THE LIMITATIONS OF CURRENT ASSESSMENT METRICS FOR COGNITION IN AGING: LESSONS FROM LONG-TERM CARE

by

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Abstract

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FOR COGNITION IN AGING:

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by

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Objectives

Accurate clinical assessment of disease among the elderly is seriously compromised by the economic constraints imposed by the healthcare system. As a direct result of limited reimbursement, many clinicians rely on quickly administered metric instruments which do not accurately adjust for the high prevalence of physical disabilities. The elderly are the fastest growing segment of the population, and these constraints have led to high rates of misdiagnoses, resulting in improper patient care, increased healthcare costs, and premature death.

The discriminative ability of the Mini-Mental Status Examination (MMSE), Cambridge Cognitive Examination Motor Examination ($CAMCOG_{ME}$), and the Unified Parkinson's Disease Rating Scale (UPDRS) are evaluated. A memory intervention which accommodates the high prevalence of physical conditions with the goal of improving cognitive function is also evaluated.

Methods

Residents in an urban long-term care facility were studied. Subjects were recruited for multiple studies and depending on the protocol, were administered the MMSE, CAMCOG, Clinical Dementia Rating (CDR), and the $UPDRS_{ME}$. Medical records information was collected on all subjects.

Results

A 97% prevalence rate for motor deficits was observed, with 50% of subjects unable to answer individual questions on the MMSE as a result of non-cognitive related reasons and only 20% were able to be evaluated on all 27 $UPDRS_{ME}$ items. Comparable discriminative ability was found using a 7-item subset of the $UPDRS_{ME}$ and 5 out of 20 MMSE items. The CAMCOG improved sensitivity to isolate cognitive deficits in a number of domains. However, areas such as perception still need to be modified to provide greater discriminative ability. The memory intervention showed improvement across all subjects for multiple areas of cognition.

Conclusions

Changes in healthcare reimbursement have resulted in the continued use of quickly administered metric instruments with decreased discriminative ability. The prevalence of co-morbid conditions has resulted in a bias for these instruments to misdiagnose the elderly

population, resulting in poor patient care, increased healthcare costs, and premature death. The identification of these problems is the first step in improving diagnostic accuracy and the success of any interventions with the growing elderly population, leading to improved patient care and decreased costs for healthcare.

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Introduction

The Limitations of Current Assessment Metrics for Cognition in Aging: Lessons From Long-Term Care

Any successful intervention or treatment strategy requires a successful diagnosis. This has become exceedingly difficult in the case of assessing mild dementia in the frail elderly long-term care (LTC) population. Reasons include coexisting age-related physical impairments, and medically-complex conditions that may bias the clinician to diagnose dementia. Accurate clinical assessment of disease among the elderly has also become seriously compromised by the economic constraints imposed by the healthcare system. As a direct result of limited reimbursement, many clinicians currently rely on quickly administered metric instruments which do not accurately adjust for the high prevalence of physical co-morbid conditions resulting in and increased rate of misdiagnoses among this population.

These factors all interact to obfuscate the diagnostic process. A false positive diagnosis of dementia in the LTC environment triggers differential treatment which is not in the best interest of a Resident (individual living in LTC) over the course of the remainder of their life, altering the level of treatment and care that they receive with regard to medical, social, and environmental support.

It is to be expected that issues, related to assessing Residents, identified in the LTC population will over the upcoming years be similar to those experienced by the

elderly residing in the community. Reasons for this include an increase in life expectancy, and the current movement in healthcare to have older individuals live in the community with increased medical and social support services. Projections for the year 2020 predict that 12 million older Americans will need LTC (American Association of Homes and Services for the Aging, 2007). By the year 2026 the number of Americans over the age of 65 will double and by 2050, 20% of all Americans will be classified as old with those 85 years and older representing a full 5% of the population. These changes can be generalized across multiple ethnic groups. By the year 2030 it is projected that 25% of the US Hispanic population will be aged 80 years or older (U.S. Department of Health and Human Services Administration on Aging, 2006).

Medical advances have resulted in the treatment and stabilization of more complex medical cases, where individuals are maintained with multiple medications with increased risk for side-effects and secondary physical and cognitive symptoms which complicate subsequent diagnoses. In this environment it becomes necessary to review the utility of current assessment strategies and instruments, and to determine the need for new strategies. This need is especially true for a population with increased rates of neurodegenerative diseases and age-related conditions where there may be an interaction between the disorder and increased sensitivity to medications, dementia, risk for falling, impaired ability to report pain, and diagnosis of depression (Espinoza, 2006; Singer & Luxenberg, 2003).

In chapter-1, I examine motor deficits related to this frail elderly population using the Unified Parkinson's Disease Rating Scale Motor Examination ($UPDRS_{ME}$) (Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease, 2003). While a number of alternative versions of the UPDRS exist (Hogan et al., 1999; Marinus et al., 2004; Martignoni, Franchignoni, Pasetti, Ferriero, & Picco, 2003; Martínez-Martín et al., 2005), the $UPDRS_{ME}$ continues to be the most widely used assessment for motor dysfunction. This study represents the first report, that I am aware of, to examine the utility of individual items from the $UPDRS_{ME}$ with the frail elderly.

In chapter-2, I look at the Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975), in this population. This instrument is the most widely used assessment tool in the U.S., for the detection of cognitive deficits. This is due to the quick administration time and psychometric properties which have been tested in a number of populations. It is also used extensively in the LTC environment even though studies have observed that alternative tests may provide better sensitivity and specificity to detect dementia (Kilada et al., 2005).

While it is used predominately as a screening tool, dementia staging cutoff scores have been developed and used by clinicians. I examine whether the instrument is sensitive to age-related physical changes, which may bias the scoring by increasing the number of false positives. There may also be a propensity for clinicians working in the LTC environment to over-emphasize test results from these instruments for the staging of dementia because of the heavy caseloads they manage, in part, based on state mandated

reimbursement guidelines. Clinical services at LTC facilities may also be outsourced to agencies where clinicians have less patient contact and are more reliant on quick and accurate assessment instruments for making diagnostic or healthcare determinations.

In chapter-3, I examine the assessment accuracy and diagnostic discriminative ability of the Cambridge Cognitive Examination (CAMCOG) (Roth, Huppert, Mountjoy, & Tym, 1998) as a cognitive assessment instrument for LTC. It has been shown to be sensitive to early cognitive changes in Alzheimer's disease and Parkinson's disease. It is also a lengthier test which incorporates testing of additional cognitive areas such as remote memory, executive function, and abstract thinking. It has also been shown to be less susceptible to ceiling effects when used with different populations. Another feature of the test, as compared to the MMSE, is that domains are tested using multiple types of stimuli. Surprisingly, while used frequently in other countries, it has not been adopted in this country. We were interested in whether the test is appropriate with this population as an assessment instrument, and whether we could differentiate Alzheimer's and Parkinson's disease diagnostic groups from frail elderly control subjects.

In chapter-4, a status report of a memory enhancement study is presented which was developed for use with LTC residents with mild cognitive impairment. Interventions in this population are becoming increasingly challenging due to the co-morbid conditions and increased frailty of this population. This requires that any successful interventions be relatively short-term in length. In addition, these interventions require that resident involvement be limited to minimize physical exertion. Any successful intervention

would also require that there be flexibility with regard to scheduling. In this chapter we describe and discuss the current status of this intervention meant to improve hippocampal/entorhinal cortex function in a LTC population at risk for developing Alzheimer's disease.

References

American Association of Homes and Services for the Aging. (2007). Aging Services: The Facts.

Espinoza, R. T. (2006). Improving the recognition and management of dementia in long-term care: Obstacles and opportunities. *Journal of the American Medical Directors Association, 7*(2), 128-130.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). 'Mini-Mental State'. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Hogan, T., Grimaldi, R., Dingemanse, J., Martin, M., Lyons, K., & Koller, W. (1999). The Parkinson's disease symptom inventory (PDSI): a comprehensive and sensitive instrument to measure disease symptoms and treatment side-effects. *Parkinsonism & Related Disorders, 5*, 93-98.

Kilada, S., Gamaldo, A., Grant, E. A., Moghekar, A., Morris, J. C., & O'Brien, R. J. (2005). Brief screening tests for the diagnosis of dementia: Comparison with the Mini-Mental State Exam. *Alzheimer Disease and Associated Disorders, 19*(1), 8-16.

Marinus, J., Visser, M., Stiggelbout, A. M., Rabey, J. M., Martínez-Martín, P., Bonuccelli, U., et al. (2004). A short scale for the assessment of motor impairments and disabilities in Parkinson's disease: the SPEC/SCOPA. *Journal of Neurology, Neurosurgery, and Psychiatry, 75*, 388-395.

Martignoni, E., Franchignoni, F., Pasetti, C., Ferriero, G., & Picco, D. (2003). Psychometric properties of the Unified Parkinson's Disease Rating Scale and of the Short Parkinson's Disease Evaluation Scale. *Neurological Science, 24*, 190-191.

Martínez-Martín, P., Benito-Léon, J., Burguera, J. A., Castro, A., Linazasaro, G., Martínez-Castrillo, J. C., et al. (2005). The SCOPA-motor scale for assessment of Parkinson's disease is a consistent and valid measure. *Journal of Clinical Epidemiology, 58*, 674-679.

Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease. (2003). The Unified Parkinson's Disease Rating Scale (UPDRS): Status and recommendations. *Movement Disorders, 18*(7), 738-750.

Roth, M., Huppert, F. A., Mountjoy, C. Q., & Tym, E. (1998). *CAMDEX-R: The Cambridge Examination for Mental Disorders of the Elderly*. Cambridge: Cambridge University Press.

Singer, C., & Luxenberg, J. (2003). Diagnosing dementia in long-term care facilities. *Journal of the American Medical Directors Association, Supplement 1, 4*(6), S134-S140.

U.S. Department of Health and Human Services Administration on Aging. (2006). *A statistical profile of Hispanic older Americans aged 65 +*

Chapter 1

Utility of the Unified Parkinson's Disease Rating Scale Motor Examination in the Frail Elderly

Abstract

We identify 7 items from the Unified Parkinson's Disease Rating Scale Motor Examination that are particularly useful in assessing motor function in the frail elderly. We studied 198 long-term care residents living in a metropolitan area nursing home. Residents were identified as elderly controls, presenting with dementia, or Parkinson's disease (PD). Participants were 85.6±8.2 years old, with 12.6±3.4 years of education and 74.7% were female.

The items were comprised of four unilateral upper extremity peripheral signs (Rest Tremor, Action Tremor, Rigidity, and Hand Grip) and three axial signs (Posture, Gait, and Postural Stability). Using a series of stepwise logistic regression models we observed that these items provide the same sensitivity and specificity as the entire 27-item section.

We also observed that while bradykinesia is a hallmark symptom of PD it was found to be less useful with this population and that 97% of our sample exhibited at least mild deficits on one or more of these items.

We conclude that the 7 items isolated are as useful in assisting in the rating and diagnosis of motoric deficits in the frail elderly as the entire motor examination. The use of this abbreviated set of items may provide a faster, accurate, method for clinicians working with the frail elderly.

Introduction

The Unified Parkinson's Disease Rating Scale (UPDRS) has gained wide acceptance and remains one of the most frequently used rating instruments. The motor subsection of this instrument ($UPDRS_{ME}$) is used in both clinical and research settings to assess and follow the severity of motor signs. Originally, it was developed predominately as an assessment scale to monitor Parkinson's disease (PD) related disabilities and impairments (Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease, 2003). Currently, it is also used to assess motor function in diseases such as Progressive Supranuclear Palsy (Cubo et al., 2000), Alzheimer's disease (Sabbagh et al., 2005) and motor function in the community dwelling elderly(Louis, Tang, & Mayeux, 2004). With time, its use has expanded to the role of a diagnostic tool for assessing diseases such as PD or Parkinsonism and the severity of their hallmark motoric manifestations (Racette et al., 2006).

Reasons for the frequent use of this instrument include the brief administration time and the inclusion of non-motor related measures. These additional sections include Mentation, Behavior and Mood, Activities of Daily Living, and Complications, which are considered more cursory with the need for supplementary instruments to augment any assessments (Ramaker, Marinus, Stiggelbout, & Van Hilten, 2002).

The consistent use of this instrument has led to a relatively well defined review of its metric properties (Martínez-Martín et al., 1994; Metman et al., 2004; Movement

Disorders Society Task Force on Rating Scales for Parkinson's Disease, 2003; Ramaker et al., 2002; Richards, Marder, Cote, & Mayeux, 1994; Siderowf et al., 2002). While these studies have supported the use of the UPDRS, they have also resulted in the instrument being used by clinicians in populations where both the metric as well as clinical properties of the instrument were not tested and are not fully understood. Assessment strategies have also been applied inconsistently across study sites to compensate for these problematic issues (Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease, 2003).

While the $UPDRS_{ME}$ has been used and shown to be appropriate in younger and healthier populations with PD. It has not been examined with regard to the frail elderly nursing home (NH) population where there is an increased frequency of related co-morbidities, and polypharmacy, with associated rates of 5% reported for idiopathic PD and 7% for parkinsonism (Lapane, Fernandez, Friedman, & Group, 1999; Tse et al., 2006). These considerations emphasize a need to examine the $UPDRS_{ME}$ with regard to reliability and utility within this population especially as the age of the general population increases with the advent of new medical treatments.

In the current study we address the utility of individual $UPDRS_{ME}$ items with the primary goal of isolating those items that are useful in assessing the frail elderly. We further examine the sensitivity and specificity of these items within frail elderly subgroups known to exhibit increasing levels of motoric change commonly assessed within the community.

Materials and Methods

This study was conducted as part of the Leir Foundation Parkinson's Disease Study at the Jewish Home & Hospital Lifecare System (JHHLCS). The JHHLCS is the largest non-profit long-term care facility in the United States. This study was approved by the JHHLCS and Mount Sinai School of Medicine Institutional Review Boards.

Assessments

All participants were administered the UPDRS (Fahn, Elton, & Committee, 1987) and Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) by a study coordinator trained by both a senior tester and neurologist trained in movement disorders. Both the senior tester and neurologist had extensive experience with the long-term care population at our facility. Basic demographic information was also collected.

The $UPDRS_{ME}$ followed the scoring range of 0-4 with .5 increments allowed. Higher scores for each item signified greater impairment. Items were not scored if they were related to a pre-existing condition such as stroke or osteoarthritis. This is a conservative approach and has been utilized in other studies (Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease, 2003). We did not control for time of Carbidopa/Levodopa administration in the PD group. All assessments were done on-state. Stebbins, Goetz, Lang, and Cubo, (1999) reported comparable internal factor structure and internal consistency between on- and off-state examinations.

MMSE items affected by pre-existing physical conditions (i.e., praxis) were not scored. Lower scores for each item signified greater impairment.

Subjects

Participants were categorized into the following subgroups:

1. Frail Elderly Control Group (FECTL). This group is representative of an older non-demented population. Subjects were assigned to this group when they met the following criteria: MMSE score $\geq$ 24, no current or prior diagnosis of PD or Parkinsonism, and no Carbidopa/Levodopa use. In addition, a complete, or partial, $UPDRS_{ME}$ must have been available. A partial $UPDRS_{ME}$ requires that 85% or 23/27 items were able to be evaluated.
2. Frail Elderly Dementia group - mixed (FEDEM). This group represents a dementia group with mixed etiologies. We have defined a mixed dementia group because this best defines the ability to determine the etiology of the disease in the community residing frail elderly as well as those in the nursing home (NH). Studies in the NH have relied on this strategy for the measurement of other behavioral related assessments (Rabinowitz et al., 2005). FEDEM assignment required a MMSE score < 24, and a prior clinical diagnosis of dementia. We restricted selection to participants with a completed MMSE, in order to eliminate bias attributable to co-morbidities which may have lowered the score due to non-

cognitive related causes. In addition, no current or prior diagnosis of PD or Parkinsonism, and no Carbidopa/Levodopa use. In addition, a complete, or partial, $UPDRS_{ME}$ must have been available.

3. Frail Elderly Parkinson's Disease group (FEPD). This group represents PD in the NH population. FEPD group assignment required a clinical diagnosis of Parkinson's disease and current use of Carbidopa/Levodopa. The MMSE was not a criterion for selection. This was due to sample size, and also to improve the comparability of this group for assessment and treatment with community dwellers. In addition, a complete, or partial, $UPDRS_{ME}$ must have been available.

Statistical Analysis

We observed that many of the $UPDRS_{ME}$ item distributions were skewed. When using parametric tests that could be affected by the irregularity of the distribution we also conducted a non-parametric equivalent. We did not observe any differences in significance values and only report the results from the parametric tests. All statistical analyses were conducted using the Statistical Package for Social Science (SPSS for Windows(Ver. 14.0.2)).

Results

Subject Selection

During the entire study we assessed 741 residents. Records were reviewed retrospectively and the application of the group inclusion and categorization criteria resulted in a total of 323 residents being isolated for participation (see Table 1).

Subjects were categorized based on the total number of $UPDRS_{ME}$ items scored. We observed that only 19.8% of subjects were able to be scored on the entire 27 $UPDRS_{ME}$ items. We restricted study inclusion to subjects with ratings on a minimum of 23 out of 27 items (85%). This was done to limit the analysis to subjects that did not have a non-movement related concomitant disorder that might affect the $UPDRS_{ME}$ ratings. Applying this cutoff resulted in a total of 198 subjects being selected for subsequent analyses (see Table 2).

We examined the comparability of demographic variables between the two samples. The only difference we observed was an increase in the score on the MMSE by 2 points in the selected sample group (n=198) ($t(284) = -2.4$, $p<.05$). However, the relative between group standing of the mean scores for this item remained identical to the scores in the larger group (n=323). Based on these findings we limited all subsequent analyses to the smaller sample.

Before proceeding with subsequent analyses we computed the mean for each $UPDRS_{ME}$ item and substituted the group mean for each missing value. An item by item analysis confirmed that there were no differences between sample group means after applying the substitution. There were also no statistically significant differences between these sample groups for $UPDRS_{ME}$ item means (see Table 3).

Demographics

Age for the FEDEM group was higher with a mean of 87.5 years as compared to 83.4 years in the FECTL and FEPD groups ($p \leq .01$ and $p \leq .05$, respectively). Education level was similar across groups. We observed that the MMSE was statistically different for each of the groups with the FECTL showing the highest level of cognitive performance (p's $\leq .001$). We also observed that while all groups were comprised primarily of females, the FEDEM group had the highest percentage with 83.2% followed by the FECTL and FEPD groups with 69.4% and 55.2%, respectively. These differences were significant between the FECTL and FEDEM groups (X^2 (1)=4.4, $p \leq .05$) and the FEPD and FEDEM groups (X^2 (1)=10.2, $P \leq .001$). Ethnicity did not differ across groups.

Age and the $UPDRS_{ME}$

Because of the observed between group differences for the demographic variables of age and gender we examined whether these variables were related to the $UPDRS_{ME}$ items. Because of the number of correlations we only considered items that were

statistically significant at the $p \leq .001$ level. We observed that none of the individual items were correlated with age or gender.

$UPDRS_{ME}$ Item Selection

Stage-1

The first objective was to examine the classification accuracy of items within, and between, each subgroup of frail elderly in this sample. It could be expected that the FEDEM group would suffer from a greater degree of impairment when compared to the FECTL group and the FEPD group would be the most severely impaired. When we examined the mean and standard deviation of $UPDRS_{ME}$ items this was the general pattern observed (see Table 4).

We conducted three comparisons contrasting the FECTL with FEDEM group, FECTL with FEPD group, and the FEDEM with the FEPD group. We included all 27 items in a logistic regression model using the forward stepwise variable entry method with selection criteria based on the likelihood ratio statistic. We isolated the items that entered into each model and provided a stable result based on a comparison of the standard error measures for each item at each step. When the standard error exceeded the value from the previous step by a value of 1000 we considered the model to be unstable and would choose the previous step as the final stopping point (see Table 5).

High overall accuracy rates were observed for both the FECTL and FEDEM groups when compared with the FEPD group (93.5% and 95.3%, respectively). In these models we observed lower rates of accuracy for the FEPD group. In the model contrasting FECTL with FEPD we accurately predicted 72.4% of cases. When contrasted with FEDEM 75.9% of the cases were correctly classified. The lowest classification accuracies occurred for the contrast between the FECTL and FEDEM groups with an overall accuracy of 75.1%. We accurately classified 83.2% of the FEDEM subjects, with only 61.3% of FECTL cases correctly identified.

Stage-2

In Stage-2, we selected the first 4 items that loaded into each of the three models (for the comparison between FECTL and FEDPD there were only 3 items). When analyses were restricted to these items, compared to all items identified in Stage-1, comparable sensitivity and specificity measures were observed.

Next we combined the items from each of the comparisons. Once accounting for overlap we derived a set of 7 items. The items were Rest Tremor-Right Upper Extremity(RUE), Action Tremor-RUE, Rigidity-RUE, Hand Grips-Right, Posture, Gait, and Postural Stability. We observed that overall accuracy rates for the models were 74.6 % between FECTL and FEDEM groups, with sensitivity for the prediction of FECTL at 58.1% and predictive accuracy for FEDEM at 84.1%. In the second model comparing the FECTL and FEPD groups, overall accuracy was 89.0%. Sensitivity for the FECTL

and FEPD groups was 93.5% and 79.3% respectively. In the final comparison between FEDEM and FEPD accuracy was 74.6%. We observed that sensitivity to predict the FEDEM group was 58.1% while specificity or accuracy to predict the FEPD group was acceptable at 84.1%.

Finally, we contrasted the specificity and sensitivity of these 7 items with the larger set of items identified in Stage 1. We repeated each group comparison and entered the 7 items in step-1 followed by all additional items, in Step-2. We observed that the additional items did not significantly add to the accuracy rates.

Discussion

While a number of alternative versions of the UPDRS exist (Hogan et al., 1999; Marinus et al., 2004; Martignoni, Franchignoni, Pasetti, Ferriero, & Picco, 2003; Martínez-Martín et al., 2005), the $UPDRS_{ME}$ continues to be the most widely used assessment for motor dysfunction. This study represents the first report that we are aware of which examines the utility of specific items from the $UPDRS_{ME}$ with the frail elderly. When compared to previous studies on the $UPDRS_{ME}$, in PD, our population is approximately 16 years older. They are also approximately 5 years older than previous studies examining the prevalence of parkinsonian signs among the elderly in the community (Louis et al., 2004; Louis, Tang, & Mayeux, 2005). Based on our sample we isolated a subset of 7 $UPDRS_{ME}$ items statistically comparable to the original 27 items in

the instrument. The items are Rest Tremor-RUE, Action Tremor-RUE, Rigidity-RUE, Hand Grips-Right, Posture, Gait, and Postural Stability.

These 7-items provide good to excellent overall accuracy. However, similar to the entire 27-item $UPDRS_{ME}$ we do observe low sensitivity between the FECTL and FEDEM group at only 58.1% accuracy. With the high sensitivity in the PD group this low value suggests that, in general, $UPDRS_{ME}$ items are more sensitive to movement function related to PD versus that of dementia.

We also recognize that the 4 peripheral items identified are isolated to the upper right extremity. This suggests that for the purpose of assessment in the frail elderly we need to account for the fact that many patients are wheelchair bound, or have limited lower body extremity ability, that may make the diagnostic use of lower body signs less sensitive. Also, approximately 90% of the population is dominant for the right side and compromised dominance may result in classification of frailty for this sample. This may also explain why bradykinesia, while a hallmark for PD, was not included in our 7 items. It was also not correlated with age which was surprising given the data available showing a relationship between age, movement disorders, and cognition (Li & Lindenberger, 2002; Pillon, Dubois, & Agid, 1996). A probable explanation for this is the frequency of co-morbidities which induce general slowness combined with an initial bias related to the decision process for selecting the NH.

As expected we observed a higher rate of movement deficits in our frail elderly sample compared to other studies that have reported a prevalence of up to 40.1% for parkinsonian signs in the elderly when using an abbreviated 10-item UPDRS (Louis et al., 2004). When we examined the prevalence of these 10 items across all study groups in our sample we observed an incidence rate of 66.2% for moderate to severe deficits ($UPDRS_{ME}$ score ≥ 2), and 74.7% of subjects showing mild deficits on at least one item ($UPDRS_{ME}$ item score = 1.0-1.5). While the prevalence observed in this sample is significantly higher than in previous reports, it represents a conservative estimate in that we did not score individual items when a deficit was clearly attributable to an etiology such as stroke or osteoarthritis. For the 7 items we observed a prevalence of 91.4% for moderate-severe and 97.0% for mild-severe deficits. The more salient items added to our set were Action Tremor, Hand Grips, Gait and Postural Stability. We also incorporate laterality into our analysis. In other studies it is assumed that deficits on both sides of the body are highly correlated across the entire sample. We observed that the strongest correlations between right and left side of the body, as interpreted by R^2, existed in the FECTL group. In this group the average correlation accounted for approximately 61% of the shared variance. In the FEDEM group this was reduced to 21%. In the FEPD group only the upper extremity items where correlated accounting for 49% or the shared variance between the two items. This suggests that while the items are correlated it is not uniform across the entire sample and may be mitigated by disease.

While we were not able to report on the side of onset for motor symptoms in these subjects. A previous study has observed differences in the severity of cognitive deficits

related to the side of onset for patients with idiopathic PD (Tomer, Levin, & Weiner, 1993). In that study PD patients with left side onset performed consistently worse on different tests of cognition which included memory, language, visuospatial ability, attention, and set shifting. It is possible that subjects in our study may have had a higher degree of left side onset. This may have resulted in a greater degree of dementia leading to a greater difficulty in attributing specific motoric deficits to appropriate etiologies versus co-morbidities. A second question that exists is whether similar results would be observed for non PD participants who present clinically with initial left sided motoric deficits. We hope to report on this in the future, giving us a better understanding of the relationship between these motoric changes and the neural pathways involved in both the PD and Non-PD observations reported in this study.

We plan to examine these issues further and hope that these findings will lead to future studies by other clinical and research facilities. We also hope that it will underscore the importance of this population for future studies related to aging, as the lifespan of the general population increases.

Table 1

Demographic Distribution of Groups (n = 323)

Group	N	Mean Age	Mean Ed Level	Mean MMSE	% Female	% White	% Black
FECTL	107	82.0±8.8	13.3±2.6[a]	26.6±1.9	70.1	78.5	12.1
FEDEM	179	87.3±7.4	12.3±3.6[b]	8.4±7.0	82.7	61.5	22.3
FEPD	37	83.7±6.8	12.7±2.8[c]	17.8±8.6	56.8	75.7	13.5

[a] Based on n= 90; [b] Based on n=146; [c] Based on n= 27

Table 2

Demographic Distribution of Groups (n=198)

Group	N	Mean Age	Mean Ed Level	Mean MMSE	% Female	% White	% Black
FECTL	62	83.4±8.5	13.1±2.5[a]	26.6±2.1	69.4	77.4	11.3
FEDEM	107	87.5±7.9	12.3±3.9[b]	10.4±6.5[+]	83.2	62.6	22.4
FEPD	29	83.4±7.2	12.7±3.1[c]	19.3±7.1	55.2	75.9	13.8

[a] Based on n= 53; [b] Based on n=87; [c] Based on n= 21

[+] Statistically different from FEDEM in larger group (n=323) p<.05

Table 3

$UPDRS_{ME}$ Item Distribution Between Samples (Mean ±Standard deviation)

$UPDRS_{ME}$ Item	**N = 323**		**N = 198**	
	n	**Mean(±SD)**	**n**	**Mean(±SD)**
Speech	307	0.66(±0.94)	195	0.57(±0.86)
Facial Expression	321	0.58(±0.97)	198	0.45(±0.84)
Resting Tremor – H/N	322	0.09(±0.36)	198	0.07(±0.26)
Resting Tremor - RUE	312	0.22(±0.58)	198	0.22(±0.58)
Resting Tremor - LUE	309	0.18(±0.50)	198	0.19(±0.50)
Resting Tremor - RLE	308	0.02(±0.19)	198	0.01(±0.11)
Resting Tremor - LLE	304	0.12(±0.15)	198	0.01(±0.05)
Action Tremor - RUE	285	0.36(±0.72)	198	0.35(±0.71)
Action Tremor - LUE	276	0.32(±0.64)	197	0.30(±0.63)
Rigidity – Neck	294	0.68(±1.12)	197	0.50(±0.98)
Rigidity – RUE	296	0.57(±0.95)	198	0.39(±0.74)
Rigidity – LUE	290	0.59(±0.99)	198	0.39(±0.76)
Rigidity – RLE	269	0.78(±1.10)	198	0.59(±0.94)
Rigidity – LLE	261	0.79(±1.15)	198	0.60(±0.98)
Finger Taps – Right	255	0.57(±0.92)	198	0.58(±0.95)
Finger Taps - Left	244	0.59(±0.95)	196	0.61(±0.98)
Hand Grips – Right	257	0.56(±0.92)	197	0.58(±0.96)
Hand Grips – Left	247	0.61(±0.97)	196	0.62(±0.97)
Rapid Alt Movement – Right	255	0.69(±0.99)	196	0.73(±1.05)
Rapid Alt Movement – Left	244	0.71(±1.04)	195	0.76(±1.07)
Leg Agility – Right	222	1.01(±1.29)	193	0.94(±1.24)
Leg Agility – Left	217	1.00(±1.23)	194	0.96(±1.20)
Arise from Chair	218	2.50(±1.28)	173	2.26(±1.23)
Posture	188	0.90(±1.08)	154	0.84(±0.99)
Gait	200	2.82(±1.26)	158	2.60(±1.27)
Postural Stability	58	1.49(±1.27)	54	1.42(±1.20)
Body Bradykinesia	225	0.78(±0.95)	168	0.80(±0.97)

H/N = Head/Neck; RUE = Right Upper Extremity; RLE = Right Lower Extremity; LUE = Left Upper Extremity; LLE = Left Lower Extremity

Table 4

Mean± SD by $UPDRS_{ME}$ Item and Group (N=198)

UPDRS Item	Group		
	FECTL n=62	**FEDEM n=107**	**FEPD n=29**
Speech	.38(±0.62)	.72(±1.00)	1.20(±1.12)
Facial Expression	.26(±0.55)	.60(±1.00)	1.40(±1.25)
Resting Tremor – Face	.05(±0.32)	.08(±0.32)	.19(±0.56)
Resting Tremor - RUE	.07(±0.34)	.21(±0.58)	.67(±0.84)
Resting Tremor - LUE	.06(±0.30)	.16(±0.45)	.62(±0.85)
Resting Tremor - RLE	.01(±0.05)	.04(±0.25)	.00(±0.00)
Resting Tremor - LLE	.00(±0.00)	.03(±0.19)	.00(±0.00)
Action Tremor - RUE	.27(±0.69)	.37(±0.73)	.56(±0.74)
Action Tremor - LUE	.23(±0.61)	.34(±0.66)	.47(±0.63)
Rigidity – Neck	.21(±0.59)	.88(±1.24)	1.07(±1.26)
Rigidity – RUE	.15(±0.37)	.69(±1.09)	1.16(±0.85)
Rigidity – LUE	.15(±0.45)	.72(±1.12)	1.15(±1.00)
Rigidity – RLE	.31(±0.66)	.92(±1.21)	1.35(±1.03)
Rigidity – LLE	.38(±0.76)	.89(±1.25)	1.24(±1.17)
Finger Taps – Right	.34(±0.60)	.59(±0.98)	1.24(±1.15)
Finger Taps - Left	.37(±0.74)	.57(±0.96)	1.29(±1.15)
Hand Grips – Right	.24(±0.54)	.64(±0.97)	1.18(±1.19)
Hand Grips – Left	.28(±0.73)	.70(±1.01)	1.16(±1.07)
Rapid Alt Movement – Right	.30(±0.65)	.77(±1.03)	1.53(±1.09)
Rapid Alt Movement – Left	.30(±0.79)	.83(±1.07)	1.42(±1.07)
Leg Agility – Right	.77(±1.14)	.97(±1.35)	1.79(±1.15)
Leg Agility – Left	.67(±1.10)	1.00(±1.27)	1.79(±1.05)
Arise from Chair	2.18(±1.21)	2.62(±1.34)	2.66(±1.05)
Posture	1.05(±0.96)	.60(±0.98)	2.02(±1.03)
Gait	2.33(±1.29)	3.00(±1.23)	2.92(±1.07)
Postural Stability	1.38(±1.10)	1.34(±1.43)	2.05(±1.27)
Body Bradykinesia	.39(±0.60)	.93(±1.04)	1.42(±0.99)

H/N = Head/Neck; RUE = Right Upper Extremity; RLE = Right Lower Extremity; LUE = Left Upper Extremity; LLE = Left Lower Extremity

Table 5

Significant Items and Order of Entry for Logistic Regression Group Comparisons (N=198)

$UPDRS_{ME}$ Item	**FECTL With FEDEM**	**FECTL With FEPD**	**FEDEM With FEPD**
Speech	12		
Facial Expression	24		
Resting Tremor – H/N	19		
Resting Tremor – RUE *	**25**	**3**	**3**
Resting Tremor – LUE	26		
Resting Tremor – RLE	17		
Resting Tremor – LLE	27		
Action Tremor – RUE *	**18**		**4**
Action Tremor – LUE	23		
Rigidity – Neck	10		5
Rigidity – RUE *	**16**	**1**	**2**
Rigidity – LUE	8		
Rigidity – RLE	21		
Rigidity – LLE	11		
Finger Taps – Right	15		
Finger Taps – Left	7		
Hand Grips – Right *	**3**		
Hand Grips – Left	14		
Rapid Alt Movement – Right	22		
Rapid Alt Movement – Left	6		
Leg Agility – Right	5		
Leg Agility – Left	13		
Arise from Chair	20		
Posture *	**1**	**2**	**1**
Gait *	**2**		
Postural Stability *	**4**		**6**
Body Bradykinesia	9		
Sensitivity	61.3%	93.5%	95.3%
Specificity	83.2%	72.4%	75.9%
Overall Accuracy	75.1%	86.8%	91.2%
P	$X^2(27)=68.3$, $p\leq.001$	$X^2(3)=66.0$, $p\leq.001$	$X^2(6)=93.8$, $p\leq.001$

H/N = Head/Neck; RUE = Right Upper Extremity; RLE = Right Lower Extremity; LUE = Left Upper Extremity; LLE = Left Lower Extremity

***** Included in final 7-Item subset of $UPDRS_{ME}$.

References

Cubo, E., Stebbins, G. T., Golbe, L. I., Nieves, A. V., Leurgans, S., Goetz, C. G., et al. (2000). Application of the Unified Parkinson's Disease Rating Scale in Progressive Supernuclear Palsy: Factor analysis of the motor scale. *Movement Disorders, 15*(2), 276-279.

Fahn, S., Elton, R. L., & Committee, M. o. U. D. (1987). Unified Parkinson's disease rating scale. In S. Fahn, C. D. Marsden & D. B. Calne (Eds.), *Recent Developments in Parkinson's Disease* (Vol. 2, pp. 153-163). Florham Park, NJ: Macmillan Healthcare Information.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). 'Mini-Mental State'. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Hogan, T., Grimaldi, R., Dingemanse, J., Martin, M., Lyons, K., & Koller, W. (1999). The Parkinson's disease symptom inventory (PDSI): a comprehensive and sensitive instrument to measure disease symptoms and treatment side-effects. *Parkinsonism & Related Disorders, 5*, 93-98.

Lapane, K. L., Fernandez, H. H., Friedman, J. H., & Group, S. S. (1999). Prevalence, clinical characteristics, and pharmacologic treatment of Parkinson's disease in residents in long-term care facilities. *Pharmacotherapy, 19*(11), 1321-1327.

Li, K. Z. H., & Lindenberger, U. (2002). Relations between aging sensory/sensorimotor and cognitive functions. *Neuroscience and Biobehavioral Reviews, 26*, 777-783.

Louis, E. D., Tang, M. X., & Mayeux, R. (2004). Factor structure of parkinsonian signs in the community-dwelling elderly. *Movement Disorders, 19*(3), 268-272.

Louis, E. D., Tang, M. X., & Mayeux, R. (2005). Functional correlates and prevalence of mild parkinsonian signs in a community population of older people. *Archives of Neurobiology, 62*, 297-302.

Marinus, J., Visser, M., Stiggelbout, A. M., Rabey, J. M., Martínez-Martín, P., Bonuccelli, U., et al. (2004). A short scale for the assessment of motor impairments and disabilities in Parkinson's disease: the SPEC/SCOPA. *Journal of Neurology, Neurosurgery, and Psychiatry, 75*, 388-395.

Martignoni, E., Franchignoni, F., Pasetti, C., Ferriero, G., & Picco, D. (2003). Psychometric properties of the Unified Parkinson's Disease Rating Scale and of the Short Parkinson's Disease Evaluation Scale. *Neurological Science, 24*, 190-191.

Martínez-Martín, P., Benito-Léon, J., Burguera, J. A., Castro, A., Linazasaro, G., Martínez-Castrillo, J. C., et al. (2005). The SCOPA-motor scale for assessment of Parkinson's disease is a consistent and valid measure. *Journal of Clinical Epidemiology, 58*, 674-679.

Martínez-Martín, P., Gil-Nagel, A., Gracia, L. M., Gómez, J. B., Martínez-Sarriés, J., & Bermejo, F. (1994). Unified Parkinson's disease rating scale characteristics and structure. *Movement Disorders, 9*(1), 76-83.

Metman, L. V., Myre, B., Hassin-Baer, S., Arzbaecher, J., Sierens, D., & Bakay, R. (2004). Test-retest reliability of UPDRS-III, dyskinesia scales, and timed motor tests in patients with advanced Parkinson's disease: An argument against multiple baseline assessments. *Movement Disorders, 19*(9), 1079-1084.

Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease. (2003). The Unified Parkinson's Disease Rating Scale (UPDRS): Status and recommendations. *Movement Disorders, 18*(7), 738-750.

Pillon, B., Dubois, B., & Agid, Y. (1996). Testing cognition may contribute to the diagnosis of movement disorders. *Neurology, 46*(2), 329-334.

Rabinowitz, J., Davidson, M., De Deyn, P. P., Katz, I., Brodaty, H., & Cohen-Mansfield, J. (2005). Factor analysis of the Cohen-Mansfield Agitation Inventory in three large samples of nursing home patients with dementia and behavioral disturbance. *American Journal of Geriatric Psychiatry, 13*(11), 991-998.

Racette, B. A., Tabbal, S. D., Jennings, D., Good, L. M., Permutter, J. S., & Evanoff, B. A. (2006). A rapid method for mass screening for parkinsonism. *NeuroToxicology, 27*, 357-361.

Ramaker, C., Marinus, J., Stiggelbout, A. M., & Van Hilten, B. J. (2002). Systematic evaluation of rating scales for impairment and disability in Parkinson's disease. *Movement Disorders, 17*(5), 867-876.

Richards, M., Marder, K., Cote, L., & Mayeux, R. (1994). Interrater reliability of the Unified Parkinson's Disease Rating Scale Motor Examination. *Movement Disorders, 9*(1), 89-91.

Sabbagh, M. N., Silverberg, N., Bircea, S., Majeed, B., Samant, S., Caviness, J. N., et al. (2005). Is the functional decline of Parkinson's disease similar to the functional decline of Alzheimer's disease? *Parkinsonism & Related Disorders, 11*(5), 311-315.

Siderowf, A., McDermott, M., Kierburtz, K., Blindauer, K., Plumb, S., Shoulson, I., et al. (2002). Test-retest reliability of the Unified Parkinson's Disease Rating Scale in

patients with early Parkinson's disease: Results from a multicenter clinical trial. *Movement Disorders, 17*(4), 758-763.

SPSS for Windows(Ver. 14.0.2).

Stebbins, G. T., Goetz, C. G., Lang, A. E., & Cubo, E. (1999). Factor analysis of the motor section of the Unified Parkinson's Disease Rating Scale during the off-state. *Movement Disorders, 14*(4), 585-589.

Tomer, R., Levin, B. E., & Weiner, W. J. (1993). Side of onset of motor symptoms influences cognition in Parkinson's disease. *Annals of Neurology, 34*, 579-584.

Tse, W., Libow, L. S., Neufeld, R., Lesser, G., Frank, J., Dolan, S., et al. (2006). Prevalence of movement disorders in an elderly nursing home population.

Chapter 2

Utility of the MMSE in Assessing Frail Elderly in Long-Term Care

Abstract

Objective

The purpose of this study was to examine the capability of individual and combined cognitive domain-specific Mini-Mental State Examination items (MMSE) to differentiate long-term care residents with dementia of the Alzheimer's type (DAT) from frail elderly residents without dementia (CTL).

Methods

The MMSE, medical, demographic, and information derived from the government-mandated Minimum Data Set were collected. We identified 134 CTL (M_{age} 84±9) and 216 DAT subjects (M_{age} 87±7), based on a prior clinical diagnosis of Alzheimer's disease and a confirmatory evaluation of dementia. A series of hierarchical logistic regression models were used to determine which patterns of item responses best differentiated the groups.

Results

We observed that 32.8% of all residents approached for assessment were unable to respond to any MMSE items because of non-cognitive related reasons such as stroke and osteoarthritic conditions. An additional 14.9% of CTL subjects were unable to answer specific items, raising the frequency to almost 50%.

The ability of MMSE items to correctly identify CTL subjects (specificity) averaged 11% lower than the correct classification of DAT subjects (sensitivity). Separate analyses for CTL and MILD-DAT groups revealed sensitivity values lower than specificity by approximately 26.4%. We also identified a subset of 5 MMSE items (What Year Is It, What Is The Name Of This Place, What Floor Are We On, Name Wristwatch, and Write Sentence) as predictive as the entire test with specificity and sensitivity, at 80.2% and 86.8% respectively. MMSE items measuring function in subcortical areas of the brain did not differentiate PD from CTL subjects.

Conclusions:

We conclude that while the MMSE is considered an exceptional clinical instrument, it provides an unacceptable level of misclassification, in this population. We strongly recommend development of new assessment instruments specific to this population.

Introduction

The purpose of this study was to determine the potential of individual items of the Mini- Mental State Examination (MMSE), as well as items grouped into specific cognitive domains, to correctly classify patients with dementia of the Alzheimer's type (DAT) from frail elderly individuals (CTL) living in long-term care. While the MMSE was developed as a gross assessment of cognitive function, specific ranges of scores are currently used to assess dementia staging. Because of the increased prevalence of non-cognitively related co-morbid conditions that directly effect the scoring of the MMSE, this test may provide unacceptable levels of false positives for the classification of dementia in this population.

Assessing dementia in the frail elderly long-term care population presents a number of difficulties for the clinician. This is increasingly evident, and problematic, as the age of the general population increases and medical advances allow for the treatment and stabilization of more complex medical cases. As a result, we have observed an increase in the life expectancy rates of the elderly residing in LTC facilities. With time, individuals living in LTC are becoming increasingly representative of the changing demographics of the US population and by the year 2020, 12 million older Americans will need LTC (American Association of Homes and Services for the Aging, 2007). It is projected that by the year 2026 the number of Americans over the age of 65 will double, and by the year 2050, 20% of all Americans will be classified as old with those 85 years and older representing a full 5% of the population. These changes can be generalized

across multiple ethnic groups, with 25% of the U.S. Hispanic population ≥ 80 years by the year 2030 (U.S. Department of Health and Human Services Administration on Aging, 2006). Many of the co-morbid age-related conditions that effect the LTC population will also affect many community-dwelling elderly because of the growing movement in healthcare to keep the elderly in the community, with increased support services. As a direct result, LTC facilities have experienced admissions of older and more medically complex residents, which have made the assessment of cognitive status increasingly difficult. In this environment it becomes necessary to review the utility of current assessment strategies and to determine the need for new strategies. This is especially true for a population with increased rates of neurodegenerative diseases and age-related conditions where there may be interactions between age and the disease state causing increased sensitivity to medications, dementia, risk for falling, impaired ability to report pain, and diagnosis of depression (Espinoza, 2006; Singer & Luxenberg, 2003).

Since the original article by Folstein, Folstein, and McHugh (1975), the MMSE has become the most widely used instrument for screening and assessing cognitive status even though studies have observed that alternative tests may provide better Sensitivity and Specificity (Kilada et al., 2005). It is comprised of questions that measure the cognitive domains of *orientation to time and place*, *registration*, *attention* and *calculation*, *recall*, and *language*. Items have also been grouped into subcortical and cortical domains showing good discriminative ability to differentiate adult patient groups with neurodegenerative diseases (Brandt, Folstein, & Folstein, 1988; Leritz, Brandt, Minor, Reis-Jensen, & Petri, 2000).

Reasons for the extensive use of the instrument include quick administration and good psychometric properties demonstrated across different patient populations. These reasons make the use of the MMSE especially appealing to clinicians working with long-term care populations (LTC) even though few validation studies have been conducted in this setting. Even so, the MMSE has been used for diverse LTC assessment purposes which include decisions for advance care planning (Allen et al., 2003), measuring the relationship of motor impairment to dementia (Camicioli & Licis, 2004), drug studies (Nelson, Hollander, Betzel, Smolen, & Mirtazapine Nursing Home Study Group, 2006), nursing home transition studies (Rosenberg et al., 2006), and issues related to assessing capacity for signed consent (Resnick et al., 2007). The MMSE has also been included in the assessment of cognitive status for both research, and clinical practice, across different ethnic groups (Alvardo-Esquivel et al., 2004; Espino, Lichtenstein, Palmer, & Hazuda, 2001; Evans & Crogan, 2006; Fountoulakis, Tsolaki, Chantzi, & Kazis, 2000; Küçükdeveci, Kutlay, Elhan, & Tennant, 2005; Lou, Dai, Huang, & Yu, 2007; Wood, Giuliano, Bignell, & Pritham, 2006).

The test properties of the MMSE are especially important in the LTC environment where residents (individuals living in LTC) may suffer from multiple co-morbidities resulting in physically frail conditions that make accurate clinical assessments more difficult and lengthy assessments unfeasible. In addition, institutional resources may be limited with increasing reliance on outsourcing for a growing number of clinical responsibilities resulting in less stable treatment teams. This may lead to decreased awareness of behavioral changes in frail residents over time, when changes may be more

difficult to detect because of medical complications and the need for early interventions are more critical. At the same time treatment team members are more reliant on test results from instruments such as the MMSE for assessment.

An additional complication is the prevalence of movement disorders in this population, which affects assessment accuracy and is higher than that of the community dwelling elderly. With the increasing age of the community residing elderly we expect this to increase over the course of the next few years. In a recent study, a prevalence rate of 7% was observed for Parkinsonism in LTC, as compared to 1-3% in the community (Tse et al., In Press), which is similar to previous reports of PD in the nursing home (Lapane, Fernandez, Friedman, & and the SAGE Study Group, 1999). Another study reported a rate of motoric deficits, as measured by the Unified Parkinson's Disease Rating Scale (UPDRS) in this LTC population of 66% for moderate-severe deficits and 75% for mild-severe deficits (Tarshish, Neufeld, & Libow, In-Preparation). This was compared to 40%, for community residing elderly reported by Louis, Tang, & Mayeux (2004), using an abbreviated 10-item version of the UPDRS motor assessment subsection. This high prevalence of motor deficits would directly impact any interpretation of the MMSE in this population because multiple items on the MMSE require physical responses such as writing or drawing.

The lack of validity and reliability studies using the MMSE in the LTC population, and changing resident demographics, such as increased age and complexity of co-morbid medical conditions, all directly effect assessment results and strategies. The

purpose of this study is to examine individual and combined items related to specific cognitive domains on the MMSE for overall classification, Sensitivity and Specificity to discriminate between residents with dementia and those without dementia, respectively, in this frail population with multiple co-morbid conditions. We focus our study of dementia on Alzheimer's disease because it is the most prevalent form of dementia observed in the LTC population. We also identify and examine a subgroup of subjects from our study with Parkinson's disease (PD). This was done to determine whether age-related neurodegenerative diseases with associated progressive physical limitations would bias the MMSE. We would expect these limitations to result in an increase in false positives with LTC residents being incorrectly classified, and ultimately diagnosed, with dementia.

Methods

This study was conducted at the Jewish Home & Hospital Lifecare System (JHHLCS), the largest non-profit academically-affiliated long-term care facility in the United States. This study was approved by the JHHLCS and Mount Sinai School of Medicine Institutional Review Boards.

As part of the study protocol all subjects were administered the MMSE (Folstein, Folstein, & McHugh, 1975). Medical, demographic, and information derived from the Minimum Data Set (MDS) were also collected as part of a systematic chart review, including the Cognitive Performance Scale (CPS) (J. N. Morris et al., 1994). All study

assessments were completed by study coordinators and supervised by a senior tester with extensive experience in the LTC environment.

Statistics

Analyses were done using SPSS for Windows (SPSS for Windows (Release 14.0.2)). For the CPS validation study we computed Pearson r and Spearman Rank-Order Correlation Coefficients.

We computed point-biserial correlations to examine the relationships between dichotomous variables including gender and diagnostic groups. We also used the Student t-test for Independent Means to examine diagnostic group differences for demographic variables. Prior to pooling the variance we computed the Levene's Test for Equality of Variances.

Hierarchical Logistic Regression Models were used to compute the probabilities for MMSE Item(s) to differentiate group membership. This was computed using a series of 2-step models. In Step-1 we controlled for the covariates of age, education, and gender. In Step-2 we entered the MMSE Item(s) of interest. Step-2 was computed using a forced entry procedure to analyze individual item or summation scores. Step-2 was also computed, using the forward stepwise variable entry method with selection criteria based on the likelihood ratio statistic, to determine which subset of items best classify subjects with dementia . For each analysis we computed the overall % correct,

Specificity to predict CTL membership ((# classified as CTL/# of actual CTL)*100), Sensitivity to predict DAT membership ((# classified as DAT/# of actual DAT)*100), χ^2, χ^2 significance level, Odds Ratio (OR), 95% Confidence Interval (CI) limits. For the OR values in the current analyses we expect to observe values below 1.0, which signify protective qualities for dementia, meaning that when subjects score an item correctly, they are more likely to be classified as CTL. This is a result of the inverse coding between the dependent variable (CTL or DAT) and the MMSE items(s) where higher scores signify better cognitive performance. We also expect relatively low values due to the effects of the restricted range of the dichotomous values coded for individual items. We present them as corroboration for the Specificity and Sensitivity analyses.

Analyses were repeated with multiple cutoff scores for the CPS to examine differences between subjects classified with mild and moderate-severe DAT. This was done to determine if specific items, or cognitive domains, on the MMSE, are correlated with severity of dementia.

Mini-Mental State Examination

We examined individual test items, and combined individual items to compute cognitive modality summation scores for *orientation to time* (Items 1-5), *orientation to place* (Items 6-10), *learning* (Item 11), *attention* (Item 12), *recall* (Item 13), *language* (Items 14-17), *commands* (Item 18), *writing* (Item 19), and *praxis* (Item 20). While the cognitive domain of *language* generally includes Items 18-20 we analyzed them

separately to determine if they were differentially affected in residents with increased motoric deficits. Summation scores were also computed for *subcortical* (Items 1-13) and *cortical* (Items 14-20) domains (Herst, Voss, & Waldman, 1990). A second Cortical/Subcortical Index Score was computed which has been sensitive for the differentiation of patients with primary subcortical diseases such as Huntington's disease and Systemic Lupus Erythematosis from those with a primary cortical neurodegenerative diseases like Alzheimer's disease or normal aging (Brandt et al., 1988; Leritz et al., 2000). In the current study, we used an available PD subgroup to test the sensitivity of this index score in this population. We focus on the discrimination of cortical and subcortical items because of the high prevalence of physical deficits which are most often attributable to subcortical etiologies which may affect a patient's ability to respond to MMSE items in this frail elderly population for reasons unrelated to cognition. This is commonly observed in diseases such as PD which is considered a disease of movement even though there are secondary changes to behavior leading to a higher incidence of dementia in this group. We contrast this to Alzheimer's disease where the initial change is in memory, and the etiology of the disease is primarily cortical.

All non-responses to MMSE items were converted to zero values (incorrect responses) regardless of whether participants were unable to complete items due to cognitive related deficits or physical limitations. For example, a subject with a history of stroke presenting with partial paralysis might be unable to complete praxis question 20, "copy figure". This scoring method would assign a 0 value even though the subject was clearly unable to respond due to a pre-existing co-morbid condition, unrelated to

cognition. Lower scores, on the MMSE, are associated with increased cognitive impairment. While this scoring method may inherently include a bias to classify borderline subjects with dementia, we utilized this method because of both clinical convention and prior research where scoring non-response items as errors was found to provide more accurate scoring than a score limited to answerable items (Fillenbaum, George, & Blazer, 1988).

Cognitive Performance Scale

The Cognitive Performance Scale (CPS) was used to assess dementia. It is computed directly from the govenrment-mandated Minimum Data Set (MDS) which is part of the Resident Assessment Instrument required by Medicare for prospective payment reimbursement. Because the MDS is required and assessed as part of standard patient care it does not require additional testing of the resident. It provides an important clinical and research tool for the staging of dementia in this population and was originally developed using both the MMSE and the Test for Severe Impairment as criterion measures (Hartmaier et al., 1995; Paquay et al., 2007). The CPS is rated on a hierarchical 7-point scale ranging from a value of 0 through 6. Scores are assigned with 0 = Intact, 1=Borderline Intact , 2 = Mild Impairment , 3 = Moderate Impairment, 4 = Moderate-Severe Impairment, 5 = Severe Impairment, and 6 = Very Severe Impairment (J. N. Morris et al., 1994). MDS assessments are done yearly, quarterly, and at the time of an adverse trigger event. We matched each subject to MDS data by minimizing the time between the MMSE administration and the MDS assessment.

CPS with MMSE

The CPS was shown to have good validity when compared to the MMSE in the nursing home setting with $r_{Spearman} = -.86$, $p<.001$ (Hartmaier et al., 1995). Because of the advanced age, and growing medical complexity of the LTC population, we examined the relationship of the MMSE and CPS in our population and observed a value of $r_{Spearman} = -.74$, $p\leq.001$ (n=350). We were not able to resolve the difference in the explained variance between the two measures by partialling out the effects of age, gender, or race. However, it might be accounted for by age associated co-morbidities in our older frail population (86±8) as compared to the study above (80±11). This is supported by an examination of subject activities of daily living (ADL) information. We computed an ADL score to assess general functional status (J. N. Morris, Fries, & Morris, 1999). This scale is computed from the ADL section of the Minimum Data Set and is coded as follows: 0= Independent, 1=Supervision, 2=limited, 3=Extensive 1, 4=Extensive 2, 5=Dependent, and 6=Total Dependence. 85% of subjects had a score of 5 or greater. We also observed that 83% of all participants needed physical assistance for self-transfer, and 91% needed assistance with moving off units, 94% with dressing, 44% with eating, 91% with hygiene. Medically, residents had co-morbid conditions including diabetes (21%), congestive heart failure (22%), hypertension (49%), and history of stroke (12%). We also looked at the number of medications taken in the week prior to assessment as an indirect measure of co-morbid conditions (Macdonald, Carpenter, Box, Roberts, & Sahu, 2002). We observed that only 19% were on fewer than 5 medications, while 81% were

on 6 or more medications, and 25% were on more than 10 medications. These measures validate the frailty and prevalence of co-morbid conditions in this population.

CPS with CDR

Because of the a smaller correlation in our frail sample between the CPS and MMSE scores ($r_{Spearman}$ = -.74), from the above mentioned study, we re-examined the validity of the CPS with the Clinical Dementia Rating (CDR) (J. C. Morris, 1993). While the CDR is not regularly administered as part of standard patient practice we had access to CDR scores on a subsample of subjects who participated in this study and a larger institutional study on Parkinson's disease in the LTC setting. The CDR is frequently used for the staging of dementia in different populations, relying on assessments of both cognitive and behavioral domains, and a cohort interview making it less susceptible to bias related co-morbid conditions. The CDR is commonly used, in research studies, for the assessment of dementia in the nursing home setting and is part of the Uniform Data Set (J. C. Morris et al., 2006) collected by The National Alzheimer's Coordinating Center (Beekly et al., 2004). We utilized the 7-point version of the CDR, which is more appropriate for our population because it expands the classification coding for advanced stages of dementia and has been used by NIH funded Aging and Dementia Research Centers around the US. This version of the CDR is scored with 0 = No Impairment, 0.5 = Questionable, 1 = Mild Dementia, 2 = Moderate Dementia, 3 = Severe Dementia, 4 = Profound Dementia, and 5 = Terminal. Terminal ratings are indicative of loss of ability to respond, comprehend, and recognize, requiring feeding, being bedridden, and suffering

from contractures. (J. C. Morris, 1993). Assessing residents with the CDR is lengthy, taking approximately 1-2 hours to complete in this setting.

CPS/CDR Validation

There were 233 residents that received both a MDS assessment from which a CPS could be derived, and a CDR. Participants had a mean age of 85±8 years (range 65-104), with a mean education level of 12±3 years. Consistent with the distribution of gender in the general JHH long-term care population, our sample consisted of 75% females. We observed a $r_{Spearman} = .70$, $p<.001$, for the association of CPS with CDR. While the effect size was not as large as that reported in some other studies, we do account for an $R^2 = .49$, and it is consistent with our observed relationship between the CPS and the MMSE. As mentioned above we assume that the smaller correlation between tests is related to the increase in age-related co-morbid conditions in our sample, making the clinical assessment of items more prone to error.

To determine the accuracy rates associated with the CPS in this population we dichotomized each test based on applied cutoff scores to classify normal and dementia groups examining the correlation, Sensitivity, and Specificity for these tests. We dichotomized the CDR classifying the normal group as having a score of 0-.5. These scores are indicative of both normal and mild cognitive impairment, both scores not meeting criteria for dementia. Dementia was categorized with scores of 1-5, indicative of mild-terminal dementia. Initially, we categorized the CPS with scores of 0-1 signifying

normal cognitive function. Participants with scores of 2 and greater were classified as having dementia. We observed a $r_{Point\ Biserial}$=.56, p<.001 for the CPS with CDR dichotomized scores. Utilizing the CDR as the gold standard, we correctly identified 65% of the normal participants (Specificity) and 90% of the demented participants (Sensitivity) on both instruments. We then modified the categorization of the CPS to cutoffs of 0-2 and 3-6, with the latter range of scores signifying dementia. We increased the identification of normal subjects to 73% with a cost to the identification of dementia participants to 86%. Based on these results we define dementia using the CPS in this study, with this latter set of cutoff scores to improve Specificity.

Subjects

We enrolled 786 subjects from the entire resident population, with a mean age of 85±9 and an education level of 12±4 years. Females made up 73% of the study group. The sample was primarily composed of White subjects (64%), followed by Blacks (20%), then Hispanic (8%). This distribution reflects the age and resident makeup of our larger LTC population.

Study inclusion was limited to English and Spanish speakers with a valid MMSE, and MDS assessment. Participants were assigned to groups based on the following inclusion criteria:

Control (CTL) - Must have a negative history for dementia as determined by either a treating community physician or JHHLCS staff physician and a score < 3 on the CPS.

Dementia of the Alzheimer's Type (DAT) - Must have a positive diagnosis of Alzheimer's disease as determined by either a treating community physician or JHHLCS staff physician and a score ≥ 3 on the CPS.

In order to examine the effects of Parkinsonism on the assessment of the MMSE we subcategorized participants from the CTL and DAT groups into two additional groups for specific analyses, listed below. All residents at the JHHLCS exhibiting motor changes symptomatic of movement disorders including Parkinson's disease (PD), Essential Tremor (ET), and Dystonia, were referred to the JHHLCS Movement Disorders Clinic.

Parkinson's Disease without Dementia (PD-CTL) - Must have a negative history for dementia as determined by either a treating community physician or JHHLCS staff physician, a score < 3 on the CPS, and a positive diagnosis of Parkinson's disease made by a neurologist trained as a Movement Disorders specialist.

Parkinson's Disease with Alzheimer's Disease (PD-DAT) - Must have a positive diagnosis for Alzheimer's disease as determined by either a treating community physician or JHHLCS staff physician, a score ≥ 3 on the CPS, and a positive diagnosis of Parkinson's disease made by a neurologist trained as a Movement Disorders specialist.

Results

Demographics

Application of the group selection criteria resulted in 350 study participants being included for study. These participants were then assigned into either the CTL (n=134), or DAT (n=216) groups. The primary reason for study exclusion was due to diffuse dementia diagnoses, such as mixed etiologies for dementia (i.e., AD plus vascular disease) or ambiguous diagnoses (i.e., unspecified source of dementia) which were suggestive of etiologies other than DAT alone. The CPS differed between groups, as expected based on classification criteria, with the CTL group averaging a score of 0.7±0.8 while the DAT group had a mean score of 4.3±1.3 ($t(348)= -32.4$, $p\leq.001$), which is consistent with moderate-severe dementia.

We compared age, years of education, gender, and race distributions for the remaining 350 subjects with those not included for study. The only significant difference was that our selected group was slightly older with a mean age of 86±8 years as compared to the subjects dropped from the study who had a mean age of 84±9 years. While statistically significant ($p\leq.05$), this only differed by approximately 1.5 years and was not considered problematic with regard to the ability to generalize, our findings, to the larger resident population.

We also observed age, and education, differences between the CTL and DAT groups. As observed in other studies the DAT group was older (87±7 and 84±9 years,

respectively; $t(249.7) = -3.1$, $p \leq .01$), in this analysis the group variances were not equivalent and we adjusted the degrees of freedom appropriately). As in other studies the CTL group was also better educated with an average 13±3 years of education as compared to the DAT group with 12±4 years ($t(348)=3.0$, $p \leq .01$). We observed that the DAT group was comprised of 80% females as compared to the CTL group with 68%. This difference was significant (χ^2 (1)=6.6, $p \leq .01$). In addition, 75% of all females in the study were in the DAT group. Finally we observed a higher percentage of Hispanics in the DAT group than the CTL group (13%, and 2%, respectively) (χ^2 (1)=12.5, $p \leq .001$). Based on the observed differences and prior research showing relationships for age, education, and gender with the MMSE we controlled for these variables in all subsequent analyses. We did not control for race because the only difference we observed was for the distribution of Hispanics between groups. Because the MMSE has been tested extensively, and validated, with both English and Spanish speaking populations we did not control for the difference in the number of Hispanic subjects between the two groups. Differences in age, education, and gender were controlled for in all analyses (see Table 1).

Mini-Mental State Examination (MMSE)

For the total 786 subjects enrolled in the larger study, 258 (33%) were unable to respond to any items on the MMSE due to non-cognitive co-morbidities. These conditions include osteoarthritis, paralysis, and aphasic conditions related to stroke.

Of the 350 subjects that met inclusion criteria for this study, we observed that in the non-dementia CTL group, up to 15% of subjects were unable to respond to all items due to non-cognitive related reasons. On average *orientation* items were able to be answered most frequently. Items requiring the ability to write or draw were the most affected across all subjects. These include the last two items of the MMSE "write sentence" (14%) and "copy figure" (13%). Item 18, "close your eyes" was also unable to be answered by 8% of CTL subjects as was "take/fold/put paper" with only 37% of subjects able to correctly complete all three manipulations (see Table 2).

MMSE Logistic Regression Analyses

To examine the ability of specific MMSE items to differentiate the CTL and DAT groups we conducted a series of hierarchical logistic regression analyses. For each analysis we entered age, years of education, and gender in step 1. We then entered the individual MMSE item(s) of interest in Step 2.

Cognitive Domains

In our first set of analyses we examined the Sensitivity, and Specificity, of the combined MMSE items grouped into cognitive domains. We observed the best overall predictive abilities with *orientation to time and place* (overall percent correct 81% and 80%, respectively). The Specificity (correct classification of CTL) was good for all domains, ranging from a high of 92% for *copying* to 70% for *learning*. In addition,

orientation to time, *orientation to place*, *attention*, *recall*, and *writing* had overall accuracy rates of 80% or greater. As shown in other studies the ability to classify dementia was lower (Wind et al., 1997). *Orientation to time* had the highest Specificity at 75%. However, *copy figure* while having a high Sensitivity only had a Specificity of 36%. *Recall* and *attention* were under 70%. All Odds Ratios were significant (see Table 3).

The next question we addressed was whether the Sensitivity and Specificity of the MMSE was affected by levels of dementia by repeating the above comparisons between the CTL and Mild-DAT and Moderate-Severe groups separately. Participants were classified with Mild-DAT, if CPS = 3. There were 98 subjects meeting criteria for this group. As compared to the analysis between the CTL and combined DAT group above, we observed a decrease in the Overall Percent Correct and associated Odds Ratios. Unexpectedly, we also observed that the ability to predict the CTL group increased at the expense of the Sensitivity rates with the lowest Overall Percent Correct for *copy figure* with a Sensitivity of 67% and Specificity at 64% (see Table 4). We found 6 items where Sensitivity decreased to below levels of chance. As an example, *learning* which had the highest Specificity in this analysis (90%) also showed a decrease in Sensitivity to 30%. This was a decrease from 70% in the previous analysis.

For the analyses between the CTL and Moderate-Severe-DAT groups, participants were classified with Moderate-Severe DAT, if CPS $\geq$ 4. This latter group included 118 subjects. As expected the Sensitivity and Specificity measures increased

predictive ability for all items. In fact the Overall Percent Correct measure ranged from 86% for *orientation to place*, down to 65% for *copy figure*, which was the only item, showing a decrease in Sensitivity at the cost of improved Specificity which rose from 36%, in the primary analysis, to 59%. We observe that items related to *orientation* show the best balance between Specificity and overall accuracy across all 2-group comparisons (see Table 5).

To examine which domains were the best at differentiating CTL from DAT we utilized a similar statistical model except, at step 2, we used a stepwise procedure to select which items were the best predictors based on the likelihood ratio statistic. We observed that the domains of *orientation to place*, *orientation to time*, and *language* were significant (ORs were .64, .70, and .53 respectively, p's $\leq$ .01). The Specificity for this analysis was 80% with Sensitivity at 87%. When we looked at the comparison between the CTL and Moderate-Severe-DAT groups we observed that *orientation to place*, *language* and *writing* differentiated the groups (ORs .50, .36, and .28 respectively), with an Overall Predictive Accuracy of 92%, with Specificity at 91%, and Sensitivity at 92%. When we looked at the final comparison between the CTL and Mild DAT groups we observed that only *orientation to time and place* entered into the model with Specificity at 84% and Sensitivity at 71% (ORs .66 and .64 respectively). Next, we entered each of the individual items, from each of the significant domains, to examine the individual ability of each item to differentiate group membership. In the analysis between the larger group of subjects we observed that of the 15 items loaded into the original model (Items 1-10, 14-17, and 19) only "Date" (OR = .27, CI = .12-.57, p$\leq$.001), "Name of Place"

(OR = .43, CI = .19-.97, p≤.05), "Floor" (OR = .36, CI = .16-.86, p≤.05), "Name wristwatch" (OR = .09, CI = .01-.72, p≤.05), and "Write Sentence" (OR = .42, CI = .20-.88, p≤.05) loaded as separate domain items (see Table 6).

When we repeated the analysis for the CTL as compared to the Moderate-Severe DAT groups we observed that for *orientation to place* only "floor" loaded into the model (OR = .08, CI = .02-.30, p≤.001). For *language* we observed both "name wristwatch" and "close your eyes" were significant discriminators between the two groups (OR = .06, CI = .01-.52, p≤.05; and OR = .23, CI = .07-.78, p≤.05, respectively). The final item loading was "write sentence" (OR = .19, CI = .06-.64, p≤.01).

In the final analysis between the CTL and Mild DAT group we found that only items related to *orientation* were significant discriminators. For *orientation to time*, "year" and "day of week" were significant (OR = .40, CI = .16-.97, p≤.05; and OR = .33, CI = .14-.76, p≤.01, respectively).

Parkinson's Disease

Because of the large number of items on the MMSE that require a motoric, or verbal, response which can be effected by age-related diseases such as Parkinson's disease (PD) we tested the ability of the cortical and subcortical items in the MMSE to differentiate a subgroup of CTL and DAT subjects with PD. For between group analyses we assumed that the cortical items would differentiate the PD-CTL and PD-DAT groups. We identified 22 subjects with PD in our sample (6.3%). There were 13 CTL (Age 82±6

years, Education 14±3 years, and 46% females) and 9 DAT subjects (Age 85±6 years, Education 12±2 years, and 56% females). While these demographic differences were consistent with that of the larger set they were not significantly different between these 2 groups, and were not included as covariates. We did observe the expected results in that only the cortical subset of items differentiated these groups (OR=.67, CI 95%=.45-.99, $p<.05$). We also observed an overall classification accuracy of 77%, with Specificity at 85%. However, Sensitivity was only 67% ($\chi 2(1)=5.1$, $p\leq.05$). To determine the contribution of individual items in the cortical subset we entered items 14-20 of the MMSE into the Logistic Regression model. We observed that Item 17 (*close your eyes*) was the only item to enter into the model (OR=.06, CI 95%=0.00-0.74, $p\leq.05$). The Overall Classification Accuracy was 79% with Specificity being high at 91% while Sensitivity was only 62%. We also examined the utility of the subcortical scale proposed by Brandt, Folstein, and Folstein (1988). In our sample, we observed that for subjects with DAT only 39% were correctly classified as having primary cortical deficits. In addition, only 54% of the PD subjects without DAT were classified as having primary subcortical deficits. This may be due to the fact that we have observed a prevalence of over 90% for movement-related deficits as measured by the Unified Parkinson's Disease Rating Scale (Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease, 2003) in our general population, which may be responsible for the lack of sensitivity of these measures in this older frail sample.

Discussion

The MMSE remains an important, and widely used, tool for cognitive screening and gross staging of dementia in the LTC environment. Reasons include minimal time and ease associated with administration, both important considerations when assessing the frail elderly, where we observe an increased prevalence of non-cognitive co-morbid conditions which can result in lower scores resulting in a higher than acceptable frequency of false positive diagnoses of DAT.

In our study, we observed that 33% of residents approached for assessment were unable to respond to any items on the MMSE due to non-cognitively related reasons. In addition, for items requiring a physical response such as "Writing a Sentence" or "Copying a Figure" we observed an additional non-response rate of 12%-15% in the non-dementia CTL group. This means that almost 50% of study participants were unable to complete these items for reasons not related to mental faculty. This is in agreement with a previous study reporting poor performance in approximately 42% of subjects ≥ 85 years in Finland (Räihä et al., 2001). Because Non-Response items are coded as errors we expected to observe a bias to misclassify a higher proportion of CTL subjects as having DAT, observed as a low percent correct rate for the classification of CTL subjects (Specificity). In fact, this was the general pattern that we observed when we compared the CTL with the DAT groups. Specificity values averaged 11% lower than the Sensitivity measures. We observed the greatest differences between Specificity and

Sensitivity for the test items of *Attention* (16%), *Commands* (17%), *Recall* (28%), and *Copy* (56%).

In contrast, Sensitivity values were on average lower than Specificity by approximately 26% when contrasting CTL with MILD-DAT. This is interpreted as a bias for items on the MMSE to classify LTC residents with MILD-DAT as not having dementia. This is the opposite of the observation seen in the other comparisons. This finding is most likely a result of the increased rate of physical limitations in this population resulting in an increase in item score variability within both the CTL and MILD-DAT groups. In these two groups where the presentation of cognitive deficits may be relatively subtle, the misclassification of Mild-DAT subjects is probably due to the fact that the MMSE items are more susceptible to differences in physical deficits which may be more severe than the cognitive deficits at this stage of impairment. We examined the difference in MMSE scores between these two groups and observed that they were lower than reported in the literature for comparable non-age matched groups (22±6, Range=4-30, and 13±7, range =0-29 respectively). These differences are related, in part, to the increased prevalence of movement deficits in this population (> 90%) which would affect the comparison of these groups most strongly by increasing between subject variability.

The best individual item predictors of CTL/DAT classification were from the domains of *orientation (*"Year", "Name of Place"*)*, *language (*"Wristwatch"*)*, and *writing (*"Write Sentence"*)*. *Orientation* and *language* require a minimum physical

response, and consistently show good accuracy for classification across groups, and is indicative of social skill and general level of activity, which is correlated to social, and ADL, abilities. *Writing* however, requires a physical response, and is disproportionately affected in the DAT group while most CTL subjects maintain the ability to adequately write a sentence (66%).

All correctly answered items on the MMSE improved the probability that individuals tested were not demented. Besides *orientation*, the items that were most sensitive were related to *recall*. *Recall* is traditionally associated with cortical diseases such as DAT and as expected did show 86% Sensitivity to discriminate DAT participants. However, we also observed that Specificity was below 60%. This is likely due to the fact that only 28% of the CTL group was able to recall all 3 words on the item, possibly due to either normal aging in the frail population or drug related memory loss, with 81% of our sample using 6 or more medications daily.

We also noted that a subset of 5 out of 20 items were as predictive as the entire test. The items "Year", "Name of Place", "Floor", "Name Wristwatch", and "Write Sentence" resulted in Specificity and Sensitivity values of 80% and 87%, respectively. These 5 items actually increased Specificity by 5% when compared to all 20 items.

MMSE subcortical and cortical items did not differentiate PD subjects from those without PD in our sample. While our PD group was small we were able to differentiate between PD-CTL and PD-DAT groups based on cortical items. While Specificity was

high we were only able to classify 67% of the DAT group. While suggestive, the size of our groups was small. However, the inability of these items to differentiate cortical from subcortical dementias in this group is further supported by our analyses with the Cortical/Subcortical Index Score. For these analyses we observed that while this scale has been observed to differentiate Huntington's disease from DAT in younger patients, it did not differentiate Parkinson's disease patients in our sample. We believe that this is due to the high prevalence of movement disorders in this general population, decreasing the Sensitivity of these questions as diagnostic items. While we did not have enough subjects with PD to test the direct effects of severe physical limitations on the scoring of the MMSE we did observe that only the cortical subset of items were able to differentiate CTL and DAT subjects. The subcortical subset did not differentiate Non-PD from PD subjects. This supports the contention that the high incidence of physical deficits in the Non-PD group, which we have observed to average over 90%, is contributory to this finding.

Conclusions

While the MMSE may be the most widely used instrument for the assessment of cognitive status, we question the high incidence of missing item data related to non-cognitive etiologies in this population. Of the original 786 participants enrolled in the study 32% were unable to respond to any of the items on the test. For subjects able to respond to items, we observed up to an additional 15% attrition rate for items requiring a motor response such as "Write Sentence" and "Draw Figure" in the CTL group, where

the expectation is that unanswered items are related to cognitive deficits. This raises the amount of missing data on specific items to almost 50%.

The instrument was inadequate with regard to detecting subcortical deficits in a sample of PD subjects. While the sample was small the instrument was still successful in differentiating PD subjects with Alzheimer's disease (PD-DAT) from those without Alzheimer's disease (PD-DAT) on cortical items which would be expected in a neurological disease such as DAT. It is important to note that while this instrument was not intended to differentiate PD from AD it was meant to provide an assessment of dementia in a clinical population. We believe that the LTC population provides a direct challenge to this and similar instruments which rely on physical responses from patients and alternative assessment strategies may be necessary.

Any changes to the MMSE should focus on items that require limited physical ability, or an alternate weighting system, for items, accounting for the limited physical abilities of a large proportion of these patients. We realize that this would alter the validity of the instrument and would require validation studies in this population as well as other sample groups. Suggestions for alternative items include the use of direct measures of physical neurological signs (Franssen & Reisberg, 1997), non-verbal tests with simplified motor response requirements, or tests of perceptual processing function (Fernandez, Kavcic, & Duffy, 2007; Scarmeas et al., 2005; Webster, Merory, & Wittwer, 2006).

While the MMSE is generally considered an exceptional clinical assessment instrument, it provides a higher than acceptable level of misclassification in this frail elderly population, with a bias to incorrectly classify dementia in non-demented individuals. We strongly recommend the need for the development of cognitive assessment instruments specific to this population. We observed comparable accuracy rates using only 5 out of the 20 items. In this population we would suggest using these items as a basis for any modifications to the MMSE for the frail elderly LTC population.

Table 1

Distribution of Demographic Variables by Group

		CTL	DAT
Number of Subjects		134	216
MDS-CPS**		1±1	4±1
MMSE**		22±6	9±8
Age*		84±9	87±7
Years of Education*		13±3	12±4
Gender (% Female)*		68%	80%
Ethnicity	White	71%	62%
	Black	18%	20%
	Hispanic**	2%	13%
	Other	9%	5%

* p≤.01; ** p≤.001

Table 2

Distribution of Non-Response Items on the MMSE Due

To Non-Cognitive Co-Morbid Conditions

	CTL	DAT
Year	0.7%	0.0%
Season	0.7%	0.0%
Month	0.0%	0.0%
Date	0.0%	0.0%
Year	0.7%	0.0%
State	1.5%	0.0%
County/Borough	1.5%	0.0%
Town or City	1.5%	0.0%
Name of Place	1.5%	0.0%
Floor	0.7%	0.0%
Immed-Apple/Table/Penny	1.5%	1.9%
WORLD Backwards	1.5%	2.8%
Recall-Apple/Table/Penny	1.5%	2.3%
Wristwatch	1.5%	2.3%
Pen	1.5%	2.3%
No ifs ands or buts	3.0%	4.6%
Close Your Eyes	7.5%	11.1%
Take/Fold/Put Paper	7.5%	5.6%
Write Sentence	14.2%	12.0%
Copy Figure	14.9%	12.5%

Table 3

MMSE Item Analysis for CTL and DAT Groups

	% Correct	Specificity	Sensitivity	$\chi 2$	P	Odds Ratio	CI (95%)
Orient-Time	**81%**	**75%**	**85%**	**139.8**	**≤.001**	**0.47**	**0.40-0.54**
Year	80%	78%	81%	109.2	≤.001	0.07	0.04-0.12
Season	75%	71%	77%	81.0	≤.001	0.11	0.06-0.18
Month	77%	77%	77%	95.8	≤.001	0.09	0.05-0.15
Date	80%	72%	85%	108.6	≤.001	0.07	0.04-0.12
Year	76%	66%	82%	78.4	≤.001	0.12	0.07-0.19
Orient-Place	**80%**	**74%**	**84%**	**147.2**	**≤.001**	**0.41**	**0.35-0.50**
State	73%	71%	74%	87.0	≤.001	0.07	0.03-0.14
County/Borough	77%	78%	77%	86.9	≤.001	0.10	0.06-0.17
Town or City	72%	66%	76%	75.6	≤.001	0.09	0.05-0.17
Name of Place	79%	67%	86%	98.9	≤.001	0.08	0.04-0.14
Floor	80%	81%	80%	123.4	≤.001	0.06	0.03-0.10
Learning	**72%**	**74%**	**70%**	**82.9**	**≤.001**	**0.27**	**0.17-0.42**
Immed-A/T/P	72%	74%	70%	82.9	≤.001	0.27	0.17-0.45
Attention	**74%**	**64%**	**80%**	**78.2**	**≤.001**	**0.59**	**0.52-0.67**
WORLD	74%	64%	80%	78.2	≤.001	0.59	0.52-0.67
Recall	**75%**	**58%**	**86%**	**78.4**	**≤.001**	**0.36**	**0.28-0.47**
Recall-A/T/P	75%	58%	86%	78.4	≤.001	0.36	0.28-0.47
Language	**76%**	**71%**	**79%**	**109.4**	**≤.001**	**0.31**	**0.23-0.42**
Wristwatch	70%	57%	78%	74.7	≤.001	0.02	0.01-0.10
Pen	69%	54%	79%	58.3	≤.001	0.06	0.02-0.16
No ifs..buts	71%	75%	68%	55.6	≤.001	0.15	0.09-0.25
Close Eyes	73%	75%	72%	80.2	≤.001	0.08	0.04-0.15
Commands	**72%**	**61%**	**78%**	**73.1**	**≤.001**	**0.37**	**0.29-0.49**
Take/Fold/Put	72%	61%	78%	73.1	≤.001	0.37	0.29-0.49
Writing	**76%**	**70%**	**80%**	**79.9**	**≤.001**	**0.09**	**0.05-0.16**
Write Sentence	76%	70%	80%	79.9	≤.001	0.09	0.05-0.16
Copy	**71%**	**36%**	**92%**	**33.9**	**≤.001**	**0.12**	**0.05-0.27**
Copy Figure	71%	36%	92%	33.9	≤.001	0.12	0.05-0.27
MMSE Total	**82%**	**75%**	**87%**	**162.4**	**≤.001**	**0.82**	**0.78-0.85**

CI = Confidence Interval

Table 4

MMSE Item Analysis for CTL and MILD DAT Groups

	% Correct	Specificity	Sensitivity	$\chi 2$	P	Odds Ratio	CI (95%)
Orient-Time	**76%**	**81%**	**69%**	**61.9**	**≤.001**	**0.54**	**0.45-0.64**
Year	77%	81%	70%	50.3	≤.001	0.12	0.06-0.22
Season	72%	80%	60%	34.0	≤.001	0.18	0.10-0.32
Month	75%	82%	64%	41.2	≤.001	0.15	0.08-0.28
Date	75%	78%	69%	46.7	≤.001	0.13	0.07-0.25
Year	73%	78%	63%	22.2	≤.001	0.26	0.15-0.46
Orient-Place	**73%**	**79%**	**65%**	**60.4**	**≤.001**	**0.49**	**0.40-0.60**
State	67%	85%	43%	26.9	≤.001	0.14	0.06-0.32
County/Borough	71%	81%	58%	27.9	≤.001	0.21	0.11-0.38
Town or City	68%	85%	46%	68.3	≤.001	0.16	0.08-0.34
Name of Place	75%	77%	71%	42.2	≤.001	0.14	0.08-0.27
Floor	75%	84%	64%	45.0	≤.001	0.13	0.07-0.24
Learning	**66%**	**90%**	**30%**	**17.4**	**≤.001**	**0.43**	**0.26-0.69**
Immed-A/T/P	66%	90%	30%	17.4	≤.001	0.43	0.26-0.69
Attention	**69%**	**77%**	**57%**	**27.5**	**≤.001**	**0.68**	**0.59-0.79**
WORLD	69%	77%	57%	27.5	≤.001	0.68	0.59-0.79
Recall	**74%**	**80%**	**67%**	**34.3**	**≤.001**	**0.45**	**0.33-0.60**
Recall-A/T/P	74%	80%	67%	34.3	≤.001	0.45	0.33-0.60
Language	**71%**	**82%**	**57%**	**29.7**	**≤.001**	**0.44**	**0.31-0.62**
Wristwatch	64%	88%	32%	14.6	≤.001	0.10	0.02-0.43
Pen	67%	89%	35%	15.0	≤.001	0.14	0.05-0.44
No ifs…buts	71%	85%	50%	16.1	≤.001	0.28	0.15-0.53
Close Eyes	66%	85%	40%	19.1	≤.001	0.20	0.10-0.43
Commands	**71%**	**81%**	**57%**	**26.7**	**≤.001**	**0.46**	**0.34-0.63**
Take/Fold/Put	70%	81%	57%	26.7	≤.001	0.46	0.34-0.63
Writing	**71%**	**81%**	**59%**	**27.1**	**≤.001**	**0.19**	**0.11-0.36**
Write Sentence	71%	81%	59%	27.1	≤.001	0.19	0.11-0.36
Copy	**65%**	**64%**	**67%**	**17.5**	**≤.001**	**0.16**	**0.06-0.42**
Copy Figure	65%	64%	67%	17.5	≤.001	0.16	0.06-0.42
MMSE Total	**75%**	**81%**	**67%**	**68.4**	**≤.001**	**0.84**	**0.80-0.88**

CI = Confidence Interval

Table 5

MMSE Item Analysis for CTL and MOD-SEVERE DAT Groups

	% Correct	Specificity	Sensitivity	$\chi 2$	P	Odds Ratio	CI (95%)
Orient-Time	**86%**	**84%**	**89%**	**148.5**	**≤.001**	**0.37**	**0.30-0.46**
Year	82%	78%	87%	109.0	≤.001	0.04	0.02-0.09
Season	79%	78%	80%	86.7	≤.001	0.07	0.04-0.13
Month	82%	79%	85%	103.5	≤.001	0.05	0.03-0.10
Date	81%	72%	92%	112.6	≤.001	0.03	0.02-0.07
Year	78%	68%	90%	103.4	≤.001	0.04	0.02-0.08
Orient-Place	**86%**	**88%**	**85%**	**170.6**	**≤.001**	**0.32**	**0.25-0.40**
State	84%	92%	74%	118.1	≤.001	0.03	0.01-0.07
County/Borough	83%	78%	88%	109.6	≤.001	0.04	0.02-0.08
Town or City	80%	90%	70%	94.4	≤.001	0.05	0.02-0.10
Name of Place	80%	70%	91%	105.6	≤.001	0.03	0.01-0.07
Floor	87%	83%	92%	150.2	≤.001	0.02	0.01-0.04
Learning	**83%**	**94%**	**70%**	**120.7**	**≤.001**	**0.19**	**0.12-0.31**
Immed-A/T/P	83%	94%	70%	120.7	≤.001	0.19	0.12-0.31
Attention	**80%**	**77%**	**83%**	**93.3**	**≤.001**	**0.49**	**0.42-0.58**
WORLD	80%	77%	83%	93.3	≤.001	0.49	0.42-0.58
Recall	**81%**	**74%**	**90%**	**82.3**	**≤.001**	**0.25**	**0.17-0.37**
Recall-A/T/P	81%	74%	90%	82.3	≤.001	0.25	0.17-0.37
Language	**85%**	**92%**	**77%**	**151.3**	**≤.001**	**0.20**	**0.13-0.29**
Wristwatch	79%	98%	58%	108.2	≤.001	0.01	0.00-0.05
Pen	75%	96%	51%	76.7	≤.001	0.03	0.01-0.09
No ifs…buts	79%	81%	78%	74.4	≤.001	0.08	0.04-0.14
Close Eyes	86%	90%	80%	116.9	≤.001	0.03	0.01-0.06
Commands	**80%**	**85%**	**74%**	**89.2**	**≤.001**	**0.30**	**0.22-0.40**
Take/Fold/Put	80%	85%	74%	89.2	≤.001	0.30	0.22-0.40
Writing	**83%**	**78%**	**87%**	**100.9**	**≤.001**	**0.03**	**0.01-0.07**
Write Sentence	83%	78%	87%	100.9	≤.001	0.03	0.01-0.07
Copy	**65%**	**59%**	**71%**	**27.2**	**≤.001**	**0.09**	**0.03-0.28**
Copy Figure	65%	59%	71%	27.2	≤.001	0.09	0.03-0.28
MMSE Total	**88%**	**88%**	**87%**	**182.8**	**≤.001**	**0.77**	**0.73-0.82**

CI = Confidence Interval

Table 6

MMSE Item Analysis For All Significant Items

	% Correct	Specificity	Sensitivity	$\chi 2$	P	Odds Ratio	CI (95%)
Orient-Time							
Year						0.27	0.12-0.57
Orient-Place							
Name of Place						0.43	0.19-0.97
Floor						0.36	0.16-0.86
Language							
Wristwatch						0.09	0.01-0.72
Writing							
Write Sentence						0.23	0.20-0.88
Total Model	**84%**	**80%**	**87%**	**4.1**	**≤.05**		

References

Allen, R., DeLaine, S. R., Chaplin, W. F., Marson, D. C., Bourgeois, M. S., Dijkstra, K., et al. (2003). Advance care planning in nursing homes: Correlates of capacity and possession of advance directives. *The Gerontologist, 43*(3), 309-317.

Alvardo-Esquivel, C., Hernández-Alvarado, A. B., Tapia-Rodríguez, R. O., Guerrero-Iturbe, Á., Rodríguez-Corral, K., & Martínez, S. E. (2004). Prevalence of dementia and Alzheimer's disease in elders of nursing homes and a senior center of Durango City, Mexico. *BMC Psychiatry, 4*(3).

American Association of Homes and Services for the Aging. (2007). Aging Services: The Facts.

Beekly, D. L., Ramos, E. M., van Belle, G., Deitrich, W., Clark, A. D., Jacka, M. E., et al. (2004). The National Alzheimer's Coordinating Center (NACC) Database: An Alzheimer's disease database. *Alzheimer Disease and Associated Disorders, 18*(4), 270-277.

Brandt, J., Folstein, S. E., & Folstein, M. F. (1988). Differential cognitive impairment in Alzheimer's disease and Huntington's disease. *Annals of Neurology, 23*, 555-561.

Camicioli, R., & Licis, L. (2004). Motor impairment predicts falls in specialized Alzheimer's care units. *Alzheimer Disease and Associated Disorders, 18*(4), 214-218.

Espino, D. V., Lichtenstein, M. J., Palmer, R. F., & Hazuda, H. P. (2001). Ethnic differences in Mini-Mental State Examination (MMSE) scores: Where you live makes a difference. *Journal of the American Geriatrics Society, 49*(5), 538-548.

Espinoza, R. T. (2006). Improving the recognition and management of dementia in long-term care: Obstacles and opportunities. *Journal of the American Medical Directors Association, 7*(2), 128-130.

Evans, B. C., & Crogan, N. L. (2006). Building a scientific base for nutrition care of hispanic nursing home residents. *Geriatric Nursing, 27*(5), 273-279.

Fernandez, R., Kavcic, V., & Duffy, C. J. (2007). Neuropsychological analyses of low- and high-level visual processing in Alzheimer's disease. *Neurology, 68*(24), 2066-2076.

Fillenbaum, G. G., George, L. K., & Blazer, D. G. (1988). Scoring nonresponse on the Mini-Mental Status Examination. *Psychological Medicine, 18*, 1021-1025.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "MINI-MENTAL STATE" A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Fountoulakis, K. N., Tsolaki, M., Chantzi, H., & Kazis, A. (2000). Mini Mental State Examination (MMSE): A validation study in Greece. *American Journal of Alzheimer's Disease and Other Dementias, 15*(6), 342-345.

Franssen, E. H., & Reisberg, B. (1997). Neurologic markers fo the progression of Alzheimer's disease. *International Psychogeriatrics, 9*(Supplement 1), 297-306.

Hartmaier, S. L., Sloane, P. D., Guess, H. A., Koch, G. G., Mitchell, C. M., & Phillips, C. D. (1995). Validation of the Minimum Data Set Cognitive Performance Scale: Agreement with the Mini-Mental State Examination. *Journal of Gerontology A:Biological Science Medical Science, 50*(2), M128-M133.

Herst, L., Voss, C. B., & Waldman, J. (1990). Cortical function assessment in the elderly. *Journal of Neuropsychiatry, 2*(4), 385-390.

Kilada, S., Gamaldo, A., Grant, E. A., Moghekar, A., Morris, J. C., & O'Brien, R. J. (2005). Brief screening tests for the diagnosis of dementia: Comparison with the Mini-Mental State Exam. *Alzheimer Disease and Associated Disorders, 19*(1), 8-16.

Küçükdeveci, A. A., Kutlay, S., Elhan, A. H., & Tennant, A. (2005). Preliminary study to evaluate the validity of the mini-mental state examination in a normal population in Turkey. *International Journal of Rehabilitation Medicine, 28*, 77-79.

Lapane, K. L., Fernandez, H. H., Friedman, J. H., & and the SAGE Study Group. (1999). Prevalence, clinical characteristics, and pharmacologic treatment of Parkinson's disease in residents in long-term care facilities. *Pharmacotherapy, 19*(11), 1321-1327.

Leritz, E., Brandt, J., Minor, M., Reis-Jensen, F., & Petri, M. (2000). "Subcortical" cognitive impairment in patients with systemic lupus erythematosis. *Journal of the International Neuropsychological Society, 6*, 821-825.

Lou, M.-F., Dai, Y.-T., Huang, G.-S., & Yu, P.-J. (2007). Identifying the most efficient items from the Mini-Mental State Examination for cognitive function assessment in older Taiwanese patients. *Journal of Clinical Nursing, 16*, 502-508.

Macdonald, A. J. D., Carpenter, G. I., Box, O., Roberts, A., & Sahu, S. (2002). Dementia and use of psychotropic medication in non- 'Elderly Mentally Infirm' nursing homes in South East England. *Age and Ageing, 31*, 58-64.

Morris, J. C. (1993). The Clinical Dementia Rating (CDR): Current version and scoring rules. *Neurology, 43*(1), 2412-2414.

Morris, J. C., Weintraub, S., Chui, H. C., Cummings, J., DeCarli, C., Ferris, S., et al. (2006). The Uniform Data Set (UDS): Clinical and cognitive variables and descriptive data from Alzheimer's Disease Centers. *Alzheimer Disease and Associated Disorders, 20*(4), 210-216.

Morris, J. N., Fries, B. E., Mehr, D. R., Hawes, C., Phillips, C., Mor, V., et al. (1994). MDS Cognitive Performance Scale. *Journal of Gerontology: Medical Sciences, 49*(4), M174-M182.

Morris, J. N., Fries, B. E., & Morris, S. A. (1999). Scaling ADLs within the MDS. *Journal of Gerontology: Medical Sciences, 54A*(11), M546-M553.

Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease. (2003). The Unified Parkinson's Disease Rating Scale (UPDRS): Status and recommendations. *Movement Disorders, 18*(7), 738-750.

Nelson, J. C., Hollander, S. B., Betzel, J., Smolen, P., & Mirtazapine Nursing Home Study Group. (2006). Mirtazapine orally disintegrating tablets in depressed nursing home residents 85 years of age and older. *International Journal of Geriatric Psychiatry, 21*, 898-901.

Paquay, L., De Lepeleire, J., Schoenmakers, B., Ylieff, M., Fontaine, O., & Buntinx, F. (2007). Comparison of the diagnostic accuracy of the Cognitive Performance Scale (Minimum Data Set) and the Mini-Mental State Exam for the detection of

cognitive impairment in nursing home residents. *International Journal of Geriatric Psychiatry, 22*, 286-293.

Räihä, I., Isoaho, R., Ojanlatva, A., Viramo, P., Sulkava, R., & Kivelä, S.-L. (2001). Poor performance in the Mini-Mental State Examination due to causes other than dementia. *Scandinavian Journal of Primary Health Care, 19*, 34-38.

Resnick, B., Gruber-Baldini, A. L., Pretzer-Aboff, I., Galik, E., Buie, V. C., Russ, K., et al. (2007). Reliability and validity of the evaluation to sign consent measure. *The Gerontologist, 47*(1), 69-77.

Rosenberg, P. B., Mielke, M. M., Samus, Q. M., Rosenblatt, A., Baker, A., Brandt, J., et al. (2006). Transition to nursing home from assisted living is not associated with dementia-related problem behaviors. *Journal of the American Medical Directors Association, 7*, 73-78.

Scarmeas, N., Albert, M., Brandt, J., Blacker, D., Hadjigeorgiou, G., Papadimitriou, A., et al. (2005). Motor signs predict poor outcomes in Alzheimer's disease. *Neurology, 64*(10), 1696-1703.

Singer, C., & Luxenberg, J. (2003). Diagnosing dementia in long-term care facilities. *Journal of the American Medical Directors Association, Supplement 1, 4*(6), S134-S140.

SPSS for Windows (Release 14.0.2).

Tarshish, C. Y., Neufeld, R. R., & Libow, L. S. (In-Preparation). Utility of the United Parkinson's Disease Rating Scale Motor Examination in the frail elderly.

Tse, W., Libow, L. S., Neufeld, R., Lesser, G., Frank, J., Dolan, S., et al. (In Press). Prevalence of movement disorders in an elderly nursing home population. *Archives of Gerontology and Geriatrics*.

U.S. Department of Health and Human Services Administration on Aging. (2006). *A statistical profile of Hispanic older Americans aged 65 +*

Webster, K. E., Merory, J. R., & Wittwer, J. E. (2006). Gait variability in community dwelling adults with Alzheimer's disease. *Alzheimer Disease and Associated Disorders, 20*(1), 37-40.

Wind, A. W., Schellevis, F., Van Staveren, G., Scholten, R. J. P. M., Jonker, C., & Van Eijk, J. T. M. (1997). Limitations of the Mini-Mental State Examination in diagnosing dementia in general practice. *International Journal of Geriatric Psychiatry, 12*, 101-108.

Wood, R. Y., Giuliano, K. K., Bignell, C. U., & Pritham, W. W. (2006).

Assessing cognitive ability in research: Use of MMSE with minority populations and elderly adults with low education levels. *Journal of Gerontological Nursing, 32*(4), 45-54.

Chapter 3

Assessment Accuracy of the CAMCOG in a Frail Elderly Long-Term Care Sample

Abstract

Objective

The primary purpose of this study was to determine the assessment accuracy of the Cambridge Cognitive Examination (CAMCOG) with the frail elderly long-term care (LTC) population. The instrument is considered sensitive to identifying early cognitive changes in elderly populations. We tested Resident (individuals living in LTC) ability to complete the test and accuracy of the instrument to measure deficits in individual cognitive domains associated with both dementia and Parkinson's disease (PD) in this population.

Methods

The CAMCOG, Mini-Mental State Examination, and Clinical Dementia Rating were administered to all subjects. Medical, demographic, and information derived from the federally-mandated Minimum Data Set were collected as part of a systematic chart review. A series of Analysis of Covariance Models controlling for age and gender were used to detect group differences among CAMCOG items in Control (n=16), Dementia (n=13), PD (n=9), and PD with dementia groups (n=12).

Results

The majority of CAMCOG items differentiated groups. The average time to complete the test was 48±16 minutes. The general pattern of cognition showed that the Control group performed best followed by the PD, PD with dementia, and Dementia groups, respectively. The total CAMCOG score was lower than seen in previously reported normative data with the Control group having the highest score (80) followed by the PD (76), PD with dementia (61), and the Dementia groups (52). Remote Memory, Abstract Thinking, and Perception related test items failed to differentiate groups.

Conclusions:

The CAMCOG is sensitive, overall, for the detection of dementia in the LTC population. Specific domains are not sensitive and require adjustment for use with the frail elderly LTC population. This is substantiated by observed total test scores, which are lower than previously reported for age, gender, and education adjusted scores.

Introduction

We evaluate the accuracy, and sensitivity, of the Cambridge Cognitive Examination – Revised (CAMCOG) to identify dementia in the frail elderly long-term care population (LTC). The CAMCOG is the cognitive assessment subsection of the Cambridge Examination for Mental Disorders of the Elderly (CAMDEX-R) diagnostic instrument (Roth, Huppert, Mountjoy, & Tym, 1998).

Studies like this are needed because of the unique impediments to the clinician in diagnosing mild-early moderate stages of dementia in this population. Concurrently, any diagnoses based on these assessments have a major impact on the "stream" of care that the Resident (individual living in long-term care) will receive because level and reimbursement of care are based directly upon expected outcome of treatment. In the last reports published by the Centers for Disease Control 68% of LTC residents are on Medicaid and 16.9% are on Medicare (Centers for Disease Control and Prevention, 2006). Services paid for in LTC are directly influenced by treatment outcomes and diagnoses of dementia and age-related neuropathological diseases such as Alzheimer's disease (AD) will have a direct effect on the services a facility can provide based on insurance reimbursement.

The LTC population is known to have a high prevalence of age-related co-morbid conditions which can affect testing accuracy. These include arthritic and aphasic conditions which would affect the ability of a Resident to accurately respond to

assessment test questions as a result of non-cognitive related reasons. These conditions plus the affects of generalized physical aging result in Residents being unable to tolerate extensive testing. Therefore, evaluation instruments must be relatively brief, accurate, and with known psychometric properties. LTC staffing patterns, which are in part dictated by State regulations, also necessitate the need for relatively brief training periods for any instruments that will be successfully adapted for use in this environment due to mandated caseloads and reimbursement scheduling.

To further obfuscate the assessment process, there is usually only sparse medical history information available on many Residents. While a complete history is collected in settings such as those of the federally-funded Aging and Dementia Research Centers, this is generally not the situation in the LTC nursing home environment. In the LTC environment it is often the case that the Resident does not have a clear recollection of their medical history. During the admissions process information may be collected from family members. However, quite often there is no informant available. When available, it is usually a child, or friend who may not have a clear recollection of information that would be useful for diagnoses such as AD or other age-related neurodegenerative diseases such as Parkinson's disease (PD) and Essential tremor, which have higher prevalence rates in the nursing home as related to community residing elderly (Tse et al., In Press). This lack of resident information forces the clinician to depend excessively on any available test or historical patient information that is available.

These issues highlight the need to utilize the most sensitive and appropriate instruments available. Over the last few years, we have observed an increase in the life expectancy rates of the elderly residing in LTC facilities. With time, individuals living in LTC are becoming increasingly representative of the changing demographics of the US population and by the year 2020, 12 million older Americans will need LTC (American Association of Homes and Services for the Aging, 2007). It is projected that by the year 2026 the number of Americans over the age of 65 will double, and by the year 2050, 20% of all Americans will be classified as old with those 85 years and older representing a full 5% of the population. These changes can be generalized across multiple ethnic groups, with 25% of the US Hispanic population ≥ 80 years by the year 2030 (U.S. Department of Health and Human Services Administration on Aging, 2006). Many of the co-morbid age-related conditions that affect the LTC population will also affect many community-dwelling elderly because of the increasing movement, in healthcare, to keep the elderly in the community, with increased support services. As a direct result, LTC facilities have experienced admissions of older and more medically complex residents, which have made the assessment of cognitive status increasingly difficult. In this environment it becomes necessary to review the utility of current assessment strategies and to determine the need for new strategies. This is especially true for a frail elderly population with increased rates of neurodegenerative and age-related conditions, where interactions between age and the disease state cause increased sensitivity to medications, dementia, risk for falling, impaired ability to report pain, and diagnosis of depression (Espinoza, 2006; Singer & Luxenberg, 2003), all of which can affect cognition. It is especially important to assess these issues now because, with time, many of the assessment issues

that are currently important for LTC will become increasingly important for the general community.

The assessment strategy for diagnosing cognition in the U.S. has been to utilize multiple instruments to assess specific domains. This is evident from the systematic approach initiated by the National Institutes of Health by funding the The National Alzheimer's Coordinating Center who require a core set of different instruments be administered at all Aging and Dementia Research Centers across the U.S. The instruments are collected as part of the Uniform Data Set which serves as the core clinical assessment for AD (Beekly et al., 2004; Morris et al., 2006). Using this type of strategy in the LTC environment is not feasible because it assumes that Residents are physically able to undergo hours of testing and to maintain sufficient levels of attention so that test results are valid. In addition, it is assumed that there is clinical staffing with a case-load that would allow for extensive testing. While there is no disagreement that this would represent the best case scenario, the simple reality is that this is not the case. In the LTC environment it becomes necessary to utilize the most accurate assessment instruments which balance the economic resources of the facility, staffing, and limits on test time, due to general Resident frailty. As part of these considerations it is also important to note that LTC facilities may not be able to utilize extensive senior clinical staff time for these assessments, relying instead on junior staff who may require increased training and supervision.

In this study we examine both the accuracy of using the CAMCOG, in this population, as well as the capability of Residents to tolerate the increased test time associated with this instrument. Specifically, can this instrument be administered successfully to LTC residents with consideration given to the physical response requirements of the test, administration time, and test sensitivity for dementia or cognitive deficits in this population.

While the CAMCOG has not gained extensive use in this country, it has been used to examine social cognition in the frail elderly nursing home population in the U.S. (Washburn, Sands, & Walton, 2003). It is widely used in countries such as Israel where a Hebrew version of the instrument has been validated and is widely used in that country by geriatric psychiatrists for assessments (Heinik, Werner, Mendel, Raikher, & Bleich, 1999). In addition the instrument has been translated and validated in a number of languages such as Italian, Dutch, Spanish, Danish, German, and Indian. In these countries it has been used with patient groups which include the visually impaired (Hartman, 2000), stroke patients (C. G. Ballard et al., 2004; Leeds, Meara, Woods, & Hobson, 2001), comparative studies between Parkinson's disease and other neurodegenerative diseases (Athey, Porter, & Walker, 2005; Hobson & Meara, 1999, , 2004), cognitive decline in Parkinson's disease (Athey & Walker, 2006) Lewy body disease (Graham, Ballard, & Saad, 1997; Tam, Burton, McKeith, Burn, & O'Brien, 2005), vascular dementia (C. Ballard et al., 2001), Alzheimer's disease (Frankfort et al., 2007; Garre-Olmo et al., 2004; Kurz et al., 1996; Nielsen, Lolk, Andersen, Andersen, & Kragh-Sørensen, 1999; Schmand, Walstra, Lindeboom, Teunisse, & Jonkers, 2000), Non-

specific dementia (Jonkers, Schmand, Lindeboom, Havekes, & Launer, 1998), Down's syndrome (Ball et al., 2004), and normal aging (Cullum et al., 2000).

The CAMCOG was revised in 1998 to include more in-depth questioning in the areas of Executive Function and Perception. The current version is considered more sensitive in detecting early stages of dementia, specifically, for Dementia of the Alzheimer's Type (DAT) and early cognitive changes in PD which have been reported to include verbal memory and executive function impairments prior to a diagnosis of dementia (Levy et al., 2002). However, the revised Executive Function items on the CAMCOG have been reported to be correlated with global function, and to be affected by depression in a sample of stroke patients, (Leeds et al., 2001). This relationship must also be considered during any assessment because of the high prevalence of depression reported in this population. While comparing favorably with other Executive Function measures such as the Raven's Coloured Progressive Matrices (Raven, 1982), the correlation between the Ravens and the CAMCOG executive function subscale was only .57, and the CAMCOG takes slightly longer to administer. The strength of the test however, is that it provides a comprehensive cognitive assessment battery which has been validated and provides testing guidelines and normative data for assessment.

This study was initiated to address the following questions:

1. Would a sample of frail elderly LTC residents be able to complete the CAMCOG? Prior studies have reported different

times for the completion of the test with Leeds, et. al (2001) reporting an administration time of 26 minutes in stroke patients who would be expected to share some similar physical impairments with subjects in this population.

2. Would items on the CAMCOG accurately measure cognitive deficits across different patient groups in this population?

Methods

This study was conducted, at the Jewish Home & Hospital Lifecare System (JHHLCS), the largest non-profit academically-affiliated long-term care facility in the United States. This study was approved by the JHHLCS and Mount Sinai School of Medicine Institutional Review Boards.

As part of the study protocol all subjects were administered the CAMCOG (Roth et al., 1998), Mini-Mental Status Examination (MMSE) (Folstein, Folstein, & McHugh, 1975), and Clinical Dementia Rating (CDR) (Morris, 1993). Medical, demographic, and information derived from the Minimum Data Set which is part of the Resident Assessment Instrument, were also collected as part of a systematic chart review. All study assessments were completed by study coordinators supervised by a senior tester with extensive experience in the LTC environment. The sequence of test administration always consisted of the MMSE and CDR being given prior to the CAMCOG.

Subjects

Fifty subjects from the entire resident population were enrolled in this study. Inclusion criteria were limited to English and Spanish speakers. Subjects were included if they had a MMSE score ≥ 15. If the MMSE score was < 24 the patient's primary care physician, or a geriatrician, acting independently of this study, would make the determination of competency to sign informed consent. The primary care physician is in daily contact with the patient, is the most informed about the subject's medical and cognitive status, and has an established relationship with the patient, family, and health care proxy. Institutionally he/she is the most capable person to assess capacity.

Once consent for participation was obtained, subjects were assigned to groups based on the following inclusion criteria:

Control (CTL) – MMSE ≥ 24, negative history for Parkinson's disease, and no current usage of PD treatment drug(s)(i.e. Sinemet, Compton, Mirapex).

Dementia (DEM) – MMSE score < 24 and ≥ 15, a negative history for Parkinson's Disease , and no current usage of PD treatment drug(s) (i.e. Sinemet, Compton, Mirapex).

Parkinson's Disease (PD) – MMSE ≥ 24, current diagnosis of PD in medical chart, and current usage of PD treatment drug(s) (i.e. Sinemet, Compton, Mirapex).

Parkinson's Disease with Dementia (PD-DEM) – MMSE < 24 and MMSE ≥ 15, current diagnosis of PD in medical chart, and current usage of PD treatment drug(s) (i.e. Sinemet, Compton, Mirapex).

We included two PD groups because the test has been used extensively with this patient group and we wanted to examine the impact of severe motor impairments on test outcome.

Statistics

Analyses were done using SPSS for Windows (SPSS for Windows Release 14.0.2).

Prior to examining data from cognitive tests we examined the distribution of demographic variables known to affect these outcome measures to determine if covariates should be included in the models. We computed analysis of variance models for each variable to determine if differences existed. Scheffé posthoc tests were used to control for multiple comparisons between groups.

Skewness and kurtosis measures were computed for each dependent variable. If either measure was greater than two standard error units, appropriate transformations were applied to normalize the distributions.

Group differences for continuous variables were analyzed using a two-stage approach. In stage-1 an Omnibus F test was computed between all groups to determine if there was a significant difference when controlling for the number of comparisons. If the F value was statistically significant ($p \leq .05$) multiple 1-way analyses of variance models were computed to determine which groups were significantly different. When necessary the appropriate data transformations were applied to normalize the distribution. Covariates were also included to control for demographic confounds, when necessary.

Group differences for gender and ethnicity were computed using the Chi-Square Test for Independence.

Pearson correlation coefficients were computed to examine the strength of association between the CAMCOG Total Score and the two MMSE test scores (collected as part of the screening protocol or derived directly from the CAMCOG).

CAMCOG

The CAMCOG was administered to all subjects. The CAMCOG follows a structured interview format that includes assessment in the areas of Orientation, Language (Comprehension and Expression), Memory (Remote, Recent, and New Learning), Attention/Calculation, Praxis, Abstract Thinking, Perception, and Executive Function. The top score on the instrument is 105 points with higher scores representing increased cognitive function. A cutoff score of < 80 was originally considered suggestive

of cognitive impairment. All questions that are not able to be answered by subjects are coded as 0 values, regardless of reason, with lower scores on the test being representative of decreased function.

This revised version of the test is an improvement over the original, in that it expands on the Executive Function section to improve sensitivity. Originally, the test was limited to category fluency for animals with an abstraction, or similarities, subcomponent. This was expanded in the current version to include ideational fluency (how many different uses can you think of for a bottle) and a visual reasoning task. This raised the score of the section from 14 to 28 points, which does not contribute to the total score on the CAMCOG. In addition, improvements were made to the visual-perceptual subsection of the test.

Because the test was developed in England there were 4 questions that were inappropriate for U.S. natives. The following alterations were made to account for these differences:

Question 172: "What is the name of the present King or Queen?"

Changed to: "What is the name of the current president of the United States?"

Question 173: "Who is likely to be the next King or Queen?"

Changed to: "Who is likely to be the next President of the United States?"

Question 174: "What is the name of the Prime Minister?"

Changed to: "What is the name of the Vice-President of the United States?"

Questions 195: If somebody went shopping and was given 15 pence as change from £1, how much did they spend?

Changed to: "If somebody went shopping and was given 15 cents as change from $1.00, how much did they spend?"

The CAMCOG also incorporates all questions from the MMSE, and a score is derived directly from the instrument.

MMSE

Even though an MMSE score is derived directly from the CAMCOG an independently administered MMSE was given to all subjects as part of the screening procedure to determine study eligibility. A second reason for doing this was to examine the reliability of a separately administered MMSE to that incorporated into the larger CAMCOG test in this population. While the MMSE portion of the CAMCOG has been validated, as part of other studies, we were concerned that in this frail older population the test would be affected by administration time and test complexity. Our prior work suggests that the increased administration time of the larger test might effect the overall scoring so that there is a bias to receive a lower MMSE score when presented as part of the larger CAMCOG where MMSE questions are distributed throughout the test.

All non-responses to MMSE items were converted to zero values (incorrect responses) regardless of whether participants were unable to complete items due to cognitive related deficits or physical limitations. For example, a subject with a history of stroke presenting with partial paralysis might be unable to complete praxis question 20, "copy figure". This scoring method would assign a 0 value even though the subject was clearly unable to respond due to a pre-existing co-morbid condition, unrelated to cognition. Lower scores, on the MMSE, were associated with increased cognitive impairment. While this scoring method may inherently include a bias to classify borderline subjects with dementia, we utilized this method because of both clinical convention and prior research where scoring non-response items as errors was found to provide more accurate scoring than a score limited to answerable items (Fillenbaum, George, & Blazer, 1988).

CDR

The CDR is frequently used for the staging of dementia in different populations, relying on assessments of both cognitive and behavioral domains and a cohort interview, making it less susceptible to bias from co-morbid conditions. The CDR is commonly used, in research studies, for the assessment of dementia in the nursing home setting and is part of the Uniform Data Set (Morris et al., 2006) collected by The National Alzheimer's Coordinating Center (Beekly et al., 2004). We utilized the 7-point version of the CDR, which is more appropriate for our population and has been used by NIH funded Aging and Dementia Research Centers around the U.S. This version of the CDR is scored with

0 = No Impairment, 0.5 = Questionable, 1 = Mild Dementia, 2 = Moderate Dementia, 3 = Severe Dementia, 4 = Profound Dementia, and 5 = Terminal. Terminal ratings are indicative of loss of ability to respond, comprehend, and recognize, requiring feeding, being bedridden, and suffering from contractures.

Results

Demographics

Study subjects had an overall mean age of 85±9 with an education level of 13±2 years. Females made up 58% of the study group. The sample was primarily composed of White subjects (82%), followed by Blacks (14%), then Hispanic (2%). We observed differences for age between the CTL and DEM groups (80±9 and 91±8 years, respectively). We also observed gender differences between the DEM and PD groups (X^2 (1) = 8.6, p≤ .01). There were no significant differences for education and ethnicity (see Table 1).

The MMSE scores for the DEM and PD-DEM groups (19±3 and 17±4, respectively) differed significantly from the CTL and PD groups without dementia (26±2 and 25±1, respectively), but not from each other, meaning that the two dementia groups were comparable with regard to gross cognitive ability. This pattern was replicated by the CDR scores.

Test Administration

The average time to administer the CAMCOG was 48±16 (range 23-99) minutes. Unexpectedly, the longest time was for the CTL group (53±22). Based on the coordinator report, and a review of records, we discovered that two subjects had a maximum test time of 99 minutes which was not related to test difficulty but an increased amount of interaction with the subject asking the tester questions and wanting to discuss the testing procedure and other non-test related issues. The tester repeatedly attempted to redirect the subject to the testing task but decided that conversing with the subject would lead to the most valid test results. If we drop these two subjects from the analysis, the mean for the group decreases to 48±16 minutes for the CTL group with the overall mean across groups dropping to 46±13 minutes. After the CTL group the PD-DEM group was the next longest followed by the DEM, and PD groups (48±9, 45±10, and 44±19, respectively).

Subjects also generally reported that they enjoyed the testing experience and would participate in future studies.

CAMCOG

Skewness and kurtosis measures were computed for each item and values greater than two standard error units were observed for a number of items. The majority of items were negatively skewed, and we applied a squared transformation on all data.

Dispersion measures were recomputed and were within appropriate limits for these analyses.

Group differences for the individual cognitive domains were examined. Initially, an Omnibus F test was computed for each domain. When the F value was significant we computed two group posthoc comparisons using an ANCOVA with covariates for age and gender in each model.

All data was analyzed using both the original and transformed data. For all comparisons across all items only one difference between the original and transformed data was observed. This was for the Attention/Calculation measure between the CTL and DEM groups, which was not significant with the transformed data. For the ease of interpretation we present our results as non-covariate adjusted, untransformed data, for all analyses described in the text (see Table 2). We also present means, adjusted for age and gender, in Table 3.

In our initial overall Omnibus F tests we observed that Remote Memory, Abstract Thinking, and Perception were not significant (p's $> .05$). We also observed that all items meeting criteria to pass the Ominibus F significantly differentiated the CTL from DEM group except for Attention/Calculation where we observed a trend ($p<.1$) with the CTL group showing superior performance over the DEM group (7.3 ± 1.9, 5.2 ± 2.4, respectively).

Orientation

This domain was sensitive to cognitive deficits related to dementia. All comparisons between the non-dementia (CTL and PD) and dementia groups (DEM and PD-DEM) were significant, while comparisons within dementia groups (DEM and PD-DEM) were not different (see Table 4). The means ranged from 9.4±0.9 in the CTL group to 5.2±2.0 in the PD-DEM group, based on a maximum score of 10.

Language

Differences were observed for Comprehension between the CTL with DEM and PD-DEM groups. The DEM group showed the greatest deficit for this item (6.7±1.2) as compared to the CTL group exhibiting the most intact ability (8.1±1.1). While performance between the CTL group was better than that of the two dementia groups the PD group performed at the same level as the PD group with dementia (PD-DEM).

Expression, which includes questions such a naming common objects, category fluency, definitions, and repetition was not as sensitive in differentiating our groups. The only significant difference observed was between the PD and DEM groups (15.9±2.0 and 14.4±2.6, respectively). The two groups with dementia scored only slightly worse than the CTL and PD groups with the PD group showing the most intact behavior.

Memory

Memory is the second most extensive category represented on the CAMCOG after Language. On the overall Omnibus F test we observed that Remote Memory was similar for all groups and is not presented.

Recent Memory was sensitive to dementia and differentiated both DEM and PD-DEM (1.5±1.5 and 2.3±1.2, respectively) from the non-dementia CTL and PD Groups (3.6±0.6 and 3.4±0.7, respectively).

New Learning which includes items such as recall and recognition of pictures and recall of address, is the only domain to differentiate the DEM and PD-DEM groups, with the DEM group scoring substantially worse on this task (4.1±2.9 and 7.3±3.0, respectively). While the CTL group performed better than the DEM group they did not perform significantly better than the PD and PD-DEM groups.

Attention/Calculation

Attention/Calculation was the only item where the PD-DEM group showed a greater deficit than the DEM group (3.4±2.2 and 5.2±2.4, respectively). For this item the DEM group performed at the same level as the CTL and PD groups (7.3±1.9 and 6.4±1.9, respectively) who performed significantly better than the PD-DEM group.

Praxis

The only group difference we observed was for the CTL and DEM groups (9.6±2.2 and 6.7±1.9, respectively). While the CTL group performed slightly better than the PD and PD-DEM groups this difference did not approach significance.

Executive Function

The DEM group (9.6±3.7) performed significantly worse than the CTL and PD groups (14.4±3.6 and 15.0±4.0, respectively). While the PD-DEM group (11.0±3.7) performed worse than PD group their performance was comparable to the CTL group.

Total Score

The combined total score was sensitive to differentiating changes related to dementia. All comparisons between the non-dementia (CTL and PD) groups and dementia groups (DEM and PD-DEM) were significant while the comparisons within dementia groups (DEM and PD-DEM) were not different. As expected, performance was best in the CTL group who scored 79.8±9.7 as compared to the DEM and PD-DEM groups (52.2±14.6, 60.9±11.5, respectively) based on a maximum score of 105.

MMSE

We compared MMSE scores from administrations given as part of the CAMCOG with that given as part of the subject screening procedure. We observed a correlation between the two MMSE tests across the combined groups of r=.71 ($p \leq .001$). The MMSE derived directly from the CAMCOG was highly correlated with the CAMCOG Total Score (r=.87, $p \leq .001$), while the correlation between the Total Score and the MMSE administered during the screening procedure was only r=.65 ($p \leq .001$). In order, to determine if this relationship was consistent within each of these groups we examined the correlations by group and observed values between the two MMSE measures ranged from r=.52 in the CTL group to -.09 in the DEM group. The strongest relationship between the two measures was found in the CTL and PD-DEM groups (r's = .52 and .34, respectively). Across groups, 56% of subjects scored higher on the MMSE given at the time of screening. Score differences ranged from 0-13 points.

Discussion

In this study the use of the CAMCOG was examined in a frail elderly LTC population. The study population consisted of CTL, Dementia, and PD subjects. PD subjects were included in the study to examine the test accuracy when administered to a subgroup with impaired physical ability. It would also allow for the determination of whether deficits reported previously for Executive Function and Visuospatial abilities would be replicated in an older frail population with PD (Cormack, Aarsland, Ballard, &

Tovée, 2004; Richards, Cote, & Stern, 1993a, , 1993b). The administration time was longer than reported in some other studies, averaging 47±16 minutes to complete, but were within acceptable limits. Longer administration times in the CTL group were reflective of the positive interaction between tester and subject.

An analysis of the overall CAMCOG score showed lower scores in our population than those previously reported. Traditionally, a cutoff score of < 80 has been used to reflect cognitive impairment. In our study we observed that the average score on the CAMCOG for the CTL group was 80±10, with 50% of the group scoring below 80 (range 95-65). A second normative study has reported age and gender adjusted median CAMCOG values which we applied to our sample (Williams, Huppert, Matthews, Nickson, & CFAS), 2003). Application of these adjusted values again shows that our group means are lower than the median values provided. This may be a result of the inability of many of the frail elderly to respond to a number of items on the CAMCOG due to non-cognitive co-morbid conditions that would effect scoring of the CAMCOG because missing items are coded as zero values. While not as sensitive to the effects of these physical conditions as the MMSE it still requires adjustments to the scoring algorithm to accommodate these conditions.

While the MMSE has shown good test-retest reliability over 12 months (Olin & Zelinski, 1991) a comparison between MMSE scores derived directly from the CAMCOG and those administered as part of the subject screening procedure were examined. This was done to determine if there was a bias towards lower MMSE scores

when administered as part of the CAMCOG which is a lengthier test and may be affected by subject frailty which should be correlated with administration time. This was not the case, even though both tests in our sample were administered an average of 11 days apart, suggesting that the association between the two MMSE administrations is based on the disease reflected in the groups under study. While the correlation between the two measures was good across all subjects (r=.75), the relationship between the two administrations of the test were significantly lower when examined within each group. The strongest test-retest reliability was observed in the CTL and PD-DEM groups (r's = .52 and .34, respectively). When examined in the DEM and PD groups these values approached 0, showing that an independent administration of the MMSE did not correlate with the one administered within approximately 11 days as part of the CAMCOG. While studies in other populations show good test-retest reliability for the MMSE, the age-related non-cognitive deficits in the LTC population decreases the reliability of brief single-administration tests in both cross-sectional and longitudinal studies. Specifically, the population is prone to issues related to frailty which may include increased fluctuations in the individual's physical health which can affect attentional ability at a specific time of testing. This was substantiated when we examined the relationship between CAMCOG administration time with scores on the MMSE derived from the CAMCOG. We did not observe any significant correlations (p's > .1), supporting a possible confound affecting test reliability which is not attributable to testing time.

This was again substantiated by the lack of observed differences using the CAMCOG to measure Attention in the DEM group when compared to the CTL and PD

groups without dementia. This forces us to rethink our assumptions about test-retest reliability in this population, and requires the need for further study of which specific factors affect these differences and how they can be controlled.

To determine whether the CAMCOG was able to differentiate across diagnostic groups we examined mean differences between CTL, PD, and dementia groups with and without PD. We observed that Remote Memory, Abstract Thinking, and Perception did not differentiate groups in our study. Our population represents an older, frail subgroup of subjects than those reported in the literature, while there are reports of Remote Memory being stable in older populations with mild dementia we observe the general pattern expected in that the CTL and PD groups show the most intact scores with the DEM group exhibiting the greatest amount of generalized deficits. The lack of sensitivity of this measure may be related to the fact that it is dependent on only 6 questions which are valued at 1 point each. This may not provide enough variability to accurately diagnose this population for this domain. Abstract Thinking is based on questions looking at similarities of objects such as two types of fruit, and was fairly well preserved across groups. Originally, sensitivity for perceptual items was expected. While this item was not statistically significant the observed means were consistent with the CTL group being the most intact followed by the PD, PD-DEM, and DEM groups, which was consistent with the overall cognitive profile across these groups.

Orientation, Recent Memory, and the Total Score provided the most consistent observable differences for groups with and without dementia. However, they were not sensitive to PD and related motor deficits.

The DEM group showed consistently poorer performance on all items except Attention/Calculation. For this item, the most severe deficits were observed in the PD-DEM group. The only significant differences existed between the NL and PD non-demented groups with the PD-DEM group. While the DEM group scored lower than the NL and PD groups this difference did not reach statistical significance.

New Learning was the only item that differentiated the DEM from PD-DEM groups. This may be a potentially important finding because it may provide a link to understanding differences that exist between the cognitive profile of patient groups with AD versus PD with dementia. Our review of the clinical diagnosis of dementia type in these two groups found 15% of cases, in the DEM group, where caused by an unknown etiology other than AD or vascular dementia. The PD-DEM group had a prevalence of 42% with unknown etiologies. This may provide a link to distinguishing PD dementia cases from AD cases as well as the associated neuropathological pathways that may contribute to the high occurrence of dementia in PD.

Praxis only differentiated the CTL and DEM groups. The DEM group had the greatest deficit on this item followed by the PD groups. While the PD groups were expected to exhibit the greatest deficits in this domain, there are prior findings that have

reported on the motor deficits associated with both DEM and PD, as well as age. These may contribute to the inability of subjects to respond to questions as a consequence of these impairments. We notice that the CTL group mean was 9.6±2.2 out of 12 points. Scores in this group ranged from 5-11, showing an inability even in the CTL subjects to answer many questions in this category, which may be due to non-cognitive co-morbid conditions affecting their ability to respond.

The use of the CAMCOG is substantiated for the identification of cognitive deficits in the LTC population. Remedial aides such as microphones and magnifiers can be used to accommodate patients with identified physical deficits such as hearing and vision loss. However, there are a number of physical conditions that impact the use of certain items on the instrument, such as Praxis. While the CAMCOG alleviates some of the problems found in the earlier version of the instrument, or in the MMSE, such as ceiling effects and a decreased range of variability for items, further modifications are necessary. The instrument must account for affected mobility in age-related diseases such as osteoarthritis as well as the need for increased variability in items related to Remote Memory, Perception and Abstract Thinking.

Conclusions

While the CAMCOG is a comprehensive cognitive assessment instrument that has gained wide acceptance in other countries, to date it has failed to gain wide acceptance in this country. This is true even though there are many studies which have examined the

reliability and validity of the instrument across different population groups. Assessment strategies in this country favor the utilization of multiple tests which focus on the assessment of individual cognitive domains. While this strategy is conceptually sound, the LTC environment would benefit from the use of more comprehensive instruments when assessment time is limited and staffing caseloads are often high due to state mandated regulations and testing may be delegated to junior clinical staff or outsourced to companies not as familiar with the patients they treat, relying more on the use of accurate assessment instruments.

The CAMCOG seems a likely candidate to fill this need. It has been tested with AD and PD populations who exhibit known disease related cognitive and movement deficits where it has been shown to be sensitive to detecting early cognitive changes in these populations. Because the frail elderly have a high prevalence of movement deficits related to co-morbid conditions an instrument shown to be sensitive and valid in similar populations should be appropriate for inclusion in any test battery administered in the LTC environment.

This instrument is sensitive to differentiating cognitive decline associated with dementia in this population. Differences in the acquisition of new information (New Learning), as measured in this instrument, may also be sensitive to the differentiation of mixed dementia from dementias associated with or concurrent with PD.

As part of this study protocol the MMSE was administered as part of the screening protocol. When examined, differences of up to 13 points were observed between this MMSE and the MMSE derived directly from the CAMCOG. These differences were not related to the length of the CAMCOG administration and highlight issues, not related to the CAMCOG, but to test reliability in this population. Reliability in this population may be directly related to frailty, which effects attention and other factors necessary for an accurate testing outcome. It may be necessary to change testing strategies using instruments such as the CAMCOG, and even the MMSE, where testing is repeated over very brief periods of time and averaged, in order to provide accurate assessment information.

While the instrument shows promise for use in the LTC environment we also observed that our subjects scored lower than expected relative to published normative data controlling for age, gender, and education. It may be necessary to adjust the published normative data to account for levels of frailty in order for this instrument to be truly useful as a diagnostic tool in this population.

We acknowledge that our sample sizes were small and require replication studies to substantiate these findings. We also hope that this study initiates future research in the U.S. with this instrument in the LTC environment. We also hope that issues raised with regard to test reliability and the need for innovative test strategies be studied in this population.

Table 1

Demographics

Group	n	Age	Education	% Female	% White	% Black	% Hispanic
CTL	16	80±9[A]	13±2	62	75	12	6
DEM	13	91±8	12±3	85	85	15	0
PD	9	82±8	12±1	22 [B]	100	0.0	0
PD-DEM	12	85±7	13±2	50	75	25	0
Overall	50	85±9	13±2	58	82	14	2

[A] Statistically Different from DEM ($F[3,46] = 4.6$, $p \leq .01$)
[B] Statistically Different from DEM ($X^2(3) = 9.0$, $p \leq .05$)

Table 2

Distribution of Actual Mean Scores (± Standard Deviation) for CAMCOG Domains

DOMAIN		GROUPS			
	Omnibus F	**CTL**	**DEM**	**PD**	**PD-DEM**
Orientation	F = 112, p≤.01	9.4±0.9	5.5±2.7	8.7±1.3	5.2±2.0
Language					
Comprehension	F = 5.1, p≤.1	8.1±1.1	6.7±1.2	7.9±1.1	7.3±1.4
Expression	F = 3.2, p≤.5	14.7±2.6	11.5±4.3	15.9±2.0	14.2±2.3
Memory					
Remote	F = 2.2, p≤ .1	4.4±1.1	2.6±1.7	4.4±1.5	3.5±1.5
Recent	F = 7.7, p≤.001	3.6±0.6	1.5±1.5	3.4±0.7	2.3±1.2
New Learning	F = 6.6, p≤.001	9.8±3.2	4.1±2.9	9.7±2.8	7.3±3.0
Attention/ Calculation	F = 7.6, p≤.001	7.3±1.9	5.2±2.4	6.4±1.9	3.4±2.2
Praxis	F = 4.3, p≤.01	9.6±2.2	6.7±1.9	7.8±2.6	7.8±2.4
Abstract Thinking	F = 0.8, NS	5.9±1.7	4.5±2.0	6.0±1.4	5.2±2.1
Perception	F = 2.5, p≤.1	6.9±1.5	3.9±3.1	5.4±1.5	4.6±2.1
Executive Function	F = 3.9, p≤.05	14.4±3.6	9.6±3.7	15.0±4.0	11.0±3.7
Total Score	F = 11.2, p≤001	79.8±9.7	52.2±14.6	75.7±9.6	60.9±11.5

Table 3

Distribution of Age and Gender Corrected Mean Scores (±Standard Deviation) for CAMCOG Domains

DOMAIN	GROUPS			
	CTL	DEM	PD	PD-DEM
Orientation	9.5±1.9	5.4±2.0	8.6±1.9	5.2±1.8
Language Comprehension	8.3±1.2	6.4±1.3	8.0±1.2	7.3±1.2
Expression	14.5±3.2	11.7±3.3	15.9±3.1	14.3±3.0
Memory Remote	4.2±1.5	2.9±1.6	4.4±1.4	3.5±1.4
Recent	3.6±1.2	1.6±1.2	3.4±1.1	2.3±1.1
New Learning	9.7±3.3	4.3±3.4	9.6±3.1	7.4±3.1
Attention/ Calculation	7.3±2.3	5.1±2.3	6.5±2.2	3.4±2.2
Praxis	9.8±2.4	6.4±2.5	7.8±2.3	7.8±2.3
Abstract Thinking	5.8±2.0	4.8±2.0	6.0±1.9	5.2±1.8
Perception	6.6±2.2	4.4±2.1	5.3±2.1	4.6±2.1
Executive Function	14.1±4.0	10.0±4.1	15.0±3.8	11.0±3.8
Total Score	79.3±12.5	53.0±12.8	75.4±11.9	61.0±11.8

Table 4

Distribution of Alpha Values for Post Hoc Comparisons for All Significant F Tests Based on Square Transformed Values

DOMAIN	GROUPS					
	CTL/ DEM	CTL/ PD	CTL/ PD-DEM	DEM/ PD	DEM/ PD-DEM	PD/ PD-DEM
Orientation	p≤.001	NS	p≤.001	p≤.01	NS	p≤.001
Language						
Comprehension	p≤.001	NS	p≤.05	P≤.05	NS	NS
Expression	NS	NS	NS	p≤.01	NS	NS
Memory						
Remote						
Recent	p≤.001	NS	p≤.01	p≤.01	NS	p≤.05
New Learning	p≤.001	NS	NS	p≤.01	p≤.05	p≤.05
Attention/ Calculation	NS	NS	p≤.001	NS	NS	p≤.01
Praxis	p≤.01	NS	NS	NS	NS	NS
Abstract Thinking						
Perception						
Executive Function	p≤.05	NS	NS	p≤.05		p≤.05
Total Score	p≤.001	NS	p≤.001	p≤.001	NS	p≤.01

References

American Association of Homes and Services for the Aging. (2007). Aging Services: The Facts.

Athey, R. J., Porter, R. W., & Walker, R. W. (2005). Cognitive assessment of a representative community population with Parkinson's disease (PD) using the Cambridge Cognitive Assessment-Revised (CAMCOG-R). *Age and Ageing, 34*, 268-273.

Athey, R. J., & Walker, R. W. (2006). Demonstration of cognitive decline in Parkinson's disease using the Cambridge Cognitive Assessment (Revised) (CAMCOG-R). *International Journal of Geriatric Psychiatry, 21*, 977-982.

Ball, S. L., Holland, A. J., Huppert, F. A., Treppner, P., Watson, P., & Hon, J. (2004). The modified CAMDEX informant interview is a valid and reliable tool for use in the diagnosis of dementia in adults with Down's syndrome. *Journal of Intellectual Disability Research, 48*(6), 611-620.

Ballard, C., O'Brien, J., Morris, C. M., Barber, R., Swann, A., Neill, D., et al. (2001). The progression of cognitive impairment in dementia with Lewy bodies, vascular dementia and Alzheimer's disease. *International Journal of Geriatric Psychiatry, 16*, 499-503.

Ballard, C. G., Morris, C. M., Rao, H., O'Brien, J. T., Barber, R., Stephens, S., et al. (2004). APOE e4 and cognitive decline in older stroke patients with early cognitive impairment. *Neurology, 63*, 1399-1402.

Beekly, D. L., Ramos, E. M., van Belle, G., Deitrich, W., Clark, A. D., Jacka, M. E., et al. (2004). The National Alzheimer's Coordinating Center (NACC) Database: An

Alzheimer's disease database. *Alzheimer Disease and Associated Disorders, 18*(4), 270-277.

Centers for Disease Control and Prevention, National Center for Health Statistics,. (2006). CDC Trends in Health and Aging. In U.S. Department of Health and Human Services (Ed.).

Cormack, F., Aarsland, D., Ballard, C., & Tovée, M. J. (2004). Pentagon drawing and neuropsychological performance in Dementia with Lewy Bodies, Alzheimer's disease, Parkinson's disease and Parkinson's disease with dementia. *International Journal of Geriatric Psychiatry, 19*, 371-377.

Cullum, S., Huppert, F. A., McGee, M., Dening, T., Ahmed, A., Paykel, E. S., et al. (2000). Decline across different domains of cognitive function in normal ageing: Results of a longitudinal population-based study using CAMCOG. *International Journal of Geriatric Psychiatry, 15*, 853-862.

Espinoza, R. T. (2006). Improving the recognition and management of dementia in long-term care: Obstacles and opportunities. *Journal of the American Medical Directors Association, 7*(2), 128-130.

Fillenbaum, G. G., George, L. K., & Blazer, D. G. (1988). Scoring nonresponse on the Mini-Mental Status Examination. *Psychological Medicine, 18*, 1021-1025.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "MINI-MENTAL STATE" A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Frankfort, S. V., Appels, B. A., de Boer, A., Tulner, L. R., van Campen, J. P. C. M., Koks, C. H. W., et al. (2007). Identification of responders and reactive domains to

rivastigmine in Alzheimer's disease. *Pharmacoepidemiology and Drug Safety, 16*, 545-551.

Garre-Olmo, J., López-Pousa, S., Vilalta-Franch, J., Turon-Estrada, A., Lozano-Gallego, M., Hernández-Ferràndiz, M., et al. (2004). Neuropsychological profile of Alzheimer's disease in women: moderate and moderately severe cognitive decline. *Archives of Women's Mental Health, 7*, 27-36.

Graham, C., Ballard, C., & Saad, K. (1997). Variables which distinguish patients fulfilling clinical criteria for dementia with Lewy Bodies from those with Alzheimer's disease. *International Journal of Geriatric Psychiatry, 12*, 314-318.

Hartman, J. A. (2000). Investigation of the use of the CAMCOG in the visually impaired elderly. *International Journal of Geriatric Psychiatry, 15*, 863-869.

Heinik, J., Werner, P., Mendel, A., Raikher, B., & Bleich, A. (1999). The Cambridge Cognitive Examination (CAMCOG): Validation of the hebrew version in elderly demented patients. *International Journal of Geriatric Psychiatry, 14*, 1006-1013.

Hobson, P., & Meara, J. (1999). The detection of dementia and cognitive impairment in a community population of elderly people with Parkinson's disease by use of the CAMCOG neuropsychological test. *Age and Ageing, 28*, 39-43.

Hobson, P., & Meara, J. (2004). Risk and incidence of dementia in a cohort of older subjects with Parkinson's disease in the United Kingdom. *Movement Disorders, 19*(9), 1043-1049.

Jonkers, C., Schmand, B., Lindeboom, J., Havekes, L. M., & Launer, L. J. (1998). Association between Apolipoprotein E e4 and the rate of cognitive decline in

community-dwelling elderly individuals with and without dementia. *Archives of Neurology, 55*, 1065-1069.

Kurz, A., Egensperger, R., Haupt, M., Lautenschlager, N., Romero, B., Graeber, M. B., et al. (1996). Apolipoprotein E e4 allele, cognitive decline, and deterioration of everyday performance in Alzheimer's disease. *Neurology, 47*, 440-443.

Leeds, L., Meara, R. J., Woods, R., & Hobson, J. P. (2001). A comparison of the new executive functioning domains of the CAMCOG-R with existing tests of executive function in elderly stroke survivors. *Age and Ageing, 30*, 251-254.

Levy, G., Jacobs, D. M., Tang, M.-X., Cote, L. J., Louis, E. D., Alfaro, B., et al. (2002). Memory and executive function impairment predict dementia in Parkinson's disease. *Movement Disorders, 17*(6), 1221-1226.

Morris, J. C. (1993). The Clinical Dementia Rating (CDR): Current version and scoring rules. *Neurology, 43*(1), 2412-2414.

Morris, J. C., Weintraub, S., Chui, H. C., Cummings, J., DeCarli, C., Ferris, S., et al. (2006). The Uniform Data Set (UDS): Clinical and cognitive variables and descriptive data from Alzheimer's Disease Centers. *Alzheimer Disease and Associated Disorders, 20*(4), 210-216.

Nielsen, H., Lolk, A., Andersen, K., Andersen, J., & Kragh-Sørensen, P. (1999). Characteristics of elderly who develop Alzheimer's disease during the next two years--A neuropsychological study using CAMCOG. The Odense Study. *International Journal of Geriatric Psychiatry, 14*, 957-963.

Olin, J. T., & Zelinski, E. M. (1991). The 12-month reliability of the Mini-Mental State Examination. *Psychological Assessment, 3*(3), 427-432.

Raven, J. C. (1982). *Revised manual for Raven's Coloured Progressive Matrices*. Windsor:UK: NFER-Nelson.

Richards, M., Cote, L. J., & Stern, Y. (1993a). Executive function in Parkinson's disease: Set-shifting or set-maintenance? *Journal of Clinical & Experimental Neuropsychology, 15*(2), 266-279.

Richards, M., Cote, L. J., & Stern, Y. (1993b). The relationship between visuospatial ability and perceptual motor function in Parkinson's disease. *Journal of Neurology, Neurosurgery, & Psychiatry, 56*(4), 400-406.

Roth, M., Huppert, F. A., Mountjoy, C. Q., & Tym, E. (1998). *CAMDEX-R: The Cambridge Examination for Mental Disorders of the Elderly*. Cambridge: Cambridge University Press.

Schmand, B., Walstra, G., Lindeboom, J., Teunisse, S., & Jonkers, C. (2000). Early detection of Alzheimer's disease using the Cambridge Cognitive Examination (CAMCOG). *Psychological Medicine, 30*, 619-627.

Singer, C., & Luxenberg, J. (2003). Diagnosing dementia in long-term care facilities. *Journal of the American Medical Directors Association, Supplement 1, 4*(6), S134-S140.

SPSS for Windows Release 14.0.2. (Version (17 Mar 2006)).

Tam, C. W. C., Burton, E. J., McKeith, I. G., Burn, D. J., & O'Brien, J. T. (2005). Temporal lobe atrophy on MRI in Parkinson's disease with dementia. *Neurology, 64*, 861-865.

Tse, W., Libow, L. S., Neufeld, R., Lesser, G., Frank, J., Dolan, S., et al. (In Press). Prevalence of movement disorders in an elderly nursing home population. *Archives of Gerontology and Geriatrics*.

U.S. Department of Health and Human Services Administration on Aging. (2006). *A statistical profile of Hispanic older Americans aged 65 +*

Washburn, l. A. M., Sands, L. P., & Walton, P. J. (2003). Assessment of social cognition in frail older adults and its association with social functioning in the nursing home. *The Gerontologist, 43*(2), 203-212.

Williams, J. G., Huppert, F. A., Matthews, F. E., Nickson, J., & CFAS), M. C. F. a. A. S. M. (2003). Performance and normative values of a concise neuropsychological test (CAMCOG) in an elderly population study. *International Journal of Geriatric Psychiatry, 18*, 631-644.

Chapter 4

A Memory Intervention for Mild Cognitive Impairment in Long-Term Care: Preliminary Findings

Abstract

Objective

The primary objective of this study was to examine the use of a computerized memory intervention in frail elderly (≥ 75 years) long-term care (LTC) residents with Mild Cognitive Impairment (MCI). The aims of the study were two-fold: first to determine whether an intervention over a period of time longer than traditionally done in this setting would be practical and useful for a frail elderly LTC population. Secondly, to examine whether any cognitive benefits, especially to memory, could be derived from this type of intervention aimed at improving hippocampal and/or entorhinal cortex function while using a paradigm structured to require minimal weekly time commitments.

Methods

In total, 20 subjects meeting criteria for MCI will be recruited and are randomly assigned to an experimental (n=10) or control (n=10) group. Both groups attend 45-minute computer sessions 1x/week for 12 weeks with the experimental group receiving a series of presentations aimed at activating the entorhinal/hippocampal areas of the brain. All subjects are assessed with the ADAS-COG at baseline, 6 weeks, 12

weeks, and 1-month post-study. Subjects also receive an assessment of Activities of Daily Living, and a study satisfaction questionnaire.

Results

To date 8 subjects have been recruited. The mean age was 84±6 years of age. Mean education level was 14±2 years (range 12-16), and 75% of subjects were female. Subjects were collapsed across groups and percent difference scores were computed between baseline and timepoint-3 (week 12). Improvements greater than 15% were observed for Orientation (60%), Naming (50%), Visual Search Task (18%), and Constructional Praxis (17%).

Conclusions

Based on these preliminary results, the feasibility of interventions of this type and length are questionable because of the frailty of this population. Out of the 10 subjects originally recruited two were dropped prior to the start of the intervention due to adverse health events. For the remaining 8 subjects there were 3 serious adverse events reported that required hospitalizations. The preliminary results from this study are positive but support shorter term interventions. The use of a computer is viable and effective. Because scheduling remains difficult the use of a flexible "memory clinic" structure, would be more effective. In addition, because of the low prevalence of MCI any intervention incorporated into the structure of a LTC facility would need to include

Residents with mild or mild-severe dementia as part of the target population to justify facility resources.

Introduction

The purpose of this study was to examine the use of a computerized memory intervention based on the consolidation of stimuli in the hippocampal area of the brain in frail elderly (≥ 75 years) long-term care (LTC) residents with Mild Cognitive Impairment (MCI). These individuals are at increased risk for developing Dementia of the Alzheimer's Type (DAT). The aims of the study were two-fold: first to examine whether an intervention over a period of time longer than traditionally done in this setting would be practical and useful for a frail elderly LTC population. This study is structured to require weekly 45-minute sessions over 12-weeks with either an intervention or control task. Information derived from this study is intended to tell us how well Residents (individuals living in a nursing home) are able, and agreeable, to tolerate non-pharmacologic interventions requiring extended time commitments. Twelve week interventions have been shown to be sufficient for observable cognitive changes with associated neuronal sprouting during pharmacologic interventions. While this is a non-pharmacologic intervention longer periods of active subject participation may not be practical or realistic with this population due to Resident frailty. We will also ascertain the usefulness of integrating a computerized intervention which would serve to standardize the presentation of the intervention, minimize staff involvement, and provide a cost-effective memory enhancement program within the LTC environment. The second purpose of the study was to examine whether any cognitive benefits, especially to memory, could be derived from this type of intervention aimed at improving

hippocampal and entorhinal cortex function while using a paradigm that was structured to require minimal weekly time commitments from Residents.

The elderly segment of the population has the highest risk for dementia and other disorders. In the United States, the population over the age of 65 is the fastest growing segment of the population with an 11-fold increase since the beginning of the last century. This is in contrast to a 3-fold increase in those under age 65. It is expected that by the year by the year 2020, 12 million older Americans will need LTC (American Association of Homes and Services for the Aging, 2007) making interventions which improve age-related memory deficits essential.

Individuals with MCI exhibit cognitive deficits primarily in memory, inconsistent with their age and education, while remaining intact on activities of daily living (ADL), and do not exhibit clinical criteria for dementia (Petersen, 1995; Petersen et al., 1999; Reisberg, Ferris, de Leon, & Crook, 1982). This group is thought to be in a transitional state between normal aging and mild dementia (American Psychiatric Association, 1994) and are at increased risk for future decline to Alzheimer's disease (AD) (Kluger, Ferris, Golomb, Mittelman, & Reisberg, 1999) . The types of memory deficits observed in MCI are consistent with the areas of the brain that have been observed to change early in the course of AD (Sramek, Veroff, & Cutler, 2000).

While the use of memory training interventions has been studied and integrated into standardized programs, studies have not examined alternative interventions more

appropriate for the older LTC Resident with MCI (Camp et al., 1993; Wolinsky et al., 2006). This study focuses on a growing segment of the population that is older and frailer than those generally studied.

The intent of this study was to examine a memory enhancement intervention within a LTC setting that would last long enough to provide Resident benefit and would then be incorporated into a "memory clinic" that could be self-initiated by Residents with minimal staffing costs. The intervention consists of an interactive computerized set of stimuli that may activate the hippocampus and entorhinal cortex. These regions of the brain have been implicated in the early memory changes observed in MCI and AD (Bobinski et al., 1999; Convit, Wolf, Tarshish, & De Leon, 2003; de Leon et al., 2006; De Santi et al., 2001; Golomb et al., 1993; Golomb et al., 1994; Golomb et al., 1996). The intervention is structured so that it can be administered by a variety of LTC facility staff with minimal training. While the majority of memory enhancing interventions involves either exercises centered on social interaction, or commercially published memory exercises, many are inappropriate for this population because of age, and disease related attention and physical limitations. This intervention utilizes larger visual stimuli, broader hand response movements, and shorter session durations to increase cooperation and effectiveness.

This study is important because it examines the use of a memory intervention program that is appropriate for the LTC population accounting for both behavioral and physical limitations that differ from more readily studied younger healthier populations.

It also addresses a group of subjects that are at high risk for developing dementia, impacting severely on their quality of life as well as the health care system via increasing facility and tax-payer health-related costs.

As the nursing home becomes more central to serving the geriatric community, it is extremely important for these centers to provide new effective, practical, and affordable interventions for age related diseases such as AD, before it is too late for treatment. Studies involving the geriatric population are extremely important because the elderly represent both the fastest growing segment of our population and have the highest risk for developing both cognitive and medical disorders. The elderly can be expected to increasingly become candidates for diagnostic and therapeutic procedures in the near future.

Methods

This study is being conducted, at the Jewish Home & Hospital Lifecare System (JHHLCS) Manhattan campus. The JHHLCS is the largest non-profit academically-affiliated long-term care facility in the United States. This study was approved by the JHHLCS and Mount Sinai School of Medicine Institutional Review Boards.

Procedures

In total, 20 subjects meeting criteria for MCI will be recruited. Previous studies with subjects meeting these criteria show that they have an increased risk of up to 12-fold for developing dementia relative to the general normal successfully aging geriatric population (Golomb et al., 1993). While up to 70% of LTC residents may have dementia (predominately AD) the remaining 30%, who are considered non-demented, include the MCI group, and are at increased risk for developing dementia over the course of their stay. While this intervention focuses on residents with MCI it may also be valuable for residents with mild dementia, thereby increasing the utility of this intervention to an even larger group of residents within LTC facilities.

After subjects have agreed to participate and have signed the appropriate consent forms they are randomly assigned to an experimental or control group. The experimental group (n=10) will attend 45-minute intervention sessions 1x/week for 12 weeks. A second control group (n=10) will receive a computerized control task of the same duration as the experimental group. All subjects will be assessed at baseline, 6 weeks, 12 weeks, and 1-month post-study. The assessment includes tests of memory, Activities of Daily Living assessment, and a satisfaction questionnaire.

The intervention consists of words flashing on a computer screen superimposed over colored blocks with sound in the background timed to the presentation of stimuli. A blank screen is then presented and the subject responds with a mouse button press as to

whether the word is spelled correctly. Subjects in the control group are presented with just a word presented on a clean screen without sound. Control subjects respond with a mouse button press as to whether the word is spelled correctly or not.

Different words are repeated at a long and short ISI for 5 minute blocks, for 45 minutes at each session. The subject has the option to rest between blocks and the session length is adjusted accordingly. Words are repeated every 4 weeks and blocks are randomized within session. Ten percent of words were incorrectly spelled and displayed randomly throughout trials.

This intervention is based on connectionist modeling on priming and stimulus integration (Antrobus, Duff, Shono, Farahani, & Numanbayraktaroglu, 2004; Henke, Weber, Kneifel, Weiser, & Buck, 1999; Kesner & Giles, 1998; Reed & Squire, 1997).

Subjects

Study inclusion criteria were:

i. Clinical Dementia Rating = .5.

ii. Mini-Mental Status Examination ≥ 24.

iii. Age ≥ 75 years.

iv. English as the primary language.

v. Physically able to sit and use computer.

vi. Must not be acutely ill, and be without unstable cardiovascular disease or other controlled chronic conditions that would interfere with the safety or conduct of the study.

vii. Has cognitive capacity to sign informed consent for study.

Original projections, for the number of subjects available for study, were done through an analysis of all Clinical Dementia Ratings (CDR) (Morris, 1993) and Mini-Mental Status Examinations (MMSE) (Folstein, Folstein, & McHugh, 1975) done on Residents during 2005. Based on this estimate it was predicted that there would be 74 subjects available for study during a given year at the Manhattan Campus. Including a 20% turnover rate in the population this would provide an additional 14 potential subjects for study inclusion.

Screening is done as part of two ongoing studies where the CDR and MMSE continue to be administered as part of the subject evaluation. These are the Behavioral Changes in Parkinson's Disease and the National Institute of Aging funded Neurobiological Factors of Aging Program Project Grant. Currently, subjects are only being screened as part of the latter study, with approximately 10 subjects being evaluated weekly.

Assessment Battery

Each test session included:

1. Alzheimer's Disease Assessment Scale-Cognitive Assessment (ADAS-COG. This battery includes the following tests:
    a. Word Recall – Subject was presented with 10 words at 1-second intervals and asked to repeat the word. Subject was then asked to recall as many words as they could. Number of words not recalled are recorded (average of 3 trials with same words).
    b. Commands – Subject was asked to follow 1-3 step commands. Number of incorrect responses are recorded.
    c. Delayed Word Recall – Subject was asked to recall as many words as they could from the Word Recall Task after a 5-minute delay. Number of words not recalled are recorded.
    d. Naming Objects and Fingers – Subject was asked the name of objects and also the name of the fingers on their hand. Number of items named incorrectly are recorded.
    e. Constructional Praxis – Subject is asked to copy a number of different forms with increasing complexity. Number of forms drawn incorrectly are recorded.
    f. Ideational Praxis – Subjects is given a piece of paper and envelope and asked to pretend to fold letter, put in envelope, seal and address envelope, write address on envelope and show

where the stamp would go. Number of incorrect components are scored.

g. Orientation – Subject is asked a number of questions regarding time and place. Number of incorrect responses are recorded.

h. Word Recognition – Subject is shown a list of words presented at 1 second intervals. Subject is then shown a second longer list and asked if the word was part of the first list of words shown. Number of incorrect responses are scored.

In addition, an Attention Visual Search Task (number cancellation) and Maze Solution Tasks were added to the original battery:

a. Visual Search Task – Subject is asked to cross out a specific number in a running list of different numbers during a 90 second period of time. Number of correct crossouts are recorded.

b. Easy and Hard Maze – Subject is asked to solve a maze. An easy version and hard version are presented. Number of seconds to complete maze is recorded.

2. The 15-Item Geriatric Depression Scale (Sheikh & Yesavage, 1986).
3. Activities of Daily Living Scale.
4. Study Satisfaction Scale.

Screening

Study inclusion criteria were reviewed with study personnel from the Parkinson's disease and Program Project Grant mentioned above. When they evaluated a potential candidate that met criteria for the memory intervention, they briefly described the study and asked them if a member of the memory study team could contact them to discuss the study further. If yes, then the Principal Investigator (CYT) would contact them for recruitment.

During the last 6-month period only 2 subjects have been identified through these procedures. One prospective subject was not appropriate for study because of a physical condition which would not let that person use a computer mouse for stimulus response. The second prospective subject passed away unexpectedly prior to being approached for recruitment.

While a diagnosis of MCI provides a small window for evaluation the primary concern has been that the LTC population is currently more medically complex and cognitively impaired than in prior years. Approximately 70% of Residents admitted to LTC are suffering from impaired cognitive ability leading to a CDR score of ≥ 1 signifying mild-severe dementia. The remaining 30% of the population is cognitively intact with a majority of these residents having entered the nursing home due to physical impairments, or conditions that have made them unable to continue living at home.

Results

Since the beginning of the study in 2006, 10 subjects have been enrolled for participation in the study. Two subjects were terminated prior to testing because of hospitalizations that resulted in their inability to continue participation. Eight subjects have been studied to date, with five subjects being assigned to the experimental group based on a randomization sequence, setup prior to the start of the study. All subjects were negative for depression based on the 15-Item Geriatric Depression Scale. There was also no current diagnosis of depression reported during a review of each subject's medical records.

Demographics

The mean age of participants was 84±6 years of age (range 75-92). Mean education level was 14±2 years (range 12-16). Seventy-five percent of participants are female (see Table 1).

ADAS-COG

With the current number of subjects in the CTL (n=3) and EXP (n=5) groups there is not enough power to conduct analyses for group differences. Group means are presented for each test for the baseline and third timepoint (see Table 2). This data is presented because it can be expected that any observable trends would be strongest

between baseline and the time when the intervention was received for the maximal period of time required in the study.

As expected, mean differences observed between baseline, and the end of the intervention period, were not statistically significant. As a measure of improvement, % change scores from baseline were computed as follows:
(((Timepoint-3 Score – Baseline Score) / Baseline Score) *100).

Of the eleven items tested on the ADAS-COG we observed trends for improvement of greater than 15% in, Naming (50%), Constructional Praxis (17%), Orientation (60%), Visual Search Task (18%), and the Easy Maze Task (41%). Commands (-25%), Delayed Word Recall (-17%), Word Recognition (-34%) showed decrements in performance. It is important to note that scoring of these tests is based on the number missed except for the Visual Search, and Maze Tasks, so increases in the mean scores at timepoint-3 reflects poorer performance.

Activities of Daily Living

These activities which included ratings on levels of assistance necessary for activities such as showering, and eating did not change during the course of the study for these individuals.

Discussion

While this report serves as a preliminary update on the status of this on-going study, there are performance increases combining the two groups at this point for Naming, Constructional Praxis, Visual Search Task, and the Easy Maze Task. While the group sizes are small, as a whole, the improvement for these items may be supported by the generalized task activity of identifying words on a screen, and responding, as a Word Recognition task even in the Control group. However, I did not observe significant changes in abilities that would traditionally reflect improved hippocampal activitiy such as on the Delayed Recall Task. One consideration is that due to the length of the intervention the decreased performance may actually be a result of health issues related to subjects' relatively frail conditions. This is supported by the two subjects that were hospitalized prior to the start of the weekly intervention/control sessions and the 3 serious adverse event related hospitalizations of subjects during the course of the study. Future research would need to include a frailty or medical complexity index score, with a score adjustment algorithm, to account for changes in health that can affect outcome measures for memory and cognition.

We did observe a substantial increase in Orientation which may be reflective of general global function in the LTC environment reflecting a Resident's ability to successfully navigate socially and cognitively in this environment.

Another question to be addressed is whether the intervention activates the hippocampus and/or entorhinal cortex. While based on work in connectionist models of priming and stimulus integration ((Antrobus et al., 2004; O'Reilly & Rudy, 2001), it is recognized that the task was never validated using neuroimaging techniques, such as fMRI or PET, and may not actually activate these areas of the brain. It will be important for future work to isolate the areas of the brain affected. The rational for not validating the task prior to this phase of the study was a direct result of the difficulty, and cost, involved to carry out neuroimaging studies on this population. While they are more easily done in younger healthier populations this would not guarantee that older frail individuals process information in the same way and that the brain does not reorganize itself as a compensatory mechanism associated with age and disease related changes occurring over time for these tasks. If the final results, are positive, and warrant further study then validations studies will be done post hoc.

Based on these preliminary results, the feasibility of interventions of this type and length with this population are questionable. This is a result of a number of factors foremost being the frailty of this population. Out of the 10 subjects originally recruited two were dropped prior to the start of the intervention due to adverse health events requiring extensive hospitalizations where the subjects where either out for an extended period of time or did not return to the facility. For the remaining 8 subjects there were 3 serious adverse events reported that required hospitalizations that disrupted the weekly intervention requirement. Disruptions lasted up to 2 weeks. The preliminary results from this study would support shorter term interventions. The use of a computer is viable and

effective for the majority of residents. Instead of the use of a mouse response button keypress, strategies used by other groups including the use of a large button response box, would be more appropriate. In addition, because scheduling remains a difficult process in the LTC environment the use of a "memory clinic" structure where Residents could come in to work on the tasks themselves, at convenient times, would be more effective. In addition, as observed by the low recruitment rate, and low prevalence of MCI currently in LTC, any intervention incorporated into the structure of a LTC facility would need to include residents with mild or mild-severe dementia as part of the target population to justify facility resources.

Table 1

Distribution of Demographic Variables by Group

		CTL	EXP
Number of Subjects		3	5
Age		82±2	85±7
Years of Education		15±1	13±1
Gender (% Female)		67%	80%
Ethnicity	White	100%	80%
	Black	0%	20%

Table 2

Distribution of Mean (±Standard Deviation) by ADAS-COG Test for Combined Subject Groups

Test	Baseline	Timepoint-3
Word Recall	5.4±1.5	5.6±1.2
Commands	0.4±0.5	0.5±0.5
Delayed Word Recall	6.4±1.3	7.5±1.6
Naming	0.4±0.7	0.2±0.5
Constructional Praxis	1.2±0.9	1.0±1.3
Ideational Praxis	0.4±0.5	0.4±0.7
Orientation	0.5±0.8	0.2±0.5
Word Recognition	6.1±4.8	8.2±2.8
Visual Search Task	14.3±4.0	16.9±5.3
Maze – Easy	25.2±14.6	35.6±40.1
Maze – Hard	96.9±70.1	99.2±88.1

References

American Association of Homes and Services for the Aging. (2007). Aging Services: The Facts.

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders* (Fourth ed.). Washington:DC.

Antrobus, J. S., Duff, M., Shono, Y., Farahani, R., & Numanbayraktaroglu, S. (2004). Word recognition and learning: Representation and process, in repetition priming: City College of the City University of New York.

Bobinski, M., De Leon, M. J., Convit, A., De Santi, S., Wegiel, J., Tarshish, C. Y., et al. (1999). MRI of entorhinal cortex in mild Alzheimer's disease. *Lancet, 353*(9146), 38-40.

Camp, C. J., Foss, J. W., Stevens, A. B., Reichard, C. C., McKitrick, L. A., & O'Hanlon, A. M. (1993). Memory training in normal and demented elderly populations: The E-I-E-I-O model. *Experimental Aging Research, 19*(3), 277-290.

Convit, A., Wolf, O. T., Tarshish, C. Y., & De Leon, M. J. (2003). Reduced glucose tolerance is associated with poor memory performance and hippocampal atrophy among normal elderly. *Proceedings of the National Academy of Science USA, 100*(4), 2019-2022.

de Leon, M. J., De Santi, S., Zinkowski, R., Mehta, P. D., Pratico, D., Segal, S., et al. (2006). Longitudinal CSF and MRI biomarkers improve the diagnosis of mild cognitive impairment. *Neurobiology of Aging, 27*(3), 394-401.

De Santi, S., De Leon, M. J., Rusinek, H., Convit, A., Tarshish, C. Y., Roche, A., et al. (2001). Hippocampal formation glucose metabolism and volume losses in MCI and AD. *Neurobiology of Aging, 22*(4), 529-539.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "MINI-MENTAL STATE" A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Golomb, J., De Leon, M. J., Kluger, A., George, A. E., Tarshish, C., & Ferris, S. H. (1993). Hippocampal atrophy in normal aging. An association with recent memory impairment. *Archives of Neurology, 50*(9), 967-973.

Golomb, J., Kluger, A., De Leon, M. J., Ferris, S. H., Convit, A., Mittelman, M. S., et al. (1994). Hippocampal formation size in normal human aging: a correlate of delayed secondary memory performance. *Learning and Memory, 1*(1), 45-54.

Golomb, J., Kluger, A., De Leon, M. J., Ferris, S. H., Mittelman, M. S., Cohen, J., et al. (1996). Hippocampal formation size predicts declining memory performance in normal aging. *Neurology, 47*(3), 810-813.

Henke, K., Weber, B., Kneifel, S., Weiser, H. G., & Buck, A. (1999). Human hippocampus associates information in memory. *Proceedings of the National Academy of Science USA, 96*, 5884-5889.

Kesner, R. P., & Giles, R. (1998). Neural circuit analysis of spatial working memory: Role of presibiculum, parasubiculum, medial and lateral entorhinal cortex. *Hippocampus, 8*, 416-423.

Kluger, A., Ferris, S. H., Golomb, J., Mittelman, M. S., & Reisberg, B. (1999). Neuropsychological prediction of decline to dementia in nondemented elderly. *Journal of Geriatric Psychiatry and Neurology, 12*(4), 168-179.

Morris, J. C. (1993). The Clinical Dementia Rating (CDR): Current version and scoring rules. *Neurology, 43*(1), 2412-2414.

O'Reilly, R. C., & Rudy, J. W. (2001). Conjunctive representations in learning and memory: Principles of cortical and hippocampal function. *Psychological Review, 108*, 311-345.

Petersen, R. C. (1995). Normal aging, mild cognitive impairment, and early Alzheimer's disease. *Neurologist, 1*, 326-344.

Petersen, R. C., Smith, G. E., Waring, S. C., Ivnik, R. J., Tangalos, E. G., & Kokman, E. (1999). Mild Cognitive Impairment: Clinical characterization and outcome. *Archives of Neurology, 56*, 303-308.

Reed, J. M., & Squire, L. R. (1997). Impaired recognition memory in patients with lesions limited to the hippocampal formation. *Behavioral Neuroscience, 111*(4), 667-675.

Reisberg, B., Ferris, S. H., de Leon, M. J., & Crook, T. (1982). The Global Deterioration Scale for assessment of primary degenerative dementi. *American Journal of Psychiatry, 139*(9), 1136-1139.

Sheikh, J. I., & Yesavage, J. A. (1986). Geriatric Depression Scale (GDS): recent evidence and development of a shorter version, in Clinical Gerontology: A Guide to Assessment and Intervention. In B. T. L. (Ed.), *Clinical Gerontology: A Guide to Assessment and Intervention* (pp. 165–173). New York: The Hawthorne Press.

Sramek, J. J., Veroff, A. E., & Cutler, N. R. (2000). Mild Cognitive Impairment: Emerging therapeutics. *The Annals of Pharmacotherapy, 34*, 1179-1188.

Wolinsky, F. D., Unverzagt, F. W., Smith, D. M., Jones, R., Stoddard, A., & Tennstedt, S. L. (2006). The ACTIVE cogntive training trial and health-related quality of life: Protection that lasts for 5 years. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences, 61*(12), 1324-1329.

Discussion

Discussion

Four studies have been described which focus on either the assessment or the enhancement of cognition, predominately memory, in the long-term care (LTC) population. During the course of these studies the term LTC was used to refer to an urban nursing home residential population. Traditionally, this population has been thought of as being older, more medically-complex, less healthy, and frailer than the community population. This view has resulted in relatively little research being done within this population with regard to improving the assessment of, or enhancing, memory function. Instead the emphasis has been on issues related to palliative care where the focus is more on physical comfort and transitional end-of-life issues.

Within the foreseeable future it should be expected that research focused on LTC will have increasing validity with regard to the general population as the average age of the U.S. population increases. Census predictions estimate that by the year 2026 the number of Americans over the age of 65 will double, and by 2050, 20% of all Americans will be classified as old with those 85 years and older representing a full 5% of the population. This trend will be seen across multiple ethnic groups, with 25% of the US Hispanic population ≥ 80 years by the year 2030 (U.S. Department of Health and Human Services Administration on Aging, 2006). It should be assumed that as the population ages we can expect that many of the co-morbid age-related conditions that currently effect the LTC population will affect the community-dwelling elderly with greater frequency. This will be exacerbated by the increasing movement in healthcare to keep

the elderly in the community, with increased support services. It can also be expected that as medical advances occur the prevalence of individuals with more medically complex conditions residing in the community will increase and will amplify the need for psychometric instruments that account for non-cognitive co-morbid conditions,

Chapter-1 describes a study that examines the prevalence of one type of co-morbid condition which can effect testing, specifically motor impairment or difficulty in movement of the body or limbs. The aim of the study was to examine the use of the Unified Parkinson's Disease Rating Scale Motor Examination ($UPDRS_{ME}$) (Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease, 2003), to measure these defecits. While a number of alternative versions of the UPDRS exist (Hogan et al., 1999; Marinus et al., 2004; Martignoni, Franchignoni, Pasetti, Ferriero, & Picco, 2003; Martínez-Martín et al., 2005), the $UPDRS_{ME}$ continues to be the most widely used assessment for motor dysfunction. This study represents the first report which looks at the diagnostic utility of individual items with the frail elderly. When compared to previous studies on the $UPDRS_{ME}$ in PD, our population was approximately 16 years older. They were also approximately 5 years older than previous studies examining the prevalence of parkinsonian signs among the elderly in the community (Louis, Tang, & Mayeux, 2004, 2005). As a measure of comparison with the larger community dwelling elderly, the prevalence of parkinsonian signs in our sample was computed using a modified 10-item $UPDRS_{ME}$ originally reported by Louis, Tang, & Mayeux (2004). While they reported a prevalence rate of 40%, a rate of 66% for moderate to severe deficits ($UPDRS_{ME}$ score ≥ 2), and 75% for mild deficits was

observed in our sample. This substantiated the higher prevalence of movement disorders in this population.

Because of the high rate of motor deficits it could be assumed that a number of items on the $UPDRS_{ME}$ would not be useful for the purpose of diagnostic evaluations assuming that many Residents (individuals living in LTC) would have comparable levels of impairment on similar items primarily as a result of aging and not disease. In fact, a subset of 7 $UPDRS_{ME}$ items were isolated that were statistically comparable to the original 27 items in the instrument. The items were Rest Tremor-RUE, Action Tremor-RUE, Rigidity-RUE, Hand Grips-Right, Posture, Gait, and Postural Stability. These items provided good to excellent overall accuracy. However, similar to the entire 27-item $UPDRS_{ME}$ we did observe low sensitivity to differentiate subjects with dementia from control subjects (58%), while high sensitivity was observed for isolating subjects with PD. This suggests that $UPDRS_{ME}$ items may be sensitive to motor function related to subcortical areas of the brain such as in PD, but not diseases where the primary lesion may affect cortical sites such as in AD. This would be expected given that the instrument was originally developed to measure change in PD patients. One reason that the $UPDRS_{ME}$ was not sensitive to differences between the CTL and DEM groups could be because many in the CTL group also suffer from deficits related to frailty and physical aging. When applying the 7-item $UPDRS_{ME}$ subset a prevalence of 91.4% for mild-severe and 97.0% for mild deficits was observed across all study groups. The more salient items added to our set, as compared to the 10-item subset reported above, were Action Tremor, Hand Grips, Gait and Postural Stability. Another difference was that we

incorporated laterality into our analysis. In other studies it was assumed that deficits on both sides of the body were highly correlated across the entire sample. We observed that the strongest correlations were in the FECTL group. In this group the average correlation accounted for approximately 61% of the shared variance. In the FEDEM group this was reduced to 21%. In the FEPD group only the upper extremity items where correlated accounting for 49% or the shared variance between the two items. This suggests that while the lateral items are correlated it is not uniform across the entire sample and may be mitigated by disease.

Chapter-2 focused on whether psychometric instruments used to assess cognition in this setting were susceptible to bias from co-morbid conditions which are not directly associated with cognition. If the answer was yes, a bias to diagnose Residents with dementia would exist. The Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) was used to determine whether a bias existed and whether this instrument was appropriate for use with the frail elderly in the LTC setting. While arguments can be made that the main function of the instrument is to assess global cognitive function, it has been used in numerous studies to both stage the severity of the deficit and to isolate deficits in specific domains (Tombaugh & McIntyre, 1992). In the LTC environment there may be a propensity to rely on these instruments because clinicians have a heavy caseload, in part, based on State-mandated reimbursement guidelines. Services are also frequently outsourced to agencies where clinicians have less patient contact and are more reliant on quick and accurate assessment instruments for making diagnostic or patient care determinations.

A full 33% of residents approached for assessment were unable to respond to any items on the MMSE due to non-cognitive related reasons. In addition, for items requiring a physical response such as "Writing a Sentence" or "Copying a Figure" there was an additional non-response rate of up to 15% in the non-dementia CTL group for subjects who were able to complete at least one item on the MMSE. This means that almost 50% of study participants were not able to complete these items for reasons unrelated to mental faculty. This is in agreement with a previous study reporting poor performance in approximately 42% of subjects ≥ 85 years (Räihä et al., 2001). Because non-response items are coded as errors a bias to misclassify a higher proportion of CTL subjects as having DAT, observed as a low % correct rate for the classification of CTL subjects (Specificity) was expected. In fact, this was the general pattern observed when comparing the CTL with the DAT groups. Specificity values averaged 11% lower than the Sensitivity measures. The greatest differences between Specificity and Sensitivity was for *Attention*(15.6%), *Commands* (17.1%), *Recall*(28.2%), and *Copy*(56.1%). A similar pattern was observed for the MOD-SEVERE DAT group when compared to the CTL group.

In contrast, Sensitivity values were on average lower than Specificity by approximately 26% when contrasting CTL with MILD-DAT. This can be interpreted as a bias for items on the MMSE to classify LTC residents with MILD-DAT as not having dementia. This is the opposite of the observation seen in the other comparisons. This finding is most likely a result of the increased prevalence of physical limitations in this

population resulting in an increase in item score variability within both the CTL and MILD-DAT groups. In these two groups where the presentation of cognitive deficits may be relatively subtle, the misclassification of Mild-DAT subjects is probably due to the fact that the MMSE items are more susceptible to differences in physical deficits which may be more severe than the cognitive deficits at this stage of impairment. We examined the difference in MMSE scores between these two groups and observed that they were lower than reported in the literature for comparable non-age matched groups (22.2±6.1, Range=4-30, and 13.1±7.4, range =0-29 respectively).

The best individual item predictors of CTL/DAT classification were from the domains of *orientation*, *language*, and *writing*. *Orientation* and *language* require a minimum physical response, and consistently show good accuracy for classification across groups, and is indicative of social skill and general level of activity, which is correlated to social, and ADL, abilities. *Writing* however, requires a physical response, and is disproportionately affected in the DAT group while most CTL subjects maintain the ability to adequately write a sentence (66.4%).

It was also noted that a subset of 5-items in the MMSE were as predictive as the entire test. "Year", "Name of Place", "Floor", "Name Wristwatch", and "Write Sentence" provided Specificity of 80%, and Sensitivity of 87%. When compared to the entire MMSE the modified 5-item set of actually increased Specificity up from 75%.

The comparison between subcortical and cortical items did not differentiate PD subjects from those without PD in our sample (Leritz, Brandt, Minor, Reis-Jensen, & Petri, 2000). While our PD group was small we were still able to differentiate between PD-CTL and PD-AD groups based on cortical items. However, the inability of these items to differentiate cortical from subcortical dementias in this group was further supported by analyses using the Cortical/Subcortical Index Score (Brandt, Folstein, & Folstein, 1988), due to the high prevalence of movement disorders in this general population, decreasing the Sensitivity of these questions as diagnostic items.

The issues observed with the MMSE led to an examination of the Cambridge Cognitive Examination (CAMCOG) (Roth, Huppert, Mountjoy, & Tym, 1998). The CAMCOG has been shown to be sensitive to early cognitive changes in Alzheimer's disease and Parkinson's disease. It is also a lengthier test which incorporates testing for additional cognitive areas such as remote memory, executive function, and abstract thinking, and is less susceptible to ceiling effects when used with different populations. Another feature of the test is that domains are tested using multiple types of stimuli. Surprisingly, while used frequently in other countries it has not been adopted in this country. We were interested in whether the test was feasible within our population and also whether we could differentiate diagnostic groups from frail elderly control subjects. Our study population consisted of CTL, Dementia, and PD subjects.

We observed that the administration time while longer than reported in some other studies, averaging 48±16 minutes to complete. A cutoff score of < 80 has been

proposed to reflect cognitive impairment. In our study we observed that while the average score on the CAMCOG for the CTL group was 80±10, 50% of the group actually scored below 80. A second normative study reported age and gender adjusted median CAMCOG values which we applied to our sample (Williams, Huppert, Matthews, Nickson, & MRC Cognitive Function and Ageing Study (MRC CFAS), 2003). Scores were still below suggested values. Again, this may be a result of the inability of many of the frail elderly to respond to a number of items on the CAMCOG due to non-cognitive co-morbid conditions. While not as sensitive to the effects of these physical conditions as the MMSE, adjustments still need to be applied to the scoring algorithm to accommodate these conditions.

To determine whether the CAMCOG was able to differentiate across diagnostic groups we examined mean differences between CTL, PD group, and dementia groups with and without PD. Orientation, Recent Memory, and the Total Score provided the most consistent observable differences for groups with and without dementia. However, they were not sensitive to PD and related motor deficits.

New Learning was the only item that differentiated the DEM from PD-DEM groups, a potentially important finding because it may provide a link to understanding differences that exist between the cognitive profile of patient groups with AD versus PD with dementia in this population. Our review of the clinical diagnosis of dementia type in these two groups found 15% of cases, in the DEM group, where caused by an unknown etiology and not AD or vascular dementia. The PD-DEM group had a prevalence of 42%

with unknown etiologies. This may provide a link to distinguishing PD dementia cases from AD cases as well as the associated neuropathological pathways that contribute to the high occurrence of dementia in PD.

Moving away from assessment Chapter-4 provides an update on the use of a 12-week computerized memory enhancement intervention. With an enrollment of only 8 subjects the data was collapsed across subjects and trends in % change from baseline were analyzed. Improvement was observed for Naming, Constructional Praxis, Visual Search Task, and the Easy Maze Task. While the group sizes were small, as a whole, the improvement in these items may be a result of the generalized task activity of identifying words on a screen, and responding to them as part of a Word Recognition task even in the Control group. However, there were no significant changes in abilities that would traditionally reflect improved hippocampal/entorhinal cortex activity such as on the Delayed Recall Task.

A subtantial increase in performance on Orientation was also observed which may be reflective of general global function in the LTC environment reflecting Residents ability to successfully navigate socially and cognitively in this environment.

A question to be addressed in future research is whether the intervention actually activates the hippocampus and/or entorhinal cortex. While based on some connectionist models of priming and stimulus integration ((Antrobus, Duff, Shono, Farahani, & Numanbayraktaroglu, 2004; O'Reilly & Rudy, 2001), it is recognized that the task was

never validated using neuroimaging techniques, such as fMRI or PET. It will be important for future work to isolate the areas of the brain affected in similar interventions. The rational for not validating the task prior to this phase of the study was a direct result of the difficulty, and cost, involved to carry out neuroimaging studies on this population. While they are more easily done in younger healthier populations this would not guarantee that older frail individuals process task information in the same way and that the brain does not reorganize itself as a compensatory mechanism associated with age and disease related changes occurring over time. If the final results, are positive, and warrant further study then validations studies will be done posthoc.

Based on these preliminary results, the feasibility of interventions of this type and length with this population are questionable. This is a result of a number of factors foremost being the frailty of this population. Out of the 10 subjects originally recruited two were dropped prior to the start of the intervention. Of the remaining 8 subjects there were 3 serious adverse events resulting in hospitalizations causing disruptions which lasted up to 2 weeks. The preliminary results from this study support interventions of shorter durations. The use of a computer proved to be viable and effective for the majority of residents. In addition, because scheduling remains a difficult process in the LTC environment the use of a "memory clinic" structure where Residents could come in to work on the tasks themselves at convenient times would be more effective. In addition, as observed by the low recruitment rate, and low prevalence of MCI currently in LTC, any intervention incorporated into the structure of a LTC facility would need to

include mild or mild-severe dementia groups as part of the target population to justify facility resources.

These studies highlight a number of problems in the current assessment instruments or strategies in testing the LTC frail elderly. Some of the issues include the increased prevalence in co-morbid conditions and physical deficits that affect the ability to derive accurate assessments from a number of psychometric tests. While the MMSE was used as an example the problems evident with this instrument such as scoring of items as deficits when due to non-cognitive etiologies is symptomatic of many tests currently used when applied to older frail patient groups. While increasing the number of items used to test specific domains is one way of circumventing this problem, as shown with the CAMCOG, it still does not resolve these issues. Future studies need to examine alterative methods for assessing cognition. This may include the use of neurological signs which stage the progression of the disease as well as weighting algorithms for the scoring of test items. One approach used in the MMSE study was to incorporate the Cognitive Performance Scale (CPS) as a staging measure. The CPS is derived directly from the Minimum Data Set (MDS) and is based on item assessments by trained nurses over a length of time, instead of at one timepoint when the Resident may not be feeling well or may be preoccupied. Future goals include the examination of different cognitive items that may be more appropriate in assessing this population. For example, test items that require minimal physical response times, or the use of techniques such as Evoked Response Potentials (ERP) to examine endogenous potentials to stimuli that would not require physical responses. While the sample size for a number of these studies was

small, future studies will be planned to both increase sample size and to provide a more ethnically diverse sample. The preliminary results of the memory intervention have been useful and exciting. They were promising with regard to overall cognitive improvement in subjects. Based on these results we will plan future interventions with Residents having a greater amount of freedom for scheduling as well as improved hardware to compensate for physical limitations.

References

Antrobus, J. S., Duff, M., Shono, Y., Farahani, R., & Numanbayraktaroglu, S. (2004). Word recognition and learning: Representation and process, in repetition priming: City College of the City University of New York.

Brandt, J., Folstein, S. E., & Folstein, M. F. (1988). Differential cognitive impairment in Alzheimer's disease and Huntington's disease. *Annals of Neurology, 23*, 555-561.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). 'Mini-Mental State'. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Hogan, T., Grimaldi, R., Dingemanse, J., Martin, M., Lyons, K., & Koller, W. (1999). The Parkinson's disease symptom inventory (PDSI): a comprehensive and sensitive instrument to measure disease symptoms and treatment side-effects. *Parkinsonism & Related Disorders, 5*, 93-98.

Leritz, E., Brandt, J., Minor, M., Reis-Jensen, F., & Petri, M. (2000). "Subcortical" cognitive impairment in patients with systemic lupus erythematosis. *Journal of the International Neuropsychological Society, 6*, 821-825.

Louis, E. D., Tang, M. X., & Mayeux, R. (2004). Factor structure of parkinsonian signs in the community-dwelling elderly. *Movement Disorders, 19*(3), 268-272.

Louis, E. D., Tang, M. X., & Mayeux, R. (2005). Functional correlates and prevalence of mild parkinsonian signs in a community population of older people. *Archives of Neurobiology, 62*, 297-302.

Marinus, J., Visser, M., Stiggelbout, A. M., Rabey, J. M., Martínez-Martín, P., Bonuccelli, U., et al. (2004). A short scale for the assessment of motor impairments and disabilities in Parkinson's disease: the SPEC/SCOPA. *Journal of Neurology, Neurosurgery, and Psychiatry, 75*, 388-395.

Martignoni, E., Franchignoni, F., Pasetti, C., Ferriero, G., & Picco, D. (2003). Psychometric properties of the Unified Parkinson's Disease Rating Scale and of the Short Parkinson's Disease Evaluation Scale. *Neurological Science, 24*, 190-191.

Martínez-Martín, P., Benito-Léon, J., Burguera, J. A., Castro, A., Linazasaro, G., Martínez-Castrillo, J. C., et al. (2005). The SCOPA-motor scale for assessment of Parkinson's disease is a consistent and valid measure. *Journal of Clinical Epidemiology, 58*, 674-679.

Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease. (2003). The Unified Parkinson's Disease Rating Scale (UPDRS): Status and recommendations. *Movement Disorders, 18*(7), 738-750.

O'Reilly, R. C., & Rudy, J. W. (2001). Conjunctive representations in learning and memory: Principles of cortical and hippocampal function. *Psychological Review, 108*, 311-345.

Olin, J. T., & Zelinski, E. M. (1991). The 12-month reliability of the Mini-Mental State Examination. *Psychological Assessment, 3*(3), 427-432.

Räihä, I., Isoaho, R., Ojanlatva, A., Viramo, P., Sulkava, R., & Kivelä, S.-L. (2001). Poor performance in the Mini-Mental State Examination due to causes other than dementia. *Scandinavian Journal of Primary Health Care, 19*, 34-38.

Roth, M., Huppert, F. A., Mountjoy, C. Q., & Tym, E. (1998). *CAMDEX-R: The Cambridge Examination for Mental Disorders of the Elderly*. Cambridge: Cambridge University Press.

Tombaugh, T. N., & McIntyre, N. J. (1992). The Mini-Mental State Examination: A comprehensive review. *Journal of the American Geriatrics Society, 40*(9), 922-935.

U.S. Department of Health and Human Services Administration on Aging. (2006). *A statistical profile of Hispanic older Americans aged 65 +*

Williams, J. G., Huppert, F. A., Matthews, F. E., Nickson, J., & MRC Cognitive Function and Ageing Study (MRC CFAS). (2003). Performance and normative values of a concise neuropsychological test (CAMCOG) in an elderly population study. *International Journal of Geriatric Psychiatry, 18*, 631-644.

Appendix A

Abbreviations List

ADAS-COG	Alzheimer's Disease Assessment Scale-Cognitive Assessment
ADL	Activities of Daily Living
CAMCOG	Cambridge Cognitive Examination
CAMDEX-R	Cambridge Examination for Mental Disorders of the Elderly
CDR	Clinical Dementia Rating
CI	Confidence Interval
CPS	Cognitive Performance Scale
CTL	Control Group
DAT	Dementia of the Alzheimer's Type
DEM	Dementia Group
ET	Essential Tremor
FECTL	Frail Elderly Control Group
FEDEM	Frail Elderly Dementia Group
FEPD	Frail Elderly Parkinson's Disease Group
JHHLCS	Jewish Home & Hospital Lifecare System
LTC	Long-Term Care
LLE	Left Lower Extremity
LUE	Left Upper Extremity
MCI	Mild Cognitive Impairment
MDS	Minimum Data Set
NH	Nursing Home

MMSE	Mini-Mental State Examination
NORCS	Naturally Occurring Retirement Communities
OR	Odds Ratio
PD	Parkinson's Disease
PD-CTL	Parkinson's Disease Control Group
PD-AD	Parkinson's Disease with Alzheimer's Disease Group
PD-DEM	Parkinson's Disease with Dementia Group
Resident(s)	Individual(s) living in Long-Term Care
RLE	Right Lower Extremity
RUE	Right Upper Extremity
UPDRS	Unified Parkinson's Disease Rating Scale
$UPDRS_{ME}$	Unified Parkinson's Disease Rating Scale Motor Examination

Appendix B

Unified Parkinson's Disease Rating Scale Motor Examination

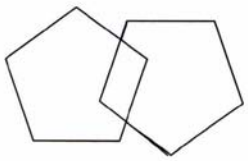
18	Speech		
19	Facial expression		
20	Tremor at rest: face, lips, chin		
	Hands: right		
	left		
	Feet: right		
	left		
21	Action tremor: right		
	left		
22	Rigidity: neck		
	Upper extremity: right		
	left		
	Lower extremity: right		
	left		
23	Finger taps: right		
	left		
24	Hand grips: right		
	left		
25	Hand pronate/supinate: right		
	left		
26	Leg agility: right		
	left		
27	Arise from chair		
28	Posture		
29	Gait		
30	Postural stability		
31	Body bradykinsesia		
	Sub-total:18-31 (maximum=108)		

Appendix C

MINI MENTAL STATUS EXAM

_____ (1)	1.	What year is it?
_____ (1)	2.	What is the season?
_____ (1)	3.	What is the month?
_____ (1)	4.	What is the date?
_____ (1)	5.	What is the day of the week?
_____ (1)	6.	What state are we in?
_____ (1)	7.	What borough are we in?
_____ (1)	8.	What city is this?
_____ (1)	9.	What is the name of this place?
_____ (1)	10.	What floor are we on?
_____ (3)	11.	Repeat: "apple, table, penny" [warn subject will be asked later] APPLE / TABLE / PENNY
_____ (5)	12.	Spell WORLD BACKWARDS ___ ___ ___ ___ ___ (Serial 7s done as part of CAMCOG Study)
_____ (3)	13.	"Can you recall the three words I asked you to remember?" APPLE / TABLE / PENNY
_____ (1)	14.	(Show wrist watch)-"What is this called?"
_____ (1)	15.	(Show Pencil)- "What is this called?"
_____ (1)	16.	"I would like you to repeat this phrase after me: 'NO IFS, ANDS, OR BUTS'."
_____ (1)	17.	"Read the words on this page out loud, then do what it says." (CLOSE YOUR EYES)
_____ (3)	18.	"I am going to give you a piece of paper. Take the paper in your right hand, fold it in half, then put it in your lap" R HAND / FOLD / LAP
_____ (1)	19.	"Please write a sentence of your choice on the line below"
_____ (1)	20.	"Make a copy of this figure right next to the drawing in the space provided."
_____ (30)		**TOTAL SCORE (30 Point Maximum)**

Sentence: _____



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_____

Examiner's Signature Date

Appendix D

Section B Cognitive examination – CAMCOG

Before commencing, make sure you have the following items:

Booklet	**Pencil**	**Wristwatch (with a second hand for timing)**
Blank sheet of paper (A4)	**Envelope**	**Coins: two coins of different value**

Ensure that calendars and clocks are not available to assist subjects in answering questions about date and time.

This section contains all 19 items of the Mini-Mental State Examination of Folstein et al. (1975). Some, but not all of these items are used in scoring the more comprehensive Cambridge Cognitive Examination (CAMCOG). A list of the items comprising each of these examinations is set out on pp. 65–66

It is important that you speak slowly and clearly. If the subject appears not to have heard or understood, repeat the question (unless the item specifically prohibits repetition).

Do not give correct answer if a wrong answer or no answer is given.

Make a note of any unusual responses including extra memory items recalled.

Coding: This section differs from other sections of the CAMDEX in that subjects who don't know, refuse to answer or give a silly answer are given a score of 0 (not 8), which is equivalent to giving an incorrect answer. Where a score of 9 or 99 is recorded, indicate why the question was not asked.

I am going to ask you some questions now which have to do with your memory and concentration. Some of them may seem rather easy, others may be difficult, but we need to ask everyone the same questions.

Orientation

Time

139. What day of the week is it?	Incorrect	0	
	Correct	1	9

What is the date today?

140. Date	Incorrect	0	
	Correct	1	9
141. Month	Incorrect	0	
	Correct	1	9
142. Year	Incorrect	0	
	Correct	1	9
143. What is the season?	Incorrect	0	
	Correct	1	9

Allow flexibility when season changes, e.g. for northern hemisphere:
March = winter/spring: June = spring/summer
September = summer/autumn: December = autumn/winter

The CAMDEX-R Schedule

Place

144. Can you tell me where we are now? For instance, what county (state) are we in?	Incorrect Correct	0 1	 9
145. What is the name of this town (city)?	Incorrect Correct	0 1	 9
146. What are two main streets nearby (or near your home)?	Incorrect Correct	0 1	 9
147. What floor of the building are we on?	Incorrect Correct	0 1	 9
148. What is the name of this place? *(or* What is this address? *if subject tested at home)*	Incorrect Correct	0 1	 9

If tested at home, the address must include enough information for mail to arrive

Language

Comprehension: Motor response

If the subject does not complete the full sequence then the whole instruction may be repeated, without change in tone or tempo, to ensure that it has been heard and understood. Prompting and coaching stage by stage are not allowed

I am going to ask you to carry out some actions, so please listen carefully

149. Please nod your head.	Incorrect Correct	0 1	 9
150. Touch your right ear with your left hand.	Incorrect Correct	0 1	 9
151. Before looking at the ceiling please look at the floor.	Incorrect Correct	0 1	 9
152. Tap each shoulder twice with two fingers keeping your eyes shut.	Incorrect Correct	0 1	 9

Comprehension: Verbal response

I am going to ask you some questions and would like you to answer 'yes' or 'no'

153. Is this place a hotel?	Incorrect Correct ('no')	0 1	 9
154. Are villages larger than towns?	Incorrect Correct ('no')	0 1	 9
155. Was there wireless/radio in this country before television was invented?	Incorrect Correct ('yes')	0 1	 9

Expression: Naming

In questions 156 and 157 accurate naming is needed. Descriptions of function or approximate answers are not acceptable. Acceptable answers may depend on local usage. Some items may have more than one correct name, as has been indicated. Errors include description of function (e.g. 'used for telling the time' for watch) and approximate answers (e.g. 'weighing machine' for scales; 'bag' or 'carrier' for suitcase; 'light' for lamp).

In the case of approximate answers, you should say 'Can you think of another word for it?'

Tick each item correctly named in questions 156 and 157 and enter number correct under Total

156. ***Show pencil***
What is this called? — Pencil ___
Show wristwatch
What is this called? — Wristwatch ___
Total |__| **9**

157. I am going to show you some objects. Please tell me the name of each one. ***Show 'Pictures for naming' in booklet.***
Shoe, sandal ___
Typewriter ___
Scales ___
Suitcase, Portmanteau ___
Barometer. ___
Table lamp, lamp ___
Total |__| **9**

Expression: Fluency

158. Name as many different animals as you can think of. You will have one minute to do this.
Number correct |__|__|

Only if subject asks for clarification, explain that animals include birds, fish, insects, humans, etc. If subject gets stuck, encourage him/her with 'Can you think of any more?' Record number correct in one minute (repetitions not to be counted but age and sexual variants should be counted e.g. calf, cow, bull)
List all items

Note: Recode: For CAMCOG score
0 = **0**
1–4 = **1**
5–9 = **2**
10–14 = **3**
15–19 = **4**
20–24 = **5**
25+ = **6**
|__| **9**

Expression: Definitions

For questions 159–162, acceptable answers may depend on local usage

159. What do you do with a hammer?
Incorrect **0**
Any correct use **1** **9**

Hit is not enough. Some other detail should be given without prompting.

160. Where do people usually go to buy medicine?
Shop (if unable to specify) **0**
Chemist, pharmacy **1** **9**

In questions 161–162 a general (abstract) definition scores 2 and a specific or limited definition scores 1. Examples are given beside each score

161. What is a bridge?
Incorrect **0**
Cross the bridge **1**
Goes across a river etc **2** **9**

162. What is an opinion?	Incorrect	0	
	A good opinion of someone	1	
	A person's ideas about something; what you think	2	9

Expression: Repetition

Only one presentation is allowed so it is essential that you read the phrase clearly and slowly, enunciating all the S's.

163. I am going to say something and I would like you to repeat it after me: 'No ifs, ands or buts'.	Incorrect	0	
	Correct	1	9
Code 1 only if entire phrase is correct			

Memory

Recall

164. Can you tell me what were the objects in the coloured pictures I showed you a little while ago?	Shoe, sandal	__	
	Typewriter	__	
	Scales	__	
	Suitcase	__	
	Barometer	__	
	Table lamp, lamp	__	
Either descriptions or names are acceptable. Tick each item correctly recalled and enter number correct under Total. If subject previously gave an incorrect name in question 157 but recalls it at this stage, score as correct	**Total**	[__]	9

Recognition

Show: 'Pictures for recognition' in booklet

Tick each item correctly recognised and enter number correct under Total

165. Which of these did I show you before?	Shoe, sandal	__	
	Typewriter	__	
	Scales	__	
	Suitcase	__	
	Barometer	__	
	Table lamp, lamp	__	
	Total	[__]	9

Retrieval of remote information

Note: Questions 166–171 should be asked if the subject was born before 1940. Questions 166a–171a should be asked if the subject was born after 1940.

Now I am going to ask you some questions about the past

166. When did the First World War begin? **(Within 1 year)**	Incorrect	0	
	1914 (in Europe)	1	9
167. When did the Second World War begin? **(Within 1 year)**	Incorrect	0	
	1939 (in Europe)	1	9
168. Who was the leader of the Germans in the Second World War?	Incorrect	0	
	Hitler	1	9

169. Who was the leader of the Russians in the Second World War?	Incorrect Stalin	0 1	 9
170. What was Mae West famous for? *Any appropriate verbal or non-verbal answer which indicates memory*	Incorrect Entertainer, Film Star, Life jacket	0 1	 9
171. Who was the famous flyer whose son was kidnapped? *Close approximations to the name are acceptable*	Incorrect Lindbergh	0 1	 9
Questions 166a–171a to be asked if subject was born after 1940			
166a. Who was the US President who was shot in Texas?	Incorrect John F. Kennedy	0 1	 9
167a. What is Yoko Ono famous for?	Incorrect Wife of Beatle, John Lennon	0 1	 9
168a. Who was the first man to set foot on the moon?	Incorrect Neil Armstrong	0 1	 9
169a. What was Edmund Hilary famous for?	Incorrect First to reach summit of Mt Everest	0 1	 9
170a. Who was the first woman Prime Minister of India?	Incorrect Indira Ghandhi	0 1	 9
171a. Who was the famous cinema actress who married Prince Rainier of Monaco? *Close approximations to the name are acceptable*	Incorrect Grace Kelly	0 1	 9
Retrieval of recent information			
172. What is the name of the present King or Queen?	Incorrect Correct	0 1	 9
173. Who is likely to be the next King or Queen?	Incorrect Correct	0 1	 9
174. What is the name of the Prime Minister? *For one month after an election, if the name of the former PM is given, ask 'Is he/she still Prime Minister?'*	Incorrect Correct	0 1	 9
175. What has been in the news in the past week or two? *If a general answer is given, e.g. 'war' ask for details*	Incorrect Correct	0 1	 9

Registration

I am going to name three objects. After I have finished saying all three, I want you to repeat them. Remember what they are because I am going to ask you to name them again in a few minutes.

176.	*Name the following three objects taking one second to say each: apple, table, penny.* *Tick which are correct on the first attempt and enter number correct under total.*	Apple Table Penny **Total**	__ __ __ [__]	**9**
177.	*If any errors or omissions are made on the first attempt, repeat all the names until subject learns all three (maximum of five repeats). Record number of repeats (record 0 if all correct on first attempt)*	Number of repeats	[__]	**9**

Attention/concentration

178.	Now I would like you to count backwards from 20.	Two or more errors One error Correct	**0** **1** **2**	**9**
179.	Now I would like you to take 7 away from 100. Now take 7 away from the number you get. Now keep subtracting 7 until I tell you to stop.	93 86 79 72 65 **Total**	__ __ __ __ __ [__]	**9**

Record answers. Score 1 point each time the difference is 7, even if a previous answer was incorrect. Maximum score = 5 points

Memory: Recall

180.	What were the three objects I asked you to repeat a little while ago?	Apple Table Penny **Total**	__ __ __ [__]	**9**

Tick each item answered correctly and enter number correct under Total

Language: Reading comprehension

Show 'Reading comprehension' in booklet.
I would like you to read this and do what it says
It is not necessary for the subject to read aloud. If subject reads instruction but fails to carry out action, say 'now do what it says'

If failure appears to be due to illiteracy, enquire whether subject learned to read. If illiterate code 7

181.	Close your eyes.	Incorrect Correct Illiterate	**0** **1** **7**	**9**

182. If you are older than 50 put your hands behind your head.	Incorrect	0	
	Correct	1	
	Illiterate	7	9

Praxis

Copying and Drawing

The subject should draw and write on the sheet of paper provided, see p. 56
Make sure the subject has finished before moving on to the next picture, e.g. by saying 'have you finished that one'?

183. Copy this design (pentagon). *Each pentagon should have 5 sides and 5 clear corners and the overlap should form a diamond*	Incorrect	0	
	Correct	1	9
184. Copy this design (spiral). *Three connected loops are required in the correct orientation.*	Incorrect	0	
	Correct	1	9
185. Copy this design (3D house). *Requires windows, door and chimney in correct position and in 3-dimensional representation*	Incorrect	0	
	Correct	1	9
186. Draw a large clock face and put all the numbers in. *When the subject has done this say,* 'Now set the hands to 10 past 11 (11.10)'.	Circle (or square)	___	
	All numbers in correct position	___	
	Correct time	___	
	Total	[...]	9
Tick each component correctly completed and enter number under Total			

Writing: Spontaneous

187. Write a complete sentence on this sheet of paper. *Indicate bottom of drawing sheet. Ask the subject what he/she has written and transcribe it onto the drawing sheet. Spelling and grammar are not important, but the sentence must have a subject (real or implied) and a verb. 'Help!' or 'Go away' are acceptable.*	Incorrect	0	
	Correct	1	
	Illiterate	7	9

Praxis: Ideational

Read the following statement and then hand a sheet of paper to the subject. Make a point of handing to the subject's midline. No repetition of this question is allowed. Speak clearly and slowly having first made sure you have the subject's full attention.

188. I am going to give you a piece of paper. When I do, take the paper in your *right* hand. Fold the paper in half with both hands, and put the paper down on your lap.	Right hand	___	
	Folds	___	
	On lap	___	
	Total	[...]	9
Do not repeat instructions or coach *Score a move as correct only if it takes place in the correct sequence.* *Tick each correct move and enter number correct under Total*			

Hand an envelope to the subject.

189. Put the paper in the envelope and seal the envelope.	Incorrect	0	
	Correct	1	9

Writing to dictation

190. Write this name and address on the envelope: Mr. John Brown 42 West Street, Bedford	Incorrect Poor but acceptable Correct Illiterate	0 1 2 7	9

Spelling and neatness are not important. Criterion is whether letter is likely to reach exact destination, e.g. 'Jon Brwn' is acceptable; '24' and 'Burford' are incorrect

Then say: Please try to remember this name and address as I shall be asking you about them later on

If the subject is unable to write, code 7 and say the address slowly, twice, and ask him/her to remember it

Praxis: Ideomotor

In questions 191–193 a correct MIME is needed. If the subject uses fingers to represent scissors or brush, say e.g. 'Pretend you are holding a toothbrush.' Score 1 if the subject makes a brushing movement but not as though holding a toothbrush

191. Show me how you wave goodbye.	Incorrect Correct	0 1	9
192. Show me how you would cut with scissors.	Incorrect Partially correct Correct	0 1 2	9
193. Show me how you would brush your teeth with a toothbrush.	Incorrect Partially correct Correct	0 1 2	9

Calculation

Mental calculation is required. Paper and pencil are not allowed.

Show the subject two different commonly used coins or notes of different value.

194. How much money does this make? *Record amount and response*	Incorrect Correct	0 1	9
195. If somebody went shopping and was given 15 pence as change from £1, how much did they spend? *Record response*	Incorrect Correct	0 1	9

Memory: Recall

196. What was the name and address you wrote on the envelope a short time ago? *Tick each item answered correctly and enter number correct under Total*	John Brown 42 West Street Bedford Total	__ __ __ __ __ [...]	9

Executive function

Abstract thinking

These questions investigate the capacity to work out the general relationships between objects. Fully correct answers score 2, partially correct answers score 1.

Examples are given beside each score. If the subject says 'They are not alike', say 'They are alike in some way. Can you tell me in which way they are alike?'

I am going to name two things and I would like you to tell me in what way they are alike. For example, a dog and a monkey are alike because they are both animals.

197.	In what way are an apple and a banana alike? *Record answer* *For this question only, if score is less than 2 say 'They are also alike because they are both fruit.'*	Round, have calories Food, grow, have peel Fruit	0 1 2	9
198.	In what way are a shirt and a dress alike? *Record answer*	Have buttons To wear, made of cloth, keep you warm Clothing or garments	0 1 2	9
199.	In what way are a table and a chair alike? *Record answer*	Wooden, have 4 legs Household objects, used for meals Furniture	0 1 2	9
200.	In what way are a plant and an animal alike? *Record answer*	Useful to man, carry germs Grow, need food, natural Living things	0 1 2	9

Ideational Fluency

200a. I am going to give you the name of a common object and I would like you to tell me as many uses for it as you can. For example, if the object was a SHEET OF PAPER it could be used to write on, to make a fan or it could be used to make a paper plane. The uses don't have to be serious – they can be ridiculous or humorous as well – so let your imagination have a free rein. The important thing is to try and think of as many uses as you possibly can in the time given. Try to make the uses as different from each other as possible.
Begin when I say the object and continue until I tell you to stop.
How many different uses can you think of for a BOTTLE?

Start timing and continue for 90 seconds, then say STOP.

Record all responses.

A correct response is any possible use of a single bottle, pieces of a bottle or numerous bottles, e.g. for strong liquid, as a weapon, as an instrument, smashed into pieces and used for art work, for juggling. Correct responses must specify a use; 'to smash', 'to stand on' are incorrect.	Number correct	|_|_|	9
	Note: Recode: >8 = 8 Enter 0–8 as above	|_|	9
A response is considered a perseveration if it is repeated verbatim or if the same idea is repeated with different examples, e.g. to store water, beer, cordial, orange juice, wine.	Number of perseverations	|_|_|	9

Visual reasoning

200b. ***Show 'Visual reasoning test' in booklet***

Show first item

Here are four boxes. Three of them have an object inside and this one is empty. Which of these objects below should go in the empty box? *Encourage subject to point to the correct response*

If subject makes an error on any of the first two items, point to the correct response and explain why it is correct.

Item 1:
The top row has a big yellow circle with a big blue circle beside it, so the bottom row needs a big blue circle.

Item 2:
The top row is blue; it has a little square beside the big circle. The bottom row is yellow, so it needs a little yellow square beside the yellow circle.

Do not make any further corrections.

If subject made an error, record which item (A to F) was chosen.

C	___	
A	___	
E	___	
D	___	
F	___	
B	___	
Total	[___]	**9**

Perception: Visual

Famous people

Show 'Recognition of famous people' in booklet

201. Who is this?

Score as correct if picture is recognised
Correct name is not required, but record any answer which does not correspond exactly to the examples given

Queen	___	
Pope, Archbishop, Bishop	___	
Total	[___]	**9**

Object constancy

Show 'Recognition of objects' in booklet

202. These are pictures of objects taken from unusual angles.
Can you tell me what they are?

Criterion is whether the object is recognised, not that it is named correctly, therefore descriptions of function are acceptable.
Tick each item answered correctly and enter number correct under Total

Spectacles	___	
Shoe	___	
Purse, suitcase	___	
Cup and saucer	___	
Telephone	___	
Pipe	___	
Total	[___]	**9**

Recognition of person/function

Indicate any two people available, e.g cleaner, doctor, nurse, patient, relative
If none available, score 9

203.	Can you tell me who this is, or what he/she does?	Incorrect Correct	0 1	9

Passage of time

204.	Without looking at your watch, can you tell me what the time is now (to the nearest hour)?	Incorrect Correct	0 1	9
205.	Without looking at your watch, can you tell me how long you think we have been talking together?	Time in minutes	|__|__|	999
206.	***Record finishing time of interview with subject.***		|__|__|	
	Actual duration of interview (minutes) *Check against starting time recorded at beginning of Section A.*	Time in minutes	|__|__|	999

References

Introduction

American Association of Homes and Services for the Aging. (2007). Aging Services: The Facts.

Espinoza, R. T. (2006). Improving the recognition and management of dementia in long-term care: Obstacles and opportunities. *Journal of the American Medical Directors Association, 7*(2), 128-130.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). 'Mini-Mental State'. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Hogan, T., Grimaldi, R., Dingemanse, J., Martin, M., Lyons, K., & Koller, W. (1999). The Parkinson's disease symptom inventory (PDSI): a comprehensive and sensitive instrument to measure disease symptoms and treatment side-effects. *Parkinsonism & Related Disorders, 5*, 93-98.

Kilada, S., Gamaldo, A., Grant, E. A., Moghekar, A., Morris, J. C., & O'Brien, R. J. (2005). Brief screening tests for the diagnosis of dementia: Comparison with the Mini-Mental State Exam. *Alzheimer Disease and Associated Disorders, 19*(1), 8-16.

Marinus, J., Visser, M., Stiggelbout, A. M., Rabey, J. M., Martínez-Martín, P., Bonuccelli, U., et al. (2004). A short scale for the assessment of motor impairments and disabilities in Parkinson's disease: the SPEC/SCOPA. *Journal of Neurology, Neurosurgery, and Psychiatry, 75*, 388-395.

Martignoni, E., Franchignoni, F., Pasetti, C., Ferriero, G., & Picco, D. (2003). Psychometric properties of the Unified Parkinson's Disease Rating Scale and of the Short Parkinson's Disease Evaluation Scale. *Neurological Science, 24*, 190-191.

Martínez-Martín, P., Benito-Léon, J., Burguera, J. A., Castro, A., Linazasaro, G., Martínez-Castrillo, J. C., et al. (2005). The SCOPA-motor scale for assessment of Parkinson's disease is a consistent and valid measure. *Journal of Clinical Epidemiology, 58*, 674-679.

Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease. (2003). The Unified Parkinson's Disease Rating Scale (UPDRS): Status and recommendations. *Movement Disorders, 18*(7), 738-750.

Roth, M., Huppert, F. A., Mountjoy, C. Q., & Tym, E. (1998). *CAMDEX-R: The Cambridge Examination for Mental Disorders of the Elderly*. Cambridge: Cambridge University Press.

Singer, C., & Luxenberg, J. (2003). Diagnosing dementia in long-term care facilities. *Journal of the American Medical Directors Association, Supplement 1, 4*(6), S134-S140.

U.S. Department of Health and Human Services Administration on Aging. (2006). *A statistical profile of Hispanic older Americans aged 65 +*

Chapter 1

Cubo, E., Stebbins, G. T., Golbe, L. I., Nieves, A. V., Leurgans, S., Goetz, C. G., et al. (2000). Application of the Unified Parkinson's Disease Rating Scale in Progressive Supernuclear Palsy: Factor analysis of the motor scale. *Movement Disorders, 15*(2), 276-279.

Fahn, S., Elton, R. L., & Committee, M. o. U. D. (1987). Unified Parkinson's disease rating scale. In S. Fahn, C. D. Marsden & D. B. Calne (Eds.), *Recent Developments in Parkinson's Disease* (Vol. 2, pp. 153-163). Florham Park, NJ: Macmillan Healthcare Information.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). 'Mini-Mental State'. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Hogan, T., Grimaldi, R., Dingemanse, J., Martin, M., Lyons, K., & Koller, W. (1999). The Parkinson's disease symptom inventory (PDSI): a comprehensive and sensitive instrument to measure disease symptoms and treatment side-effects. *Parkinsonism & Related Disorders, 5*, 93-98.

Lapane, K. L., Fernandez, H. H., Friedman, J. H., & Group, S. S. (1999). Prevalence, clinical characteristics, and pharmacologic treatment of Parkinson's disease in residents in long-term care facilities. *Pharmacotherapy, 19*(11), 1321-1327.

Li, K. Z. H., & Lindenberger, U. (2002). Relations between aging sensory/sensorimotor and cognitive functions. *Neuroscience and Biobehavioral Reviews, 26*, 777-783.

Louis, E. D., Tang, M. X., & Mayeux, R. (2004). Factor structure of parkinsonian signs in the community-dwelling elderly. *Movement Disorders, 19*(3), 268-272.

Louis, E. D., Tang, M. X., & Mayeux, R. (2005). Functional correlates and prevalence of mild parkinsonian signs in a community population of older people. *Archives of Neurobiology, 62*, 297-302.

Marinus, J., Visser, M., Stiggelbout, A. M., Rabey, J. M., Martínez-Martín, P., Bonuccelli, U., et al. (2004). A short scale for the assessment of motor impairments

and disabilities in Parkinson's disease: the SPEC/SCOPA. *Journal of Neurology, Neurosurgery, and Psychiatry, 75*, 388-395.

Martignoni, E., Franchignoni, F., Pasetti, C., Ferriero, G., & Picco, D. (2003). Psychometric properties of the Unified Parkinson's Disease Rating Scale and of the Short Parkinson's Disease Evaluation Scale. *Neurological Science, 24*, 190-191.

Martínez-Martín, P., Benito-Léon, J., Burguera, J. A., Castro, A., Linazasaro, G., Martínez-Castrillo, J. C., et al. (2005). The SCOPA-motor scale for assessment of Parkinson's disease is a consistent and valid measure. *Journal of Clinical Epidemiology, 58*, 674-679.

Martínez-Martín, P., Gil-Nagel, A., Gracia, L. M., Gómez, J. B., Martínez-Sarriés, J., & Bermejo, F. (1994). Unified Parkinson's disease rating scale characteristics and structure. *Movement Disorders, 9*(1), 76-83.

Metman, L. V., Myre, B., Hassin-Baer, S., Arzbaecher, J., Sierens, D., & Bakay, R. (2004). Test-retest reliability of UPDRS-III, dyskinesia scales, and timed motor tests in patients with advanced Parkinson's disease: An argument against multiple baseline assessments. *Movement Disorders, 19*(9), 1079-1084.

Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease. (2003). The Unified Parkinson's Disease Rating Scale (UPDRS): Status and recommendations. *Movement Disorders, 18*(7), 738-750.

Pillon, B., Dubois, B., & Agid, Y. (1996). Testing cognition may contribute to the diagnosis of movement disorders. *Neurology, 46*(2), 329-334.

Rabinowitz, J., Davidson, M., De Deyn, P. P., Katz, I., Brodaty, H., & Cohen-Mansfield, J. (2005). Factor analysis of the Cohen-Mansfield Agitation Inventory in three large

samples of nursing home patients with dementia and behavioral disturbance. *American Journal of Geriatric Psychiatry, 13*(11), 991-998.

Racette, B. A., Tabbal, S. D., Jennings, D., Good, L. M., Permutter, J. S., & Evanoff, B. A. (2006). A rapid method for mass screening for parkinsonism. *NeuroToxicology, 27*, 357-361.

Ramaker, C., Marinus, J., Stiggelbout, A. M., & Van Hilten, B. J. (2002). Systematic evaluation of rating scales for impairment and disability in Parkinson's disease. *Movement Disorders, 17*(5), 867-876.

Richards, M., Marder, K., Cote, L., & Mayeux, R. (1994). Interrater reliability of the Unified Parkinson's Disease Rating Scale Motor Examination. *Movement Disorders, 9*(1), 89-91.

Sabbagh, M. N., Silverberg, N., Bircea, S., Majeed, B., Samant, S., Caviness, J. N., et al. (2005). Is the functional decline of Parkinson's disease similar to the functional decline of Alzheimer's disease? *Parkinsonism & Related Disorders, 11*(5), 311-315.

Siderowf, A., McDermott, M., Kierburtz, K., Blindauer, K., Plumb, S., Shoulson, I., et al. (2002). Test-retest reliability of the Unified Parkinson's Disease Rating Scale in patients with early Parkinson's disease: Results from a multicenter clinical trial. *Movement Disorders, 17*(4), 758-763.

SPSS for Windows(Ver. 14.0.2).

Stebbins, G. T., Goetz, C. G., Lang, A. E., & Cubo, E. (1999). Factor analysis of the motor section of the Unified Parkinson's Disease Rating Scale during the off-state. *Movement Disorders, 14*(4), 585-589.

Tomer, R., Levin, B. E., & Weiner, W. J. (1993). Side of onset of motor symptoms influences cognition in Parkinson's disease. *Annals of Neurology, 34,* 579-584.

Tse, W., Libow, L. S., Neufeld, R., Lesser, G., Frank, J., Dolan, S., et al. (2006). Prevalence of movement disorders in an elderly nursing home population.

Chapter 2

Allen, R., DeLaine, S. R., Chaplin, W. F., Marson, D. C., Bourgeois, M. S., Dijkstra, K., et al. (2003). Advance care planning in nursing homes: Correlates of capacity and possession of advance directives. *The Gerontologist, 43*(3), 309-317.

Alvardo-Esquivel, C., Hernández-Alvarado, A. B., Tapia-Rodríguez, R. O., Guerrero-Iturbe, Á., Rodríguez-Corral, K., & Martínez, S. E. (2004). Prevalence of dementia and Alzheimer's disease in elders of nursing homes and a senior center of Durango City, Mexico. *BMC Psychiatry, 4*(3).

American Association of Homes and Services for the Aging. (2007). Aging Services: The Facts.

Beekly, D. L., Ramos, E. M., van Belle, G., Deitrich, W., Clark, A. D., Jacka, M. E., et al. (2004). The National Alzheimer's Coordinating Center (NACC) Database: An Alzheimer's disease database. *Alzheimer Disease and Associated Disorders, 18*(4), 270-277.

Brandt, J., Folstein, S. E., & Folstein, M. F. (1988). Differential cognitive impairment in Alzheimer's disease and Huntington's disease. *Annals of Neurology, 23,* 555-561.

Camicioli, R., & Licis, L. (2004). Motor impairment predicts falls in specialized Alzheimer's care units. *Alzheimer Disease and Associated Disorders, 18*(4), 214-218.

Espino, D. V., Lichtenstein, M. J., Palmer, R. F., & Hazuda, H. P. (2001). Ethnic differences in Mini-Mental State Examination (MMSE) scores: Where you live makes a difference. *Journal of the American Geriatrics Society, 49*(5), 538-548.

Espinoza, R. T. (2006). Improving the recognition and management of dementia in long-term care: Obstacles and opportunities. *Journal of the American Medical Directors Association, 7*(2), 128-130.

Evans, B. C., & Crogan, N. L. (2006). Building a scientific base for nutrition care of hispanic nursing home residents. *Geriatric Nursing, 27*(5), 273-279.

Fernandez, R., Kavcic, V., & Duffy, C. J. (2007). Neuropsychological analyses of low- and high-level visual processing in Alzheimer's disease. *Neurology, 68*(24), 2066-2076.

Fillenbaum, G. G., George, L. K., & Blazer, D. G. (1988). Scoring nonresponse on the Mini-Mental Status Examination. *Psychological Medicine, 18*, 1021-1025.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "MINI-MENTAL STATE" A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Fountoulakis, K. N., Tsolaki, M., Chantzi, H., & Kazis, A. (2000). Mini Mental State Examination (MMSE): A validation study in Greece. *American Journal of Alzheimer's Disease and Other Dementias, 15*(6), 342-345.

Franssen, E. H., & Reisberg, B. (1997). Neurologic markers fo the progression of Alzheimer's disease. *International Psychogeriatrics, 9*(Supplement 1), 297-306.

Hartmaier, S. L., Sloane, P. D., Guess, H. A., Koch, G. G., Mitchell, C. M., & Phillips, C. D. (1995). Validation of the Minimum Data Set Cognitive Performance Scale: Agreement with the Mini-Mental State Examination. *Journal of Gerontology A:Biological Science Medical Science, 50*(2), M128-M133.

Herst, L., Voss, C. B., & Waldman, J. (1990). Cortical function assessment in the elderly. *Journal of Neuropsychiatry, 2*(4), 385-390.

Kilada, S., Gamaldo, A., Grant, E. A., Moghekar, A., Morris, J. C., & O'Brien, R. J. (2005). Brief screening tests for the diagnosis of dementia: Comparison with the Mini-Mental State Exam. *Alzheimer Disease and Associated Disorders, 19*(1), 8-16.

Küçükdeveci, A. A., Kutlay, S., Elhan, A. H., & Tennant, A. (2005). Preliminary study to evaluate the validity of the mini-mental state examination in a normal population in Turkey. *International Journal of Rehabilitation Medicine, 28*, 77-79.

Lapane, K. L., Fernandez, H. H., Friedman, J. H., & and the SAGE Study Group. (1999). Prevalence, clinical characteristics, and pharmacologic treatment of Parkinson's disease in residents in long-term care facilities. *Pharmacotherapy, 19*(11), 1321-1327.

Leritz, E., Brandt, J., Minor, M., Reis-Jensen, F., & Petri, M. (2000). "Subcortical" cognitive impairment in patients with systemic lupus erythematosis. *Journal of the International Neuropsychological Society, 6*, 821-825.

Lou, M.-F., Dai, Y.-T., Huang, G.-S., & Yu, P.-J. (2007). Identifying the most efficient items from the Mini-Mental State Examination for cognitive function assessment in older Taiwanese patients. *Journal of Clinical Nursing, 16,* 502-508.

Macdonald, A. J. D., Carpenter, G. I., Box, O., Roberts, A., & Sahu, S. (2002). Dementia and use of psychotropic medication in non- 'Elderly Mentally Infirm' nursing homes in South East England. *Age and Ageing, 31,* 58-64.

Morris, J. C. (1993). The Clinical Dementia Rating (CDR): Current version and scoring rules. *Neurology, 43*(1), 2412-2414.

Morris, J. C., Weintraub, S., Chui, H. C., Cummings, J., DeCarli, C., Ferris, S., et al. (2006). The Uniform Data Set (UDS): Clinical and cognitive variables and descriptive data from Alzheimer's Disease Centers. *Alzheimer Disease and Associated Disorders, 20*(4), 210-216.

Morris, J. N., Fries, B. E., Mehr, D. R., Hawes, C., Phillips, C., Mor, V., et al. (1994). MDS Cognitive Performance Scale. *Journal of Gerontology: Medical Sciences, 49*(4), M174-M182.

Morris, J. N., Fries, B. E., & Morris, S. A. (1999). Scaling ADLs within the MDS. *Journal of Gerontology: Medical Sciences, 54A*(11), M546-M553.

Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease. (2003). The Unified Parkinson's Disease Rating Scale (UPDRS): Status and recommendations. *Movement Disorders, 18*(7), 738-750.

Nelson, J. C., Hollander, S. B., Betzel, J., Smolen, P., & Mirtazapine Nursing Home Study Group. (2006). Mirtazapine orally disintegrating tablets in depressed nursing

home residents 85 years of age and older. *International Journal of Geriatric Psychiatry, 21*, 898-901.

Paquay, L., De Lepeleire, J., Schoenmakers, B., Ylieff, M., Fontaine, O., & Buntinx, F. (2007). Comparison of the diagnostic accuracy of the Cognitive Performance Scale (Minimum Data Set) and the Mini-Mental State Exam for the detection of cognitive impairment in nursing home residents. *International Journal of Geriatric Psychiatry, 22*, 286-293.

Räihä, I., Isoaho, R., Ojanlatva, A., Viramo, P., Sulkava, R., & Kivelä, S.-L. (2001). Poor performance in the Mini-Mental State Examination due to causes other than dementia. *Scandinavian Journal of Primary Health Care, 19*, 34-38.

Resnick, B., Gruber-Baldini, A. L., Pretzer-Aboff, I., Galik, E., Buie, V. C., Russ, K., et al. (2007). Reliability and validity of the evaluation to sign consent measure. *The Gerontologist, 47*(1), 69-77.

Rosenberg, P. B., Mielke, M. M., Samus, Q. M., Rosenblatt, A., Baker, A., Brandt, J., et al. (2006). Transition to nursing home from assisted living is not associated with dementia-related problem behaviors. *Journal of the American Medical Directors Association, 7*, 73-78.

Scarmeas, N., Albert, M., Brandt, J., Blacker, D., Hadjigeorgiou, G., Papadimitriou, A., et al. (2005). Motor signs predict poor outcomes in Alzheimer's disease. *Neurology, 64*(10), 1696-1703.

Singer, C., & Luxenberg, J. (2003). Diagnosing dementia in long-term care facilities. *Journal of the American Medical Directors Association, Supplement 1, 4*(6), S134-S140.

SPSS for Windows (Release 14.0.2).

Tarshish, C. Y., Neufeld, R. R., & Libow, L. S. (In-Preparation). Utility of the United Parkinson's Disease Rating Scale Motor Examination in the frail elderly.

Tse, W., Libow, L. S., Neufeld, R., Lesser, G., Frank, J., Dolan, S., et al. (In Press). Prevalence of movement disorders in an elderly nursing home population. *Archives of Gerontology and Geriatrics*.

U.S. Department of Health and Human Services Administration on Aging. (2006). *A statistical profile of Hispanic older Americans aged 65 +*

Webster, K. E., Merory, J. R., & Wittwer, J. E. (2006). Gait variability in community dwelling adults with Alzheimer's disease. *Alzheimer Disease and Associated Disorders, 20*(1), 37-40.

Wind, A. W., Schellevis, F., Van Staveren, G., Scholten, R. J. P. M., Jonker, C., & Van Eijk, J. T. M. (1997). Limitations of the Mini-Mental State Examination in diagnosing dementia in general practice. *International Journal of Geriatric Psychiatry, 12*, 101-108.

Wood, R. Y., Giuliano, K. K., Bignell, C. U., & Pritham, W. W. (2006).

Assessing cognitive ability in research: Use of MMSE with minority populations and elderly adults with low education levels. *Journal of Gerontological Nursing, 32*(4), 45-54.

Chapter 3

American Association of Homes and Services for the Aging. (2007). Aging Services: The Facts.

Athey, R. J., Porter, R. W., & Walker, R. W. (2005). Cognitive assessment of a representative community population with Parkinson's disease (PD) using the Cambridge Cognitive Assessment-Revised (CAMCOG-R). *Age and Ageing, 34*, 268-273.

Athey, R. J., & Walker, R. W. (2006). Demonstration of cognitive decline in Parkinson's disease using the Cambridge Cognitive Assessment (Revised) (CAMCOG-R). *International Journal of Geriatric Psychiatry, 21*, 977-982.

Ball, S. L., Holland, A. J., Huppert, F. A., Treppner, P., Watson, P., & Hon, J. (2004). The modified CAMDEX informant interview is a valid and reliable tool for use in the diagnosis of dementia in adults with Down's syndrome. *Journal of Intellectual Disability Research, 48*(6), 611-620.

Ballard, C., O'Brien, J., Morris, C. M., Barber, R., Swann, A., Neill, D., et al. (2001). The progression of cognitive impairment in dementia with Lewy bodies, vascular dementia and Alzheimer's disease. *International Journal of Geriatric Psychiatry, 16*, 499-503.

Ballard, C. G., Morris, C. M., Rao, H., O'Brien, J. T., Barber, R., Stephens, S., et al. (2004). APOE e4 and cognitive decline in older stroke patients with early cognitive impairment. *Neurology, 63*, 1399-1402.

Beekly, D. L., Ramos, E. M., van Belle, G., Deitrich, W., Clark, A. D., Jacka, M. E., et al. (2004). The National Alzheimer's Coordinating Center (NACC) Database: An

Alzheimer's disease database. *Alzheimer Disease and Associated Disorders, 18*(4), 270-277.

Centers for Disease Control and Prevention, National Center for Health Statistics,. (2006). CDC Trends in Health and Aging. In U.S. Department of Health and Human Services (Ed.).

Cormack, F., Aarsland, D., Ballard, C., & Tovée, M. J. (2004). Pentagon drawing and neuropsychological performance in Dementia with Lewy Bodies, Alzheimer's disease, Parkinson's disease and Parkinson's disease with dementia. *International Journal of Geriatric Psychiatry*, *19*, 371-377.

Cullum, S., Huppert, F. A., McGee, M., Dening, T., Ahmed, A., Paykel, E. S., et al. (2000). Decline across different domains of cognitive function in normal ageing: Results of a longitudinal population-based study using CAMCOG. *International Journal of Geriatric Psychiatry*, *15*, 853-862.

Espinoza, R. T. (2006). Improving the recognition and management of dementia in long-term care: Obstacles and opportunities. *Journal of the American Medical Directors Association, 7*(2), 128-130.

Fillenbaum, G. G., George, L. K., & Blazer, D. G. (1988). Scoring nonresponse on the Mini-Mental Status Examination. *Psychological Medicine, 18*, 1021-1025.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "MINI-MENTAL STATE" A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Frankfort, S. V., Appels, B. A., de Boer, A., Tulner, L. R., van Campen, J. P. C. M., Koks, C. H. W., et al. (2007). Identification of responders and reactive domains to

rivastigmine in Alzheimer's disease. *Pharmacoepidemiology and Drug Safety*, *16*, 545-551.

Garre-Olmo, J., López-Pousa, S., Vilalta-Franch, J., Turon-Estrada, A., Lozano-Gallego, M., Hernández-Ferràndiz, M., et al. (2004). Neuropsychological profile of Alzheimer's disease in women: moderate and moderately severe cognitive decline. *Archives of Women's Mental Health, 7*, 27-36.

Graham, C., Ballard, C., & Saad, K. (1997). Variables which distinguish patients fulfilling clinical criteria for dementia with Lewy Bodies from those with Alzheimer's disease. *International Journal of Geriatric Psychiatry, 12*, 314-318.

Hartman, J. A. (2000). Investigation of the use of the CAMCOG in the visually impaired elderly. *International Journal of Geriatric Psychiatry, 15*, 863-869.

Heinik, J., Werner, P., Mendel, A., Raikher, B., & Bleich, A. (1999). The Cambridge Cognitive Examination (CAMCOG): Validation of the hebrew version in elderly demented patients. *International Journal of Geriatric Psychiatry, 14*, 1006-1013.

Hobson, P., & Meara, J. (1999). The detection of dementia and cognitive impairment in a community population of elderly people with Parkinson's disease by use of the CAMCOG neuropsychological test. *Age and Ageing, 28*, 39-43.

Hobson, P., & Meara, J. (2004). Risk and incidence of dementia in a cohort of older subjects with Parkinson's disease in the United Kingdom. *Movement Disorders, 19*(9), 1043-1049.

Jonkers, C., Schmand, B., Lindeboom, J., Havekes, L. M., & Launer, L. J. (1998). Association between Apolipoprotein E e4 and the rate of cognitive decline in

community-dwelling elderly individuals with and without dementia. *Archives of Neurology, 55*, 1065-1069.

Kurz, A., Egensperger, R., Haupt, M., Lautenschlager, N., Romero, B., Graeber, M. B., et al. (1996). Apolipoprotein E e4 allele, cognitive decline, and deterioration of everyday performance in Alzheimer's disease. *Neurology, 47*, 440-443.

Leeds, L., Meara, R. J., Woods, R., & Hobson, J. P. (2001). A comparison of the new executive functioning domains of the CAMCOG-R with existing tests of executive function in elderly stroke survivors. *Age and Ageing, 30*, 251-254.

Levy, G., Jacobs, D. M., Tang, M.-X., Cote, L. J., Louis, E. D., Alfaro, B., et al. (2002). Memory and executive function impairment predict dementia in Parkinson's disease. *Movement Disorders, 17*(6), 1221-1226.

Morris, J. C. (1993). The Clinical Dementia Rating (CDR): Current version and scoring rules. *Neurology, 43*(1), 2412-2414.

Morris, J. C., Weintraub, S., Chui, H. C., Cummings, J., DeCarli, C., Ferris, S., et al. (2006). The Uniform Data Set (UDS): Clinical and cognitive variables and descriptive data from Alzheimer's Disease Centers. *Alzheimer Disease and Associated Disorders, 20*(4), 210-216.

Nielsen, H., Lolk, A., Andersen, K., Andersen, J., & Kragh-Sørensen, P. (1999). Characteristics of elderly who develop Alzheimer's disease during the next two years--A neuropsychological study using CAMCOG. The Odense Study. *International Journal of Geriatric Psychiatry, 14*, 957-963.

Olin, J. T., & Zelinski, E. M. (1991). The 12-month reliability of the Mini-Mental State Examination. *Psychological Assessment, 3*(3), 427-432.

Raven, J. C. (1982). *Revised manual for Raven's Coloured Progressive Matrices*. Windsor:UK: NFER-Nelson.

Richards, M., Cote, L. J., & Stern, Y. (1993a). Executive function in Parkinson's disease: Set-shifting or set-maintenance? *Journal of Clinical & Experimental Neuropsychology, 15*(2), 266-279.

Richards, M., Cote, L. J., & Stern, Y. (1993b). The relationship between visuospatial ability and perceptual motor function in Parkinson's disease. *Journal of Neurology, Neurosurgery, & Psychiatry, 56*(4), 400-406.

Roth, M., Huppert, F. A., Mountjoy, C. Q., & Tym, E. (1998). *CAMDEX-R: The Cambridge Examination for Mental Disorders of the Elderly*. Cambridge: Cambridge University Press.

Schmand, B., Walstra, G., Lindeboom, J., Teunisse, S., & Jonkers, C. (2000). Early detection of Alzheimer's disease using the Cambridge Cognitive Examination (CAMCOG). *Psychological Medicine, 30*, 619-627.

Singer, C., & Luxenberg, J. (2003). Diagnosing dementia in long-term care facilities. *Journal of the American Medical Directors Association, Supplement 1, 4*(6), S134-S140.

SPSS for Windows Release 14.0.2. (Version (17 Mar 2006)).

Tam, C. W. C., Burton, E. J., McKeith, I. G., Burn, D. J., & O'Brien, J. T. (2005). Temporal lobe atrophy on MRI in Parkinson's disease with dementia. *Neurology, 64*, 861-865.

Tse, W., Libow, L. S., Neufeld, R., Lesser, G., Frank, J., Dolan, S., et al. (In Press). Prevalence of movement disorders in an elderly nursing home population. *Archives of Gerontology and Geriatrics*.

U.S. Department of Health and Human Services Administration on Aging. (2006). *A statistical profile of Hispanic older Americans aged 65 +*

Washburn, l. A. M., Sands, L. P., & Walton, P. J. (2003). Assessment of social cognition in frail older adults and its association with social functioning in the nursing home. *The Gerontologist, 43*(2), 203-212.

Williams, J. G., Huppert, F. A., Matthews, F. E., Nickson, J., & CFAS), M. C. F. a. A. S. M. (2003). Performance and normative values of a concise neuropsychological test (CAMCOG) in an elderly population study. *International Journal of Geriatric Psychiatry, 18*, 631-644.

Chapter 4

American Association of Homes and Services for the Aging. (2007). Aging Services: The Facts.

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders* (Fourth ed.). Washington:DC.

Antrobus, J. S., Duff, M., Shono, Y., Farahani, R., & Numanbayraktaroglu, S. (2004). Word recognition and learning: Representation and process, in repetition priming: City College of the City University of New York.

Bobinski, M., De Leon, M. J., Convit, A., De Santi, S., Wegiel, J., Tarshish, C. Y., et al. (1999). MRI of entorhinal cortex in mild Alzheimer's disease. *Lancet, 353*(9146), 38-40.

Camp, C. J., Foss, J. W., Stevens, A. B., Reichard, C. C., McKitrick, L. A., & O'Hanlon, A. M. (1993). Memory training in normal and demented elderly populations: The E-I-E-I-O model. *Experimental Aging Research, 19*(3), 277-290.

Convit, A., Wolf, O. T., Tarshish, C. Y., & De Leon, M. J. (2003). Reduced glucose tolerance is associated with poor memory performance and hippocampal atrophy among normal elderly. *Proceedings of the National Academy of Science USA, 100*(4), 2019-2022.

de Leon, M. J., De Santi, S., Zinkowski, R., Mehta, P. D., Pratico, D., Segal, S., et al. (2006). Longitudinal CSF and MRI biomarkers improve the diagnosis of mild cognitive impairment. *Neurobiology of Aging, 27*(3), 394-401.

De Santi, S., De Leon, M. J., Rusinek, H., Convit, A., Tarshish, C. Y., Roche, A., et al. (2001). Hippocampal formation glucose metabolism and volume losses in MCI and AD. *Neurobiology of Aging, 22*(4), 529-539.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "MINI-MENTAL STATE" A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Golomb, J., De Leon, M. J., Kluger, A., George, A. E., Tarshish, C., & Ferris, S. H. (1993). Hippocampal atrophy in normal aging. An association with recent memory impairment. *Archives of Neurology, 50*(9), 967-973.

Golomb, J., Kluger, A., De Leon, M. J., Ferris, S. H., Convit, A., Mittelman, M. S., et al. (1994). Hippocampal formation size in normal human aging: a correlate of delayed secondary memory performance. *Learning and Memory, 1*(1), 45-54.

Golomb, J., Kluger, A., De Leon, M. J., Ferris, S. H., Mittelman, M. S., Cohen, J., et al. (1996). Hippocampal formation size predicts declining memory performance in normal aging. *Neurology, 47*(3), 810-813.

Henke, K., Weber, B., Kneifel, S., Weiser, H. G., & Buck, A. (1999). Human hippocampus associates information in memory. *Proceedings of the National Academy of Science USA, 96*, 5884-5889.

Kesner, R. P., & Giles, R. (1998). Neural circuit analysis of spatial working memory: Role of presibiculum, parasubiculum, medial and lateral entorhinal cortex. *Hippocampus, 8*, 416-423.

Kluger, A., Ferris, S. H., Golomb, J., Mittelman, M. S., & Reisberg, B. (1999). Neuropsychological prediction of decline to dementia in nondemented elderly. *Journal of Geriatric Psychiatry and Neurology, 12*(4), 168-179.

Morris, J. C. (1993). The Clinical Dementia Rating (CDR): Current version and scoring rules. *Neurology, 43*(1), 2412-2414.

O'Reilly, R. C., & Rudy, J. W. (2001). Conjunctive representations in learning and memory: Principles of cortical and hippocampal function. *Psychological Review, 108*, 311-345.

Petersen, R. C. (1995). Normal aging, mild cognitive impairment, and early Alzheimer's disease. *Neurologist, 1*, 326-344.

Petersen, R. C., Smith, G. E., Waring, S. C., Ivnik, R. J., Tangalos, E. G., & Kokman, E. (1999). Mild Cognitive Impairment: Clinical characterization and outcome. *Archives of Neurology, 56*, 303-308.

Reed, J. M., & Squire, L. R. (1997). Impaired recognition memory in patients with lesions limited to the hippocampal formation. *Behavioral Neuroscience, 111*(4), 667-675.

Reisberg, B., Ferris, S. H., de Leon, M. J., & Crook, T. (1982). The Global Deterioration Scale for assessment of primary degenerative dementi. *American Journal of Psychiatry, 139*(9), 1136-1139.

Sheikh, J. I., & Yesavage, J. A. (1986). Geriatric Depression Scale (GDS): recent evidence and development of a shorter version, in Clinical Gerontology: A Guide to Assessment and Intervention. In B. T. L. (Ed.), *Clinical Gerontology: A Guide to Assessment and Intervention* (pp. 165–173). New York: The Hawthorne Press.

Sramek, J. J., Veroff, A. E., & Cutler, N. R. (2000). Mild Cognitive Impairment: Emerging therapeutics. *The Annals of Pharmacotherapy, 34*, 1179-1188.

Wolinsky, F. D., Unverzagt, F. W., Smith, D. M., Jones, R., Stoddard, A., & Tennstedt, S. L. (2006). The ACTIVE cogntive training trial and health-related quality of life: Protection that lasts for 5 years. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences, 61*(12), 1324-1329.

Discussion

Antrobus, J. S., Duff, M., Shono, Y., Farahani, R., & Numanbayraktaroglu, S. (2004). Word recognition and learning: Representation and process, in repetition priming: City College of the City University of New York.

Brandt, J., Folstein, S. E., & Folstein, M. F. (1988). Differential cognitive impairment in Alzheimer's disease and Huntington's disease. *Annals of Neurology, 23,* 555-561.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). 'Mini-Mental State'. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Hogan, T., Grimaldi, R., Dingemanse, J., Martin, M., Lyons, K., & Koller, W. (1999). The Parkinson's disease symptom inventory (PDSI): a comprehensive and sensitive instrument to measure disease symptoms and treatment side-effects. *Parkinsonism & Related Disorders, 5*, 93-98.

Leritz, E., Brandt, J., Minor, M., Reis-Jensen, F., & Petri, M. (2000). "Subcortical" cognitive impairment in patients with systemic lupus erythematosis. *Journal of the International Neuropsychological Society, 6*, 821-825.

Louis, E. D., Tang, M. X., & Mayeux, R. (2004). Factor structure of parkinsonian signs in the community-dwelling elderly. *Movement Disorders, 19*(3), 268-272.

Louis, E. D., Tang, M. X., & Mayeux, R. (2005). Functional correlates and prevalence of mild parkinsonian signs in a community population of older people. *Archives of Neurobiology, 62*, 297-302.

Marinus, J., Visser, M., Stiggelbout, A. M., Rabey, J. M., Martínez-Martín, P., Bonuccelli, U., et al. (2004). A short scale for the assessment of motor impairments

and disabilities in Parkinson's disease: the SPEC/SCOPA. *Journal of Neurology, Neurosurgery, and Psychiatry, 75*, 388-395.

Martignoni, E., Franchignoni, F., Pasetti, C., Ferriero, G., & Picco, D. (2003). Psychometric properties of the Unified Parkinson's Disease Rating Scale and of the Short Parkinson's Disease Evaluation Scale. *Neurological Science, 24*, 190-191.

Martínez-Martín, P., Benito-Léon, J., Burguera, J. A., Castro, A., Linazasaro, G., Martínez-Castrillo, J. C., et al. (2005). The SCOPA-motor scale for assessment of Parkinson's disease is a consistent and valid measure. *Journal of Clinical Epidemiology, 58*, 674-679.

Movement Disorders Society Task Force on Rating Scales for Parkinson's Disease. (2003). The Unified Parkinson's Disease Rating Scale (UPDRS): Status and recommendations. *Movement Disorders, 18*(7), 738-750.

O'Reilly, R. C., & Rudy, J. W. (2001). Conjunctive representations in learning and memory: Principles of cortical and hippocampal function. *Psychological Review, 108*, 311-345.

Olin, J. T., & Zelinski, E. M. (1991). The 12-month reliability of the Mini-Mental State Examination. *Psychological Assessment, 3*(3), 427-432.

Räihä, I., Isoaho, R., Ojanlatva, A., Viramo, P., Sulkava, R., & Kivelä, S.-L. (2001). Poor performance in the Mini-Mental State Examination due to causes other than dementia. *Scandinavian Journal of Primary Health Care, 19*, 34-38.

Roth, M., Huppert, F. A., Mountjoy, C. Q., & Tym, E. (1998). *CAMDEX-R: The Cambridge Examination for Mental Disorders of the Elderly*. Cambridge: Cambridge University Press.

Tombaugh, T. N., & McIntyre, N. J. (1992). The Mini-Mental State Examination: A comprehensive review. *Journal of the American Geriatrics Society, 40*(9), 922-935.

U.S. Department of Health and Human Services Administration on Aging. (2006). *A statistical profile of Hispanic older Americans aged 65 +*

Williams, J. G., Huppert, F. A., Matthews, F. E., Nickson, J., & MRC Cognitive Function and Ageing Study (MRC CFAS). (2003). Performance and normative values of a concise neuropsychological test (CAMCOG) in an elderly population study. *International Journal of Geriatric Psychiatry, 18,* 631-644.