [a]				
Paragraph-I	**-.567***	<.0005	**-.526***	<.0005
Paragraph-D	**-.531***	<.0005	**-.673***	<.0005
Digit Symbol	**-.529***	<.0005	**-.681***	<.0005
Paired Associates-I	**-.427***	<.0005	**-.552***	<.0005
Paired Associates-D	**-.411***	<.0005	**-.570***	<.0005
Vocabulary	**-.334***	.002	**-.535***	<.0005
Memory for Designs	**-.404***	<.0005	**-.557***	<.0005
B. Depression [b]				
Work and Activities	**.446***	<.0005	**.366***	.001
Retardation	**.637***	<.0005	**.226***	.045
HDRS-total score	**.347***	.002	**.378***	.001

[a] Controlling for age, sex, and education.
[b] Controlling for age, sex, education, and 7 cognitive tests.
*Significant at .05 by Holm multiple comparison procedure.
Note: I = Initial, D = Delayed, HDRS = Hamilton Depression Rating Scale.

Appendix B
Association Between Baseline Predictors and Baseline GDS (1 -5) among Hispanics and Their Corresponding Whites

	Spanish Match (n = 56)				English Match (n = 33)			
	Hispanics		Whites		Hispanics		Whites	
Predictor	Partial *r*	*p*	Partial *r*	*p*	Partial *r*	*p*	Partial *r*	*p*
A. Neuropsychological Tests [a]								
Paragraph-I	**-.574***	<.0005	**-.611***	<.0005	**-.531***	.003	-.353	.056
Paragraph-D	**-.473***	<.0005	**-.834***	<.0005	**-.559***	.001	**-.366**	.047
Digit Symbol	**-.401***	.003	**-.787***	<.0005	**-.670***	<.0005	**-.464**	.010
Paired Associates-I	**-.430***	.001	**-.629***	<.0005	-.349	.059	-.331	.074
Paired Associates-D	**-.342***	.012	**-.655***	<.0005	**-.425**	.019	**-.407**	.026
Vocabulary	**-.365***	.007	**-.613***	<.0005	-.248	.186	-.300	.107
Memory for Designs	**-.451***	.001	**-.676***	<.0005	-.292	.118	-.260	.166
B. Depression [b]								
Work and Activities	**.430***	.003	.109	.471	**.477***	.022	.339	.113
Retardation	**.675***	<.0005	.269	.071	**.575***	.004	.200	.360
HDRS-total score	**.321***	.030	.178	.238	**.456***	.029	**.490**	.018

[a] Controlling for age, sex, education.
[b] Controlling for age, sex, education, and 7 cognitive tests.
*Significant at .05 by Holm multiple comparison procedure.
Note: I = Initial, D = Delayed, HDRS = Hamilton Depression Rating Scale.

Appendix C

Mean (*SEM*) Baseline Performance among Hispanics and Their Corresponding Whites, according to the Primary Language of the Hispanic Participant

	Spanish (*n* = 51 pairs)			English (*n* = 33 pairs)		
	n	Hispanics	Whites	*n*	Hispanics	Whites
A. Neuropsychological Tests						
Paragraph-I						
GDS 1-2	26	4.4 (.38)	7.1 (.52)	21	5.8 (.39)	6.5(.54)
GDS 3	13	3.9 (.51)	5.6 (.70)	8	3.5 (.65)	4.8 (.23)
GDS 4	12	2.5 (.55)	3.2 (.75)	4	2.3 (.93)	4.4 (1.3)
Paragraph-D						
GDS 1-2	26	5.0 (.51)	7.9 (.54)	21	7.5 (.53)	8.1 (.57)
GDS 3	13	4.3 (.69)	6.2 (.74)	8	4.6 (.87)	6.9 (.93)
GDS 4	12	2.6 (.73)	1.7 (.79)	4	2.4 (1.2)	3.7 (1.3)
WAIS-Digit Symbol						
GDS 1-2	26	35.3 (2.3)	54.5 (2.1)	21	50.1 (2.4)	50.6 (2.2)
GDS 3	13	36.3 (3.2)	46.2 (2.9)	8	37.1 (4.0)	51.0 (3.7)
GDS 4	12	28.5 (3.4)	30.9 (3.1)	4	22.8 (5.7)	24.9 (5.3)
Paired Associates-I						
GDS 1-2	26	3.3 (.35)	4.6 (.42)	21	3.8 (.37)	4.7 (.44)
GDS 3	13	2.9 (.48)	3.3 (.58)	8	3.7 (.60)	3.9 (.73)
GDS 4	12	2.0 (.51)	1.4 (.62)	4	.99 (.87)	2.6(1.0)

Paired Associates-D						
GDS 1-2	26	3.1 (.37)	4.9 (.47)	21	4.3 (.39)	5.1 (.49)
GDS 3	13	3.3 (.51)	3.6 (.64)	8	3.7 (.64)	3.8 (.80)
GDS 4	12	1.9 (.54)	1.0 (.68)	4	1.1 (.92)	1.8 (1.2)
WAIS-Vocabulary						
GDS 1-2	26	55.9 (2.5)	69.0 (2.5)	21	59.4 (2.6)	67.3 (2.6)
GDS 3	13	47.1 (3.4)	59.6 (3.4)	8	50.9 (4.3)	65.7 (4.3)
GDS 4	12	50.9 (3.6)	54.1 (3.6)	4	49.9 (6.1)	53.5 (6.1)
Memory for Designs						
GDS 1-2	26	4.8 (.43)	5.7 (.43)	21	4.8 (.45)	5.2 (.44)
GDS 3	13	4.0 (.58)	4.6 (.58)	8	4.1 (.74)	6.0 (.73)
GDS 4	12	3.0 (.62)	2.3 (.62)	4	2.9 (.1.1)	1.8 (1.1)
B. Depression Measures						
Work and Activities						
GDS 1-2	26	.33 (.16)	.37 (.21)	21	.14 (.17)	.43 (.22)
GDS 3	13	.46 (.22)	1.24 (.29)	8	.60 (.28)	1.16 (.36)
GDS 4	12	1.42 (.24)	2.02 (.31)	4	2.41 (.40)	1.22 (.52)
Retardation						
GDS 1-2	26	.02 (.09)	.17 (.13)	21	.00 (.10)	.24 (.14)
GDS 3	13	.29 (.13)	1.06 (.18)	8	.21 (.16)	.33 (.23)
GDS 4	12	1.00 (.13)	1.08 (.19)	4	1.81 (.23)	.80 (.33)
HDRS-total score						
GDS 1-2	26	4.84 (.87)	2.21 (.67)	21	2.40 (.90)	2.23 (.70)
GDS 3	13	5.30 (1.8)	7.77 (.92)	8	5.70 (1.49)	5.59 (1.15)
GDS 4	12	7.34 (1.26)	6.56 (.98)	4	11.06 (2.14)	6.32 (1.66)

Note: *Mean* (*SEM*) based on analysis of covariance controlling for age, sex, and education.

Appendix D

HAMILTON PSYCHIATRIC RATING SCALE FOR DEPRESSION

For each item select the one "answer" which best characterizes the patient and check the corresponding numbered box.

1. DEPRESSED MOOD (Sadness, hopeless, worthless)

0 = Absent.
1 = These feeling states indicated only on questioning.
2 = These feeling states spontaneously reported verbally.
3 = Communicates feeling states non-verbally - i.e., through facial expression, posture, voice, and tendency to weep.
4 = Patient reports VIRTUALLY ONLY these feeling states in his spontaneous verbal and non-verbal communication.

0	1	2	3	4

2. FEELINGS OF GUILT

0 = Absent.
1 = Self reproach, feels he has let people down.
2 = Ideas of guilt or rumination over past errors or sinful deeds.
3 = Present illness as a punishment. Delusions of guilt.
4 = Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations.

0	1	2	3	4

3. SUICIDE

0 = Absent.
1 = Feels life is not worth living.
2 = Wishes he were dead or any thoughts of possible death to self.
3 = Suicide ideas or gesture.
4 = Attempts at suicide (any serious attempt rates 4).

0	1	2	3	4

4. INSOMNIA EARLY

0 = No difficulty falling asleep.
1 = Complains of occasional difficulty falling asleep - i.e., more than 1/2 hour.
2 = Complains of nightly difficulty falling asleep.

0	1	2

5. INSOMNIA MIDDLE

0 = No difficulty.
1 = Patient complains of being restless and disturbed during the night.
2 = Waking during the night - any getting out of bed rates 2 (except for purposes of voiding).

0	1	2

6. INSOMNIA LATE

0 = No difficulty.
1 = Waking in early hours of the morning but goes back to sleep.
2 = Unable to fall asleep again if he gets out of bed.

0	1	2

7. WORK AND ACTIVITIES

0 = No difficulty.
1 = Thoughts and feelings of incapacity, fatigue or weakness related to activities; work or hobbies.
2 = Loss of interest in activity; hobbies or work - either directly reported by patient, or indirect in listlessness, indecision and vacillation (feels he has to push self to work or activities).
3 = Decrease in actual time spent in activities or decrease in productivity. In hospital, rate 3 if patient does not spend at least 3 hours/day activities (hospital job or hobbies) exclusive of ward chores.
4 = Stopped working because of present illness. In hospital, rate 4 if patient engages in no activities except ward chores, or if patient fails to perform ward chores.

0	1	2	3	4

8. RETARDATION (Slowness of thought and speech; impaired ability to concentrate; decreased motor activity)

0 = Normal speech and thought.
1 = Slight retardation at interview.
2 = Obvious retardation at interview.
3 = Interview difficult.
4 = Complete stupor.

0	1	2	3	4

9. AGITATION

0 = None.
1 = "Playing with" hands, hair, etc.
2 = Hand wringing, nail biting, hair pulling, biting of lips.

0	1	2

10. ANXIETY PSYCHIC

0 = No difficulty.
1 = Subjective tension and irritability.
2 = Worrying about minor matters.
3 = Apprehensive attitude apparent in face or speech.
4 = Fears expressed without questioning.

0	1	2	3	4

11. ANXIETY SOMATIC

0 = Absent
1 = Mild
2 = Moderate
3 = Severe
4 = Incapacitating

Physiological concomitants of anxiety, such as: Gastro-intestinal-dry mouth, wind, indigestion, diarrhea, cramps, belching, headaches, cardio-vascular-palpitations, urinary frequency, respiratory-hyperventilation, sighing, sweating.

0	1	2	3	4

12. SOMATIC SYMPTOMS GASTROINTESTINAL

0 = None.
1 = Loss of appetite but eating without staff encouragement. Heavy feelings in the abdomen.
2 = Difficulty eating without staff urging. Requests or requires laxatives or medication for bowels or medication for G.I. symptoms.

0	1	2

13. SOMATIC SYMPTOMS GENERAL

0 = None.
1 = Heaviness in limbs, back of head. Backaches, headaches, muscle aches. Loss of energy and fatigability.
2 = Any clear-cut symptom rates 2.

0	1	2

14. GENITAL SYMPTOMS

0 = Absent
1 = Mild
2 = Severe

Symptoms such as: loss of libido, menstrual disturbances.

0	1	2

15. HYPOCHONDRIASIS

0 = Not present.
1 = Self-absorption (bodily).
2 = Preoccupation with health.
3 = Frequent complaints, requests for help, etc.
4 = Hypochondriacal delusions.

0	1	2	3	4

16. LOSS OF WEIGHT Rate either A or B

A. When Rating By History:

NOTE: RATE ACCORDING TO "A" AT FIRST VISIT, AND "B" AT OTHER VISITS.

0 = No weight loss.
1 = Probable weight loss associated with present illness.
2 = Definite (according to patient) weight loss.

0	1	2

B. On Weekly Ratings By Ward Psychiatrist, When Actual Weight Changes Are Measured:

0 = Less than 1 lb. weight loss in a week.
1 = Greater than 1 lb weight loss in a week.
2 = Greater than 2 lb weight loss in a week.

17. INSIGHT

0 = Acknowledges being depressed and ill.
1 = Acknowledges illness but attributes causes to bad food, climate, overwork, virus, need for rest, etc.
2 = Denies being ill at all.

0	1	2

18. DIURNAL VARIATION

a. Note whether symptoms are worse in the morning or evening. If NO diurnal variation, mark none.

0 = None
1 = Mild
2 = Severe

PLEASE CIRCLE ONE: AM PM

0	1	2

19. DEPERSONALIZATION AND DEREALIZATION

0 = Absent
1 = Mild
2 = Moderate
3 = Severe
4 = Incapacitating

Such as: feelings of unreality, nihilistic ideas.

0	1	2	3	4

20. PARANOID SYMPTOMS

0 = None
1 = Suspicious
2 = Ideas of reference
3 = Delusions of reference and persecution

0	1	2	3

21. OBSESSIONAL AND COMPULSIVE SYMPTOMS

0 = Absent
1 = Mild
2 = Severe

0	1	2

CLINICIAN: _____ TOTAL: _____

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