Screening for MCI in Older Adults

Joseph Barsuglia, M.A. ~ 12/05/2012

Dementia & Alzheimer's Disease

Alzheimer's disease (AD) is the most common form of dementia (National Institute on Aging, 2007).

In the US, approximately 5.4 million suffer from AD
and this statistic is anticipated
to grow as the current cohort of older adults become older
(Alzheimer's Association, 2012)

50 percent of individuals over age 65 report cognitive deficits and virtually all respondents worry that perceived changes in their memory may be early signs of Alzheimer's disease or dementia.
(Chertkow et al., 2008; Jonker, Geerlings & Schmand, 2000; Ritchie, Artero & Touchon, 2001).

Population Growth, Aging & Memory Concerns

By the year 2030, the number of individuals over the age of 65 is estimated to practically double to 75 million

(Administration on Aging, 2009).

By the year 2025, the number of individuals with Alzheimer's disease over the age of 65 is expected to increase 30 percent, from 5.2 million to 6.7 million

(Hebert, Scherr, Bienias, Bennett, & Evans, 2003).

With the estimated increase in the aging population and life expectancy in the US, there will be an estimated four-fold increase in individuals over the age of 85 by the year 2050. By 2050, the number of individuals over the age of 65 with Alzheimer's disease is expected to triple

(Hebert et al., 2003).

Healthy Aging & AAMI

Normal cognitive aging consists of changes due to the natural course of aging, rather than a neurodegenerative condition.

The criteria for AAMI:

- over age 50
- report subjective declines in memory
- perform at least 1 SD below the mean on memory scores compared to young adults

(Crook et al., 1986).

Debate over whether AAMI is a result of normal aging or early prodromal phase of a neurodegenerative process

Mild Cognitive Impairment

The original MCI criteria includes:

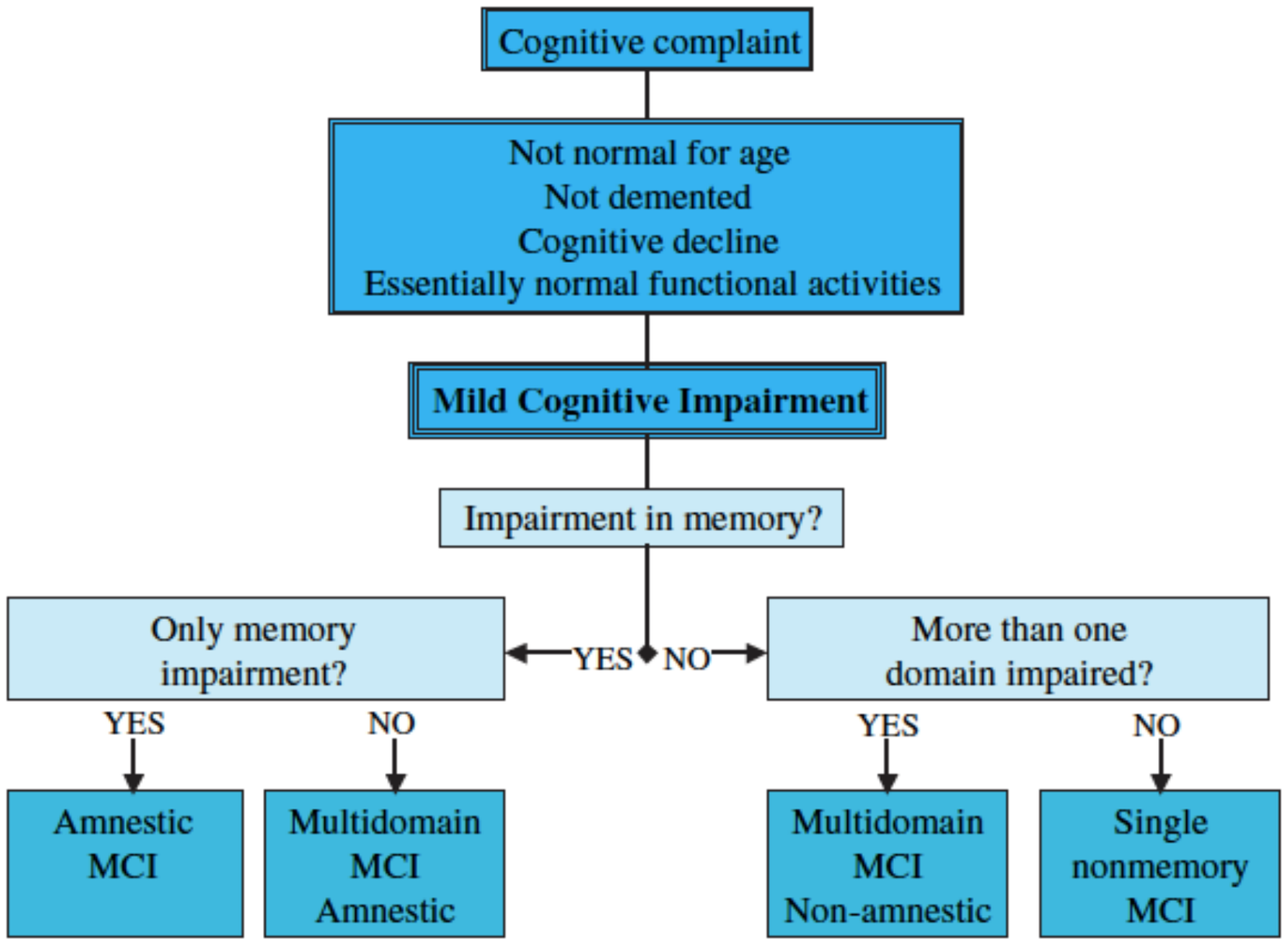
- subjective memory concerns
- performance in memory tests 1.5 SD below age- education-matched controls.
- preserved activities of daily living
- absence of dementia
- CDR 0.5

(Petersen et al., 1995; Petersen et al., 1999).

A workgroup later nuanced Petersen's initial definition of MCI, to account for multi-domain and non-amnestic variants of MCI

(Winblad, et al., 2004)

Mild Cognitive Impairment



Mild Cognitive Impairment

Most MCI studies have focused on the amnestic form (a-MCI) as individuals with this variant have the highest rates of progression to AD

(Petersen et al., 1999).

The infrequency of the pure amnestic MCI subtype makes it likely that MCI study samples include a combination of both amnestic single and amnestic multi-domain subtypes

(Alladi et al., 2006; Lonie, Tierney & Ebmeier, 2009).

Mild Cognitive Impairment remains the most frequently used term to describe cognitive impairment in older adults

(Petersen et al., 1999; Petersen et al., 2001)

American Journal of Alzheimer's Disease & Other Dementias®
27(7) 520-529

DOI: 10.1177/1533317512459798
http://aja.sagepub.com
SAGE

Neuropsychological and Neuroimaging Markers in Early Versus Late-Onset Alzheimer's Disease

Natalie C. Kaiser, PhD[1], Rebecca J. Melrose, PhD[2], Collin Liu, MD[1], David L. Sultzer, MD[1,2], Elvira Jimenez, MPH[1], Michael Su, MD[2], Lorena Monserratt, MA[1], and Mario F. Mendez, MD, PhD[1]

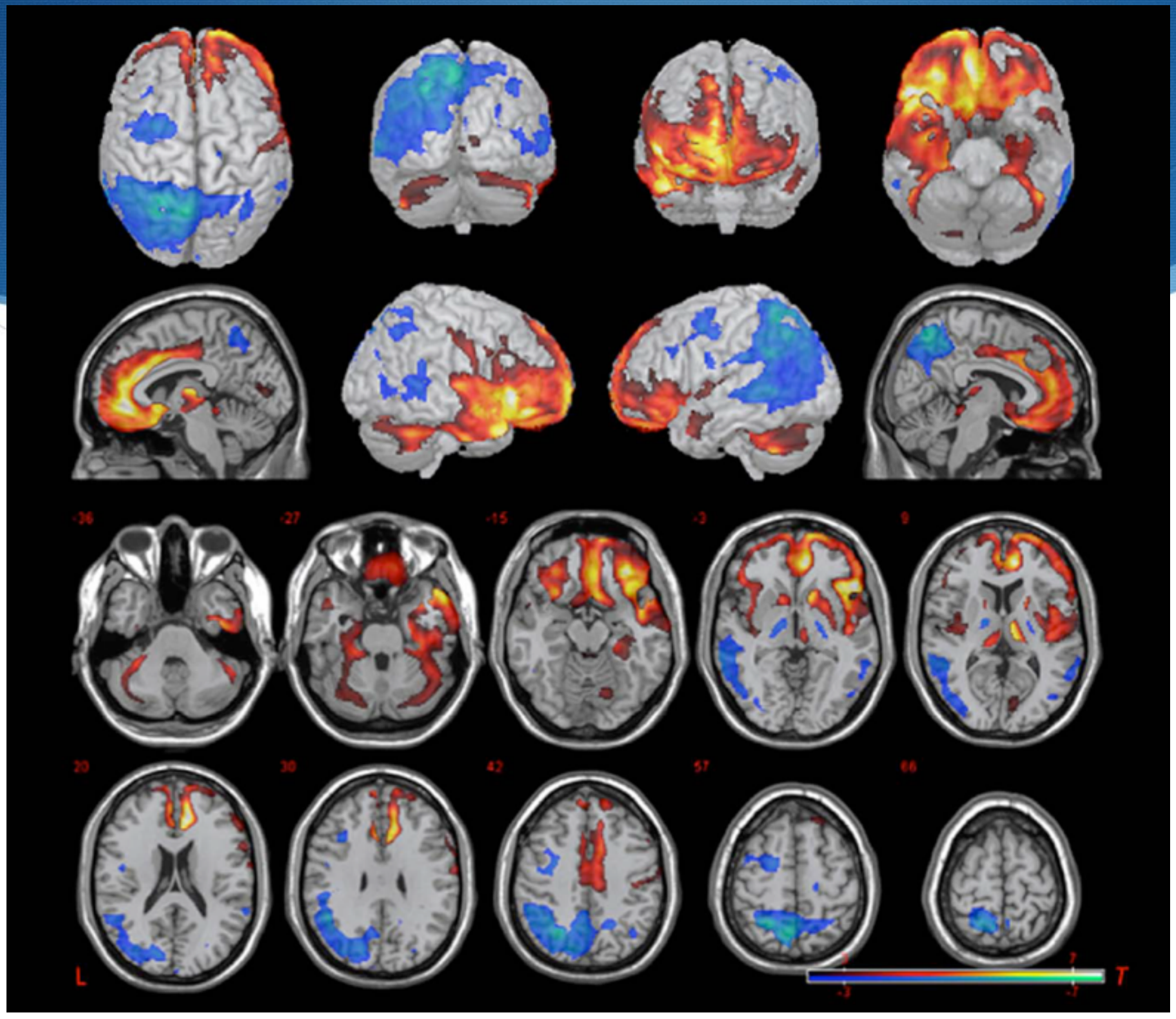


Figure 1. Base comparison of EOAD relative to LOAD. Two-sample *t* test comparison shows relative hypometabolism in the EAD group (blue) and relative hypometabolism in the LAD group (red; uncorrected $P = .01$, $T = 2.43$, $k_c = 10$ voxels). Picture is in neurological convention; brain's left is your left. EOAD indicates early-onset Alzheimer's disease; LOAD, late-onset Alzheimer's disease.

Mild Cognitive Impairment
Risk factors

A number of risk factors for developing Mild Cognitive Impairment are identified in research literature

- Age
- subjective complaints of memory
- history of early or late onset depression
- less education
- female gender
- African American ethnicity
- with cardiovascular risk factors such as hypertension or stroke

(Elliott, Horgas & Marsiske, 2008; Geerlings, den Heijer, Koudstaal, Hofman & Breteler, 2008; Kryscio, Schmitt, Salazar, Mendiondo, & Markesbery, 2006; Ownby, Crocco, Acevedo, John & Loewenstein, 2006; Reisberg & Gauthier, 2008; Wang et al., 2004; Barnes, Alexopoulos, Lopez, Williamson & Yaffe, 2006).

Mild Cognitive Impairment Prevalence

Prevalence estimates for MCI in the elderly generally range from 14–18%, with the amnestic variant of MCI (a-MCI) being more frequent than non-amnestic forms

(Petersen, 2009).

Mayo Clinic study included a randomized sample of approximately 3000 non-demented between the ages of 70 to 90s and revealed a prevalence of MCI estimated at 15 percent with a ratio of 2 to 1 of MCI amnestic type to non-amnestic MCI

(Roberts et al., 2008).

Mild Cognitive Impairment Conversion Rates

Petersen (2004) reported a conversion rate of 12% per year, and up to 80% after six years.

Rates of progression in epidemiological studies from MCI to dementia are about 6–10 percent per year

(Petersen et al., 2009).

Individuals with the amnestic, plus other domain of MCI show the highest rates of conversion to dementia.

Importance of Early Detection

Many individuals with MCI remain undiagnosed for years
(Hashimoto, Matsumoto, Nakano, Yasuda & Mori, 2005).

In the primary care setting, diagnosis often delayed for 8 to 32 months from the onset of symptoms.
(Brodaty, Low, Gibson & Burns, 2006).

If the onset of MCI could be delayed 5 years through treatment strategies, the prevalence of dementia would drop by 50%
(Burns & O'Brien, 2006; Hendrie, 1998; Petersen et al., 2001).

Importance of Early Detection

With early detection, intervene w/ evidence based interventions:

- Acetylcholinesterase inhibitors
- Environmental or lifestyle changes
- Educate family members
- Cognitive training or rehabilitation.
- Psychotherapy can enhance adjustment

Artero & Ritchie, 2003; Belleville et al., 2006; Brodaty, 2010; Elliot et al., 2008).
Moniz-Cook, Wang & Campion 2001; Willis et al., 2006

Cognitive Screening In Residential Care for Elders

Currently, 13 million older American adults require residential care or assisted living

(Schumacher, 2006).

By the year 2050, the number needing these services will increase to 27 million people

(U.S. Department of Health and Human Services, 2003).

Top Reasons for Nursing Home Admission

- Medical issues
- Cognitive impairment
- Lack of social support
- Functional impairment

(Gaugler, Duval, Anderson & Kane 2007; Miller & Weissert, 2000
Gaugler, Yu, Krichbaum & Wyman, 2009).

MCI In Elderly Residential Facilities

A Sample of 130 elderly participants (aged 82.5 years) residing in nursing homes, assisted living facilities, and senior housing found a breakdown of residents:

- Cognitively intact (50.8%)
- Amnestic MCI (19.2%)
- Probable dementia (30%)

(Elliot, et al., 2008).

At least half of those residents had cognitive impairment

(US General Accounting Office, 1997).

14% of residents diagnosed with Alzheimer disease

(Gaugler, et al, 2009; Magaziner, et al., 2000; National Center for Health, 2006).

Need for Screening Measures

Standard Neuropsychological Batteries

- Time consuming (administration, scoring, reports)
- Complex assessment
- Arduous process
- Expensive

Screening Measures

- Easy to administer
- Cost-effective measures
- Quick
- Need high predictive value

(Bernstein, et al., 2010; Shulman, 2000).

Need for Screening Measures

General practice, primary care, or nursing home setting where individuals with MCI are most likely to present

(Artero & Ritchie, 2003).

Nurses and social workers most likely to do screening

(Winblad, et al., 2004)

Inconsistent and insensitive screening measures likely contribute to under diagnosis

(Stoppe et al., 2007).

The Mini-Mental State Examination

Domains:
Orientation, concentration/working memory, recall and short-term memory, language, written command, verbal command, sentence construction, basic visuoconstruction

(Bernstein et al., 2010).

- 30-points
- Dubbed "the gold standard" (Lerch et al., 2010).
- Distributed by Psychological Assessment Resources (PAR)
- Copyrighted and costs approximately 1 dollar per copy.

MMSE Limitations

Ceiling effect on the MMSE can hide severity of cognitive deficits.

(Ismail, et al., 2010).

Insensitive to frontal-executive and subcortical functioning

Pendlebury, Cuthbertson, Welch, Mehta & Rothwell, 2010

Limited value in helping to identify MCI

(Mitchell & Malladi, 2010

Most individuals with MCI score higher than suggested cutoff of 26

(Nasreddine et al., 2005).

A high percentage of MCI develop AD, yet score in the normal range

(Diniz et al., 2007).

The Montreal Cognitive

The Montreal Cognitive Assessment (MoCA) is a screening test that was developed for cognitive assessment in elderly persons (Koski, Xie & French, 2009).

Domains: Visuospatial, Executive, language, Memory, Attention, Abstraction, Orientation

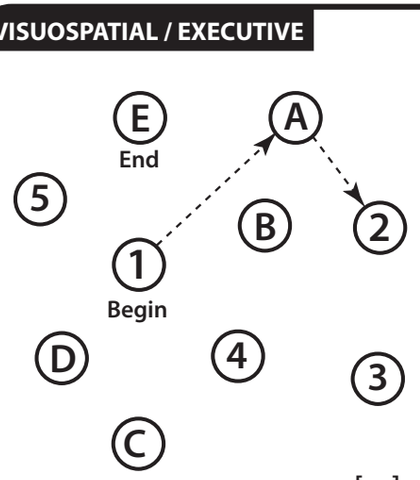
(Bernstein et al., 2010).

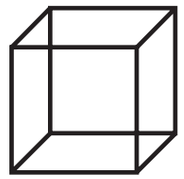
- 30-questions
- 1 page, 10 minutes to adminster
- In 35 languages
- Free & available for public download at www.mocatest.org.

MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE





Copy cube

[ ] [ ]

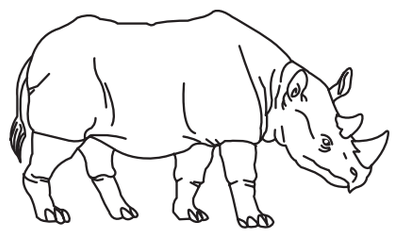
Draw CLOCK (Ten past eleven)
(3 points)

[ ] Contour [ ] Numbers [ ] Hands

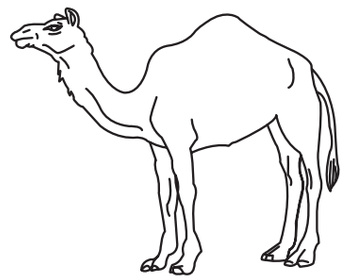
POINTS ___/5

NAMING

[ ]



[ ]



[ ]

___/3

MEMORY

Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful.
Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION

Read list of digits (1 digit/ sec.).
Subject has to repeat them in the forward order [ ] 2 1 8 5 4
Subject has to repeat them in the backward order [ ] 7 4 2

___/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

___/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

___/3

LANGUAGE

Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ]

___/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

___/1

ABSTRACTION

Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

___/2

DELAYED RECALL

	Has to recall words **WITH NO CUE**	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only
Optional	Category cue						
	Multiple choice cue						

___/5

ORIENTATION

[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

___/6

 Version 7.1 **www.mocatest.org** Normal ≥ 26 / 30

TOTAL ___/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

The MoCA Overview

The MoCA separated into 7 subsections with score values:

(1) Visuospatial three points for clock-drawing, one point for cube copying

(2) Executive one point for modified Trail making B task, one point for phonemic fluency, two points for 2-item verbal abstraction

(3) Language three points for animal naming of low-familiarity animals lion, camel, and rhinoceros, two points for sentence repetition

(4) Memory five points for delayed recall of five nouns

(5) Attention one point for target detection using tapping, 3 points for serial subtraction, and 2 points for digits forward and backward

(6) Abstraction 2 points

(7) Orientation 6 points for orientation to time and place

MoCA Norms

Initial Canadian sample population (N = 90) with a mean age of 72.8 (SD = 7.03) and mean education of 13.33 (SD = 3.40) years.
A score below 26 is indicative of cognitive impairment.
In the initial sample, with a cut-off score of 26 or below,
sensitivity of the MoCA for MCI and AD (90% and 100%)
specificity was (87%) (Nasreddine et al., 2005).

Participants with 12 years of education were given one additional point for their total MoCA score if they scored below 30 points.

A later study proposed addition of two points to the total MoCA score for patients with 4-9 years of education, and 1 point for 10-12 years of education (Johns et al., 2010).

MoCA Psychometrics

Validated in a variety of settings including

- older adults in a British memory clinic population (Smith et al., 2007),
- a geriatric cognitive disorders clinic in Canada (Koski, Xie & Finch, 2009)
- a Southeastern United States population (Luis et al., 2009)
- outpatient Parkinson's disease clinic (Gill, Freshman, Blender & Ravina, 2008)
- preventive medicine clinic, cardiac outpatients, and a population-based sample in Texas (Bernstein, Lacritz, Barlow, Weiner & Defina, 2010).

Several alternate language forms

- Korean form in an outpatient population (Lee et al., 2008),
- the Japanese form in an outpatient memory clinic (Fujiwara et al., 2010)
- Arabic Version in patients in geriatric clubs in Cairo (Rahman & Gaafary, 2009).

MoCA Psychometrics

The MoCA has moderate to high 1-month test–retest reliability values (70–92%) (Nasreddine et al., 2005).

Good internal consistency (Cronbach's alpha = 0.83; Nasreddine et al., 2005).

Moderately strong positive correlations between MoCA scores and education (Bernstein, et al., 2010).

MoCA scores generally do not correlate with gender and correlate with age only in clinical populations (Bernstein et al, 2010).

MoCA Psychometrics

Good criterion validity from standardized neuropsychological testing: correlation coefficient between the MoCA and a neuropsychological battery was 0.72 (Gill, 2008).

Correlations of the MoCA with standard neuropsychological measures by domain as follows:

Memory (CVLT) strongest ($r = 0.84$, $p < 0.001$)

Executive/ Visuospatial (Trails B/Rey-Osterrieth) ($r = 0.60$, $p < 0.001$),

Attention (Stroop & Digit Symbol) ($r = 0.62$, $p < 0001$)

Language (Boston Naming & Word fluency) ($r = 0.61$, $p < 0.001$).

Critiques of MoCA

MoCA lacks specificity and standard cut off misclassifies normal individuals as being cognitively impaired. (Coen, Cahill & Lawlor, 2011).

Standard Cut off has high risk of False positives (Smith, Gildeh & Holmes, 2007).

The MoCA has poor reliability in non-clinical groups (Coen, Cahill & Lawlor, 2011).

Lack of demonstrated test-test reliability at frequently identified intervals, such as 6 months or 12 months (Lonie et al., 2009).

Relatively new instrument with only five to six years of research to support its use vs MMSE has over 30 years support (Koski et al., 2009)

Somewhat complex administration (Coen et al., 2011).

MoCA Versus MMSE

MoCA vs. MMSE

Nasreddine et al. (2005) created the MoCA with the explicit purpose of addressing the limitations of the MMSE.

The MoCA spans a wider range of cognitive abilities than the MMSE (Diniz et al., 2007; Ravaglia et al., 2005).

The MoCA has more difficult measures than the MMSE, which makes up for the low ceiling and false negative rates (Dong et al., 2010).

One analysis of the MMSE indicated that normative data should be used when interpreting an MMSE based upon age and education (Crum et al., 1993).

MoCA vs. MMSE

MoCA demonstrated superior sensitivity and specificity than the MMSE in detecting cognitive impairment (Nasreddine et al., 2005).

MoCA is a better predictor of progression from MCI to AD than the MMSE (Bernstein et al., 2010).

The MoCA more sensitive to amnestic MCI (83%-90%) and Alzheimer's dementia (94%-100%)

MoCA demonstrated a high sensitivity in identifying MCI (83%) and dementia (94%) vs. MMSE (17% and 25%, respectively).

The established cut-off score of 24 on the MMSE demonstrated false negatives for detecting dementia in 32% of patients (Lerch et al., 2010).

MoCA Lower Cut Score

Nasreddine (2005) found a cutoff score of 26 for a diagnosis of MCI, Sensitivity of (90%) for MCI and 100% for AD, specificity (87%).

Subsequent studies found lower specificity at Nasreddine's original cutoff points (Coen et al., 2011).

Damian et al. (2011) cutoff score 24, sensitivity (87%) specificity (75%).

Luis et al. (2009) found cut-off score of 26, too high and only yielded specificity of 35%.

> A lower score (23 or below for abnormality) improved the specificity of the MoCA to 95%, without compromising the sensitivity (96%) for detecting MCI.

Addition of Tests to MoCA

The addition of brief neuropsychological measures to the MoCA may improve its diagnostic utility.

Nakata et al. (2009) found most important aspect of a screening measure in detecting MCI is that it contains a sampling from a number of domains

Combination of two or more screening measures offers superior diagnostic accuracy than a single measure due to increased exposure to differing cognitive domains (Lonie et al., 2009).

Some patients perform well on screeners, yet exhibit cognitive impairment on standard neuropsychological tests measuring language or executive functioning by semantic verbal fluency test, Trail Making Test part B, or the Stroop Color Word Test. Gagnon et al. (2010)

Semantic Verbal Fluency & MCI

The 'Animals' semantic verbal fluency test from the COWAT (Benton & Hamsher, 1976) would be a valuable addition to the MoCA, as part of a brief screening battery for MCI.

The MoCA contains a subtest with letter fluency consisting of words that begin with the letter F, however lacks a measure of semantic fluency.

Semantic fluency compared to phonemic fluency is differentially impacted by medial temporal lobe degeneration characteristic of Alzheimer's disease (Bartha, et al., 2003).

Several studies have validated differences in performance between letter fluency and semantic category fluency to differentiate individuals with MCI from healthy elderly controls. Murphy et al. (2006)

Semantic Verbal Fluency & MCI

Several studies have found verbal fluency to be an effective cognitive screening tool in detecting differences between healthy older adults and MCI (Beinhoff, Hilbert, Bittner, Gron, & Riepe, 2005; Miller, Bedics, Kaplan, Giurgius, & Small, 2007).

Lopez (2011) found that the Animals semantic fluency task could be utilized as an effective screening tool in the detection of MCI.

Both semantic and phonemic fluency were significant predictors of diagnostic classification between individuals with a-MCI and AAMI, although semantic fluency was the most significant predictor in the model.

Current Study

Current research supports the superiority of the MoCA over the MSME in detecting MCI in a variety of settings.

Original normative data (Nasreddine et al., 2005) for the MoCA been challenged in terms of the set cutoff (26) for discriminating healthy individuals from those with MCI (Coen et al., 2011; Luis et al. 2009).

The MoCA is early in its development as a clinical and diagnostic tool and has yet to be validated in older cohorts in a residential population.

The present study will expand the clinical applicability with a cohort of older (M age = 81.57) and more highly educated adults (M years of education = 16.11) than the original normative sample (M age = 72.8 and M years of education =13.33 years).

Current Study

The semantic verbal fluency task Animals independently established as a powerful screening tool for detecting MCI, yet the combined predictive power of the MoCA and Animals have not yet evaluated.

The goal of the current study is to establish a valuable combination screening tool that most effectively characterizes healthy older adults from those with MCI, in order to aid in early diagnosis and intervention.

Methods

Archival data that was collected by the Aging and Memory Research Center at the UCLA Semel Institute for Neuroscience and Human Behavior.

The neuropsychological data was gathered as part of a baseline evaluation in a larger cognitive training study in older adults in assisted living and residential home settings.

Individuals were assessed on site, at three different nursing homes in the Southern California area.

Participants were screened for the absence of dementia

For this study, participants will be divided into two groups: normal healthy older adults, which include individuals with AAMI and subjects with MCI. Individuals with MCI were defined as such according to modified Petersen's criteria (Petersen et al., 1995; Petersen et al., 1999)

Diagnostic Method

•The control group was pooled from “Normals” and individuals with AAMI.

•Criteria for inclusion in the control group included (1) performances below -1.00 standard deviation from normative data on more than one test in a cognitive domain.

•Cognitive domains included attention, information processing speed, language, visuospatial skills, memory, and executive functioning.

•Criteria for MCI was specific to the study guidelines and defined as follows:

•inclusion in the MCI group included performance below -1.00 standard deviation on 2 or more tests in in one of the aforementioned domains,

•with MMSE score greater than or equal to 25.

•Individuals with dementia with dementia were not included in the study, as classified by MMSE score < 25, with performance of -2.00 SD or more on majority of memory tests.

Population

The current sample includes 98 participants:

63 normal aging older adults (49 women, 14 men, M_{age} = 80.7, SD = 5.7) and 35 individuals with MCI (19 women, 16 men, M_{age} = 82.43, SD = 7.25).

MCI group was pooled from

14 with a-MCI single domain,

8 with MCI Non-Amnestic single or multiple domains,

13 with a-MCI multiple domains.

The sample is highly educated (average years of education, M = 16.11). The sample is predominantly Caucasian (90 Caucasian, 5 Asian American, 1 African American, 1 Biracial/Other).

Procedure & Measures

Each participant received a brief interview and neuropsychological evaluation. After the initial evaluation, some subjects also received a follow-up neuropsychological evaluation using the same measures approximately several months later, as part of a follow-up and treatment comparison. Only the baseline evaluations are used in the current study.

Mini-Mental Status Examination
Montreal Cognitive Assessment
Semantic Fluency: Animals (Newcombe, 1969)

Full Neuropsy Battery

Logical Memory, Verbal Pairs, and Visual Reproduction from the WMS-III, 1997
Rey Osterreith Complex Figure Test (ROCFT; Osterrieth, 1944; Rey, 1941)
Buschke Selective Reminding Test (BSRT, 1985)
Hopkins Verbal Learning Test-Revised (HVLT-R, 2001).
Boston Naming Test (BNT; Kaplan, Goodlass, & Weintraub, 1983)
Controlled Oral Word Association Test: FAS (Benton & Hamsher, 1976),
Geriatric Depression Scale (GDS) (Yesavage et al., 1983)
Stroop Test (Comali Version) (Comali, Wapner, & Werner, 1962),
Trailmaking Test Parts A & B, (TMT) (Army Individual Test Battery, 1944),
Wechsler Adult Intelligence Scale Third Edition (WAIS-III) subtests Digit Span, Digit Symbol, Letter-Number Sequencing, and Similarities (Wechsler, 1997).

The following measures were utilized in the statistical analyses,
the Animal Naming Semantic Fluency Test (Newcombe, 1969),
the Folstein Mini Mental Status Examination (Folstein, Fostein, & McHugh, 1975),
the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005)
the Wechsler Test of Adult Reading (WTAR) (The Psychological Corporation, 2001).

Review of Study Hypotheses

1. MoCA will have greater sensitivity and specificity than MMSE for detecting MCI

2. Lower cutoff score on the MoCA will have greater sensitivity and specificity than cutoff score from original norms (<26, Nasreddine et al., 2005) in this older sample of older adults.

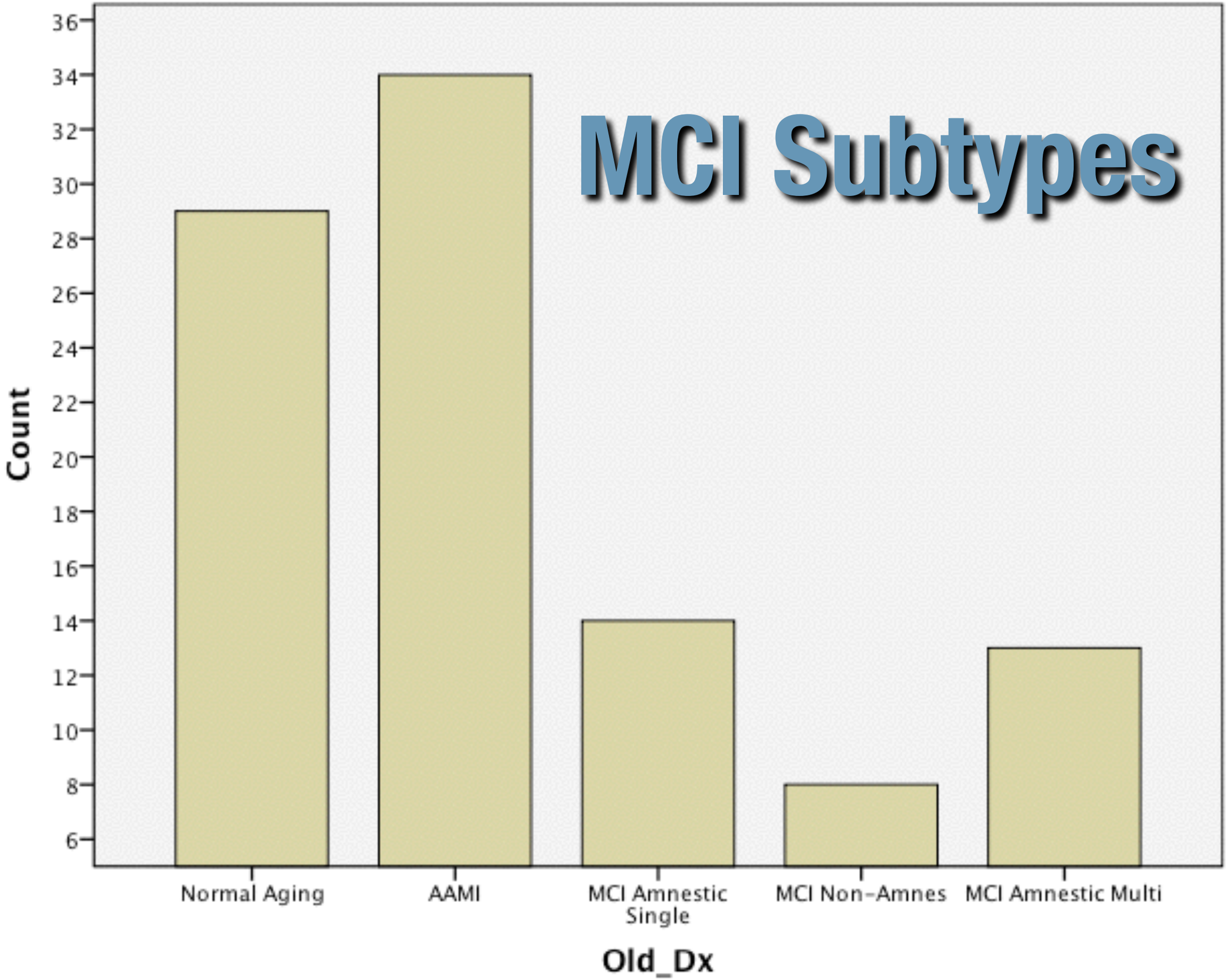
3. An analysis of domains on the MOCA will indicate deficits in (1) visuospatial/executive, (2) delayed recall, and (3) language have greater predictive value in distinguishing MCI from Normal Older Adults.

4. Combining MoCA and the Animals fluency scores will add greater predictive value to the MoCA.

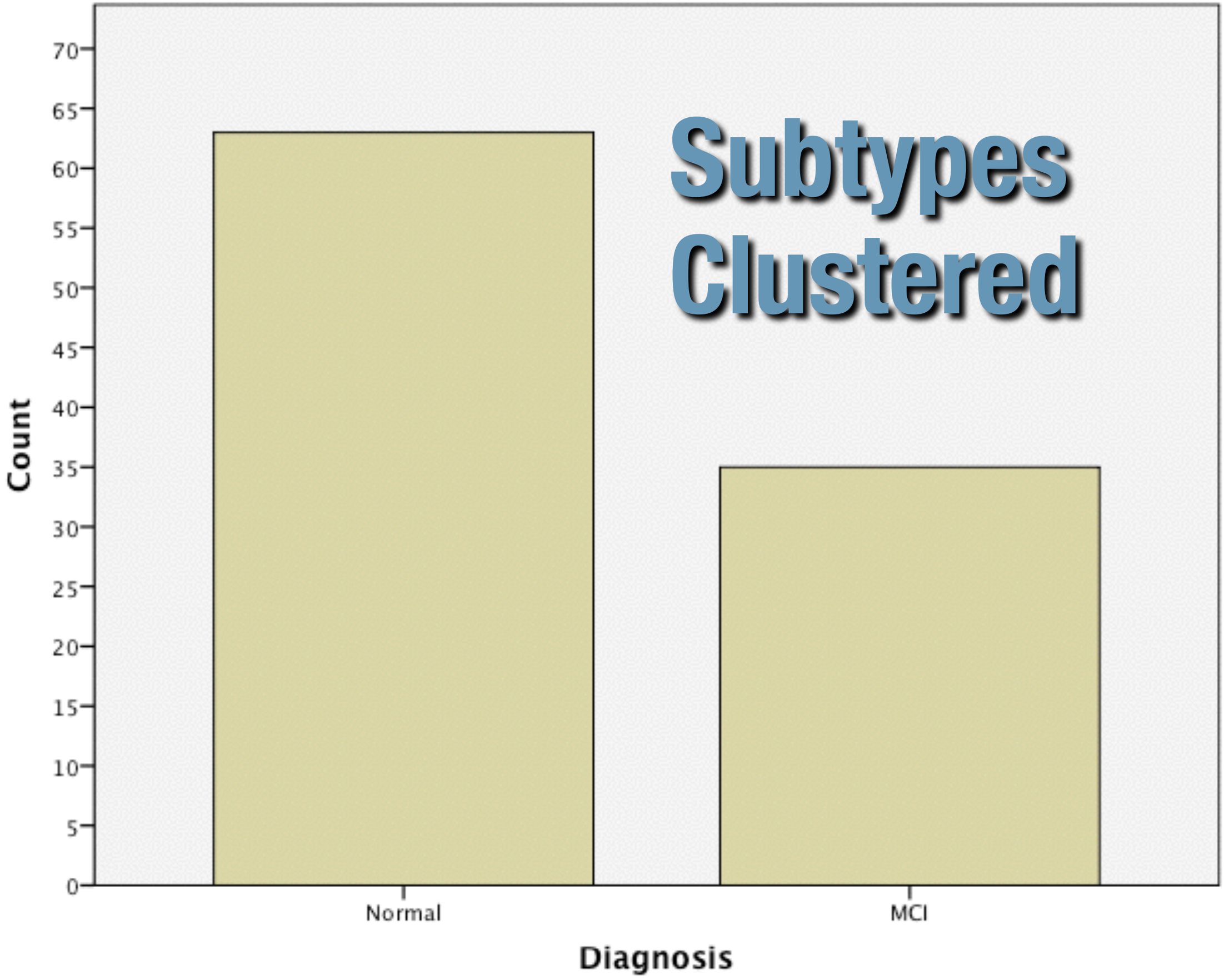
DEMOGRAPHICS & PREDICTORS

* SEE DOC TABLES 1-4

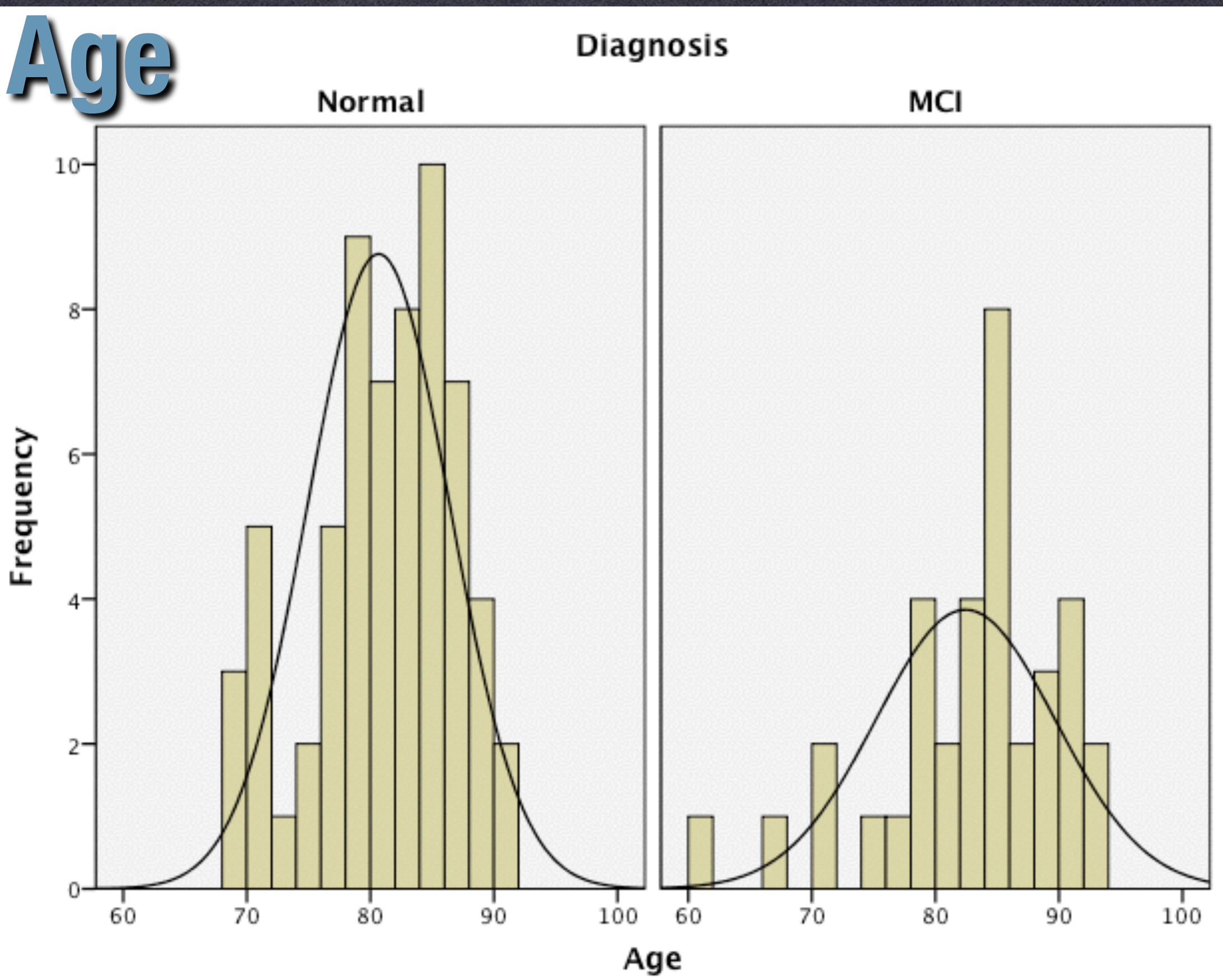
MCI Subtypes



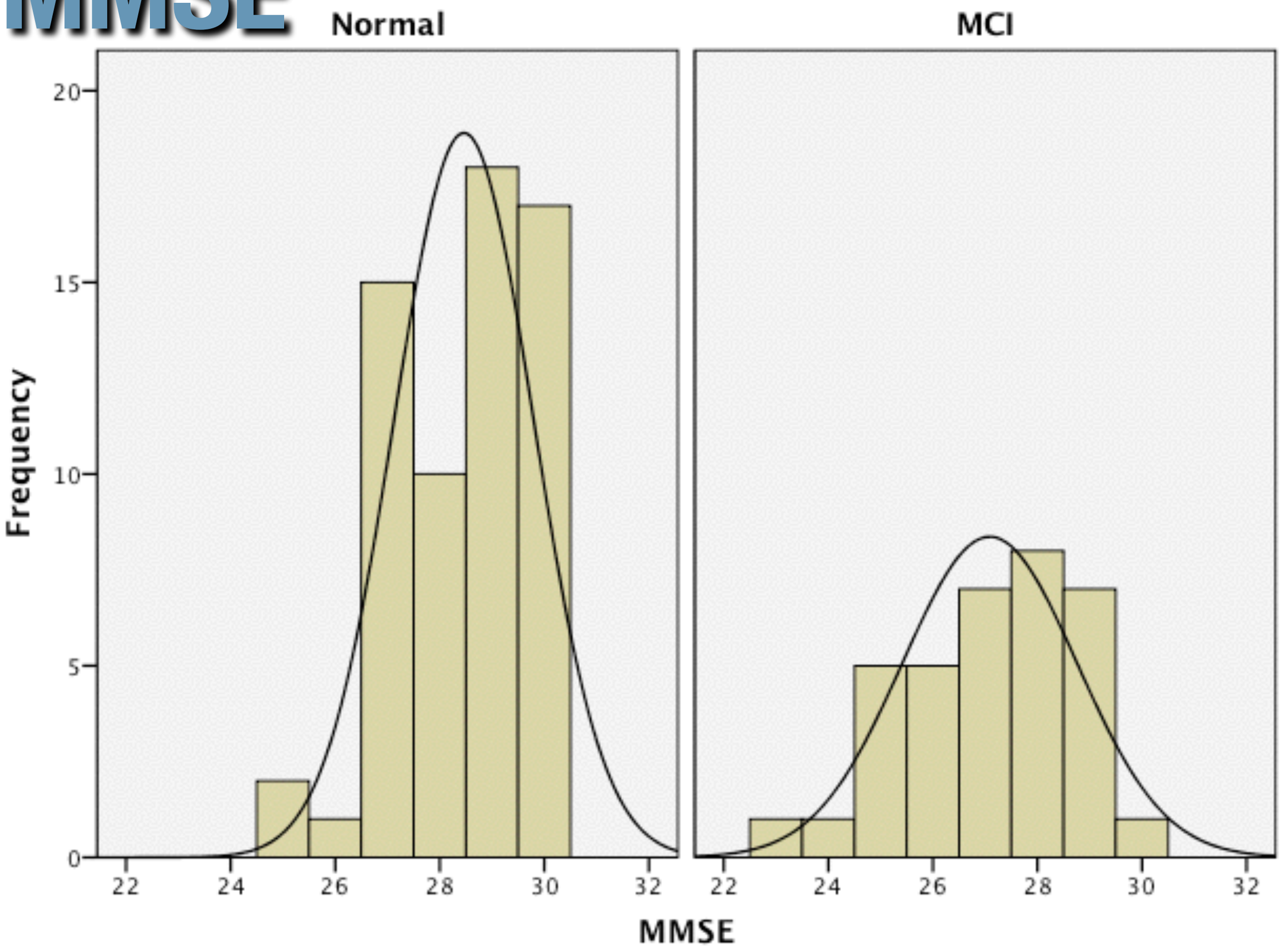
Subtypes Clustered



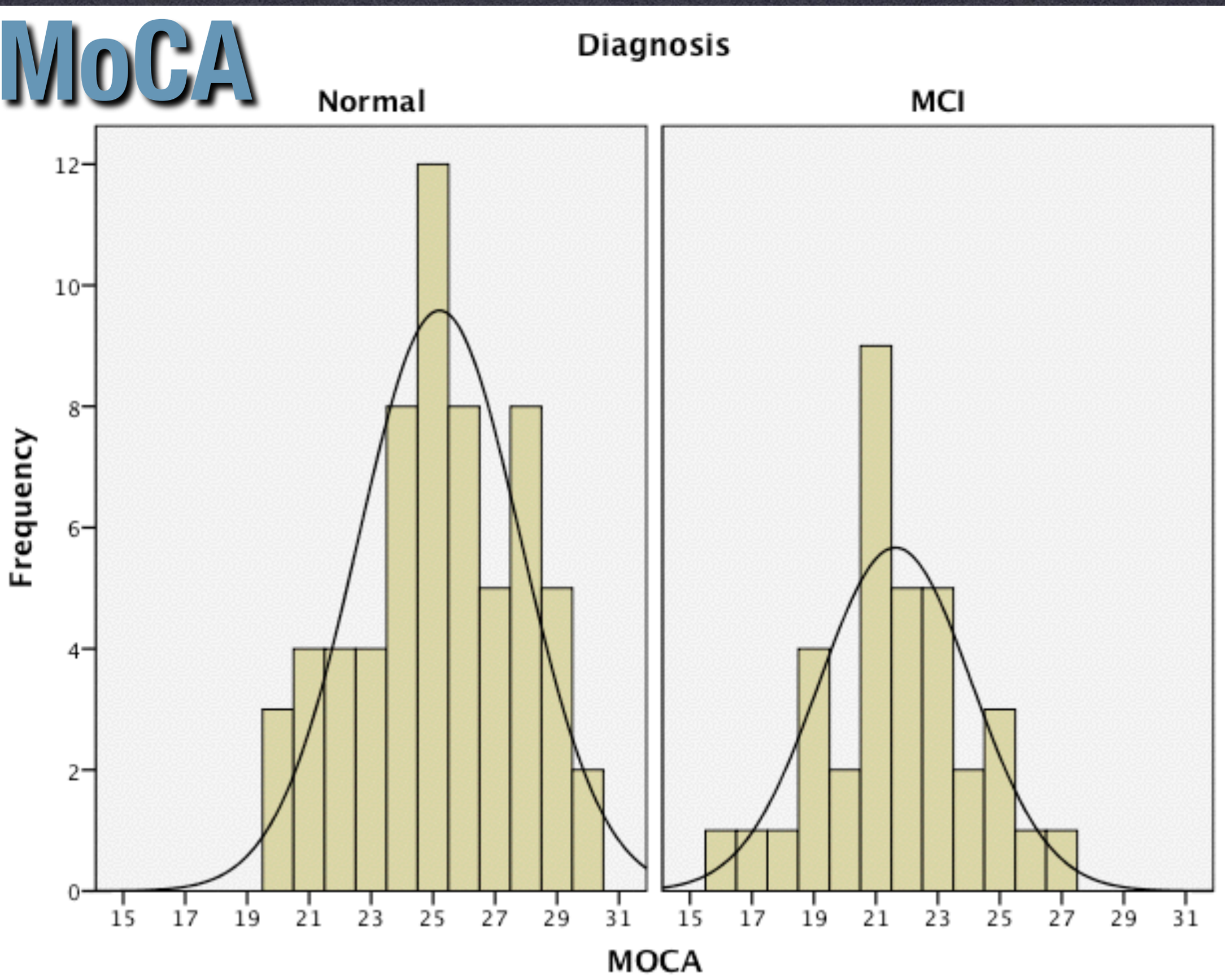
Age



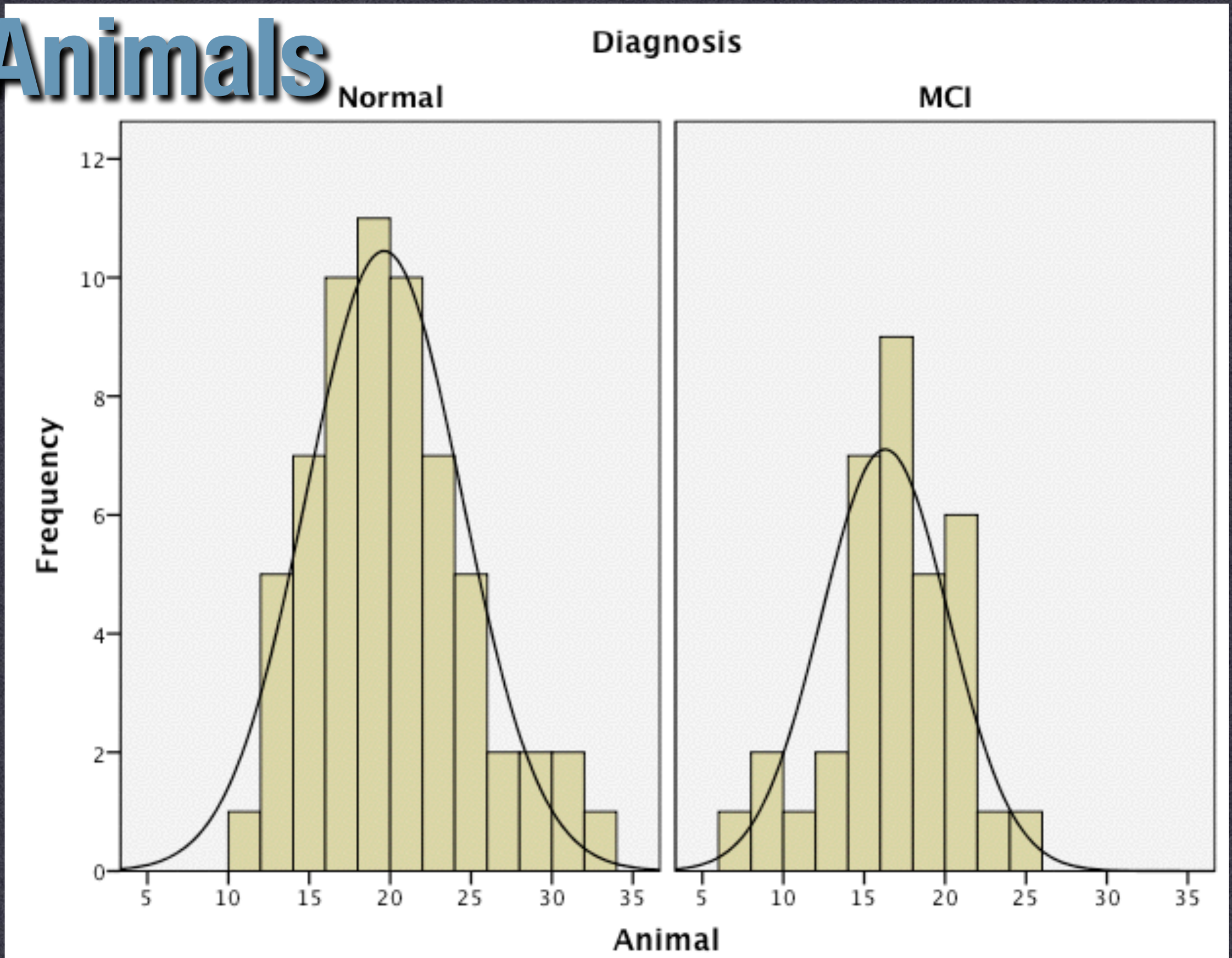
MMSE


Diagnosis
Normal
MCI
Frequency
20
15
10
5
0
22
24
26
28
30
32
MMSE

MoCA


Diagnosis
Normal
MCI
Frequency
12
10
8
6
4
2
0
15
17
19
21
23
25
27
29
31
MOCA

Animals


Diagnosis
Normal
MCI
Frequency
0
2
4
6
8
10
12
5
10
15
20
25
30
35
Animal

Review of Test Psychometric Terms

Sensitivity - Test correctly identifies individuals with MCI (True Positive)

Specificity - Test correctly identifies individuals as Normal (True Negative)

Positive Predictive Value - Proportion of individuals who test + MCI / (actual # MCI)

Negative Predictive Value - Proportion of individuals who test Normal / (actual # Controls)

ROC Area Under the Curve - Compares sensitivity versus specificity across a range of MoCA values for the ability to predict diagnosis. Values closer to 1 are desirable. 0.8 deemed “useful”. Plot of Sensitivity versus 1-specificity over all possible values of the test.

Youden Index - Useful for determining specific cutoff value of a test. Highest value is considered the best cutoff value. At each value YI = Sensitivity + Specificity -1

Review of Logistic Regression Symbols & Terms

Binary Logistic Regression - Regression used for predicting a categorical outcome variable with multiple predictors (diagnosis = Control vs. MCI).

Wald's χ^2 - contribution of individual predictors to the model. Higher values indicate greater contribution.

Odds Ratio (e^{β}) - Odds of outcome given a one unit change in the predictor. i.e. odds of being diagnosed as MCI given a one unit change in MoCA score. A type of measure of effect size. Higher value indicates greater odds.

-2 Log likelihood - Indicator of how much unexplained information there is after the model has been fitted. Measure of of overall fit of the model. Lower values indicate a better model.

R^2 = (Cox & Snell) - Analogue to R^2 in multiple regression, although value is suppressed.

Hypothesis #1

"MoCA will have greater sensitivity and specificity than MMSE for detecting MCI"

Analyses Used:

1) Receiver Operating Characteristic - Area under Curve - Tables 6-8 & Figure 1
2) 3 Binary Logistic Regression Models using Enter Method
   (a) MoCA + Covariates (WTAR & Sex) - Table 9
   (b) MMSE + Covariates (WTAR & Sex) - Table 10
   (c) MoCA + MMSE + Covariates - Table 11
3) Binary Logistic Regression w/ Stepwise Forward Likelihood Ratio - Table 15

Hypothesis #1

"MoCA will have greater sensitivity and specificity than MMSE for detecting MCI"

<u>Summary of Results Found:</u>

1) MoCA (<24) has greater sensitivity & specificity and Area Under the Curve than MMSE (<29).

2) MoCA explains more variance in the regression model than MMSE, even when entered with MMSE.

3) MoCA adds significant contribution to the regression model after the MMSE and all covariates are retained in the model.

Hypothesis #2

"A cross-validation of the MOCA with an older cohort will indicate a lower cutoff score than the recommended (<26) and will yield greater specificity in the detection of MCI."

Analyses Used:

1) Receiver Operating Characteristic - Area under the Curve - Tables 6-8
2) Compared cutoff value from original article based on Nasreddine et al., 2005 - Table 17

Hypothesis #2

"A cross-validation of the MOCA with an older cohort will indicate a lower cutoff score than the recommended (<26) and will yield greater specificity in the detection of MCI."

Summary of Results Found:

1) Cutoff from original article (< 26) had better sensitivity (.94 versus .80) but worse specificity (.44 versus .76). Youden index was highest at < 24 for optimal cutoff.

2) Finding of lower cutoff supported based on performance of MoCA in comparable studies

Hypothesis #3

"An analysis of domains on the MOCA will indicate deficits in (1) visuospatial/executive, (2) delayed recall, and (3) language will yield greater predictive value in distinguishing MCI from Normal Controls."

Analyses Used:

1) One-way ANOVA w/ Subscale Scores - Tables 12
2) Receiver Operating Characteristic - Area under the Curve - Table 13 & Figure 2
3) Binary Logistic Regression w/ Subscale Scores - Table 14

Hypothesis #3

"An analysis of domains on the MOCA will indicate deficits in (1) visuospatial/executive, (2) delayed recall, and (3) language will yield greater predictive value in distinguishing MCI from Normal Controls."

<u>Summary of Results Found:</u>

1) Subscales significant between groups in ANOVA from largest effect size:

   (a) recall, (b) attention, (c) language, (d) vis/exec.

2) Area under the curve in order from largest area under the curve:

   (a) recall, (b) attention, (c) language, (d) vis/exec.

3) In regression largest Wald $\chi 2$ values:

   (a) recall (b) attention (c) vis/exec (d) language

Hypothesis #4

"Combining the MoCA and Animals semantic fluency scores will add greater predictive value than MoCA or semantic fluency alone. "

Analyses Used:

1) One-way ANOVA - Table 2
2) Receiver Operating Characteristic - Area under the Curve - Table 8
3) Binary Logistic Regression w/ Stepwise Forward Likelihood Ratio - Table 15

Hypothesis #4

"Combining the MoCA and Animals semantic fluency scores will add greater predictive value than MoCA or semantic fluency alone. "

<u>Summary of Results Found:</u>

1) Animals was significant between groups with small effect size in ANOVA (.11)
2) Animals less predictive than premorbid IQ in ROC with poor AUC value (.68), although was significant predictor.
3) In the stepwise regression model Animals was removed from the model and was no longer a significant predictor after MoCA, MMSE, WTAR, and Sex were in the model

Limitations & Questions

1) Education was significant predictor of MoCA score, need to adjust for this?

2) Subscales different in various studies, need to do an item analysis? Not sure if assumptions met because of minimal score ranges on these scales.

3) How to explain WTAR findings? Premorbid IQ is a protective factor?

4) How to explain gender findings? Is this because greater proportion of females in control group?

5) Remove Age Outliers for paper?