The MCI Screen combines high precision with practical administration in clinical and research settings. Embic Corporation continually enhances its products and capabilities through directed research efforts and through collaboration with leading researchers in the field. The results of these efforts have been published in medical journals and presented at industry conferences.

## HIGH PRECISION OF THE MCI SCREEN

### High Accuracy in All Stages of Memory Impairment

The MCI Screen has high overall accuracy, sensitivity and specificity in distinguishing normal aging from all stages of memory impairment from Normal to MCI to Dementia.

| | Overall Accuracy | Sensitivity | Specificity |
|---|---|---|---|
| MCI vs. Normal | 97% | 95% | 88% |
| MCI/Mild Dementia vs. Normal | 98% | 97% | 88% |
| Mild Dementia vs. Normal | 99% | 96% | 99% |

Proceedings of National Academy of Science. 2005; 102(13):4919-24.

### More Accurate than Commonly Used Assessments

The MCI Screen has much higher accuracy compared to commonly used assessments in physicians' offices. In fact, no other instrument in the published literature can reliably distinguish MCI from Normal, whereas the MCI Screen does so with 97% accuracy.

| | Overall Accuracy | Sensitivity | Specificity |
|---|---|---|---|
| MCI Screen | 96% | 94% | 97% |
| Mini Mental State Exam | 62% | 71% | 36% |
| Clock Drawing | 54% | 59% | 39% |

Journal of Alzheimer's Disease. 2007; 11(3):323-335.

## WHY IS PRECISION SO IMPORTANT?

### Better Traffic Control Needed in Primary Care Settings

The aging public is concerned about cognitive health. To ensure timely intervention against all causes of impairment, without over-utilization of diagnostic tests, physicians need a simple but accurate tool for assessing cognition in primary care. With such a tool, physicians can prescribe further diagnostic evaluation for those with an underlying medical condition, without over-utilizing healthcare resources on the worried-well.

### Currently AD Is Detected Too Late

Over 2/3 of patients with Alzheimer's disease are detected in the mild to moderate dementia stage when treatment efficacy is marginal. This is partly due to the lack of assessment tools that can identify more subtle cognitive impairment at the MCI stage.

# Detecting Cognitive Impairment in Primary Care: Performance Assessment of Three Screening Instruments

Douglas L. Trenkle, D.O.[1], William R. Shankle, M.D.[2,3], Stanley P. Azen, Ph.D.[4]

1 Maine Coast Memorial Hospital, Ellsworth, Maine; 2 Medical Care Corporation; 3 Department of Cognitive Sciences, University of California, Irvine; 4 Department of Preventive Medicine, Keck School of Medicine, University of Southern California

Early detection of Alzheimer's disease and related disorders (**ADRD**) is important, especially in primary care settings. We compared performances of two common screening tests, the Mini-Mental State Exam (**MMSE**) and Clock Drawing Test (**CDT**), with that of the MCI Screen (**MCIS**) in 254 patients over 65. None had previous diagnosis of ADRD, and 81% were asymptomatic by Functional Assessment Staging Test (**FAST**) (FAST=1). 215 patients completed all screening tests - 141 had ≥1 abnormal result, 121/141 completed standardized diagnostic assessment, and the remaining 74/215 (34%) screened entirely normally and weren't further evaluated. Potential bias due to unevaluated cases was statistically adjusted. Among diagnosed cases: AD=43%, cerebrovascular disease=36%, other causes=21%. Bias-adjusted MCI prevalence for FAST stages 1 and 1-3 were 13.9-20.3% and 23.0-28.3%. Bias-adjusted results for the CDT, MMSE and MCIS were: clinical diagnosis validity (kappa statistic) = {-0.02 (p=.61), 0.06 (p=.23), 0.92 (p<.0001)}; sensitivity = {59%, 71%, 94%}; specificity = {39%, 36%, 97%}; overall accuracy = {54%, 62%, 96%}; positive predictive value = {16%, 17%, 86%}; and negative predictive value = {83%, 87%, 96%}. The MMSE and CDT were not valid for early detection, while the MCIS had high validity and accuracy in the primary care cohort.

Reference:
Trenkle D, Shankle WR, Azen SP. Detecting Cognitive Impairment in Primary Care: Performance Assessment of Three Screening Instruments. Journal of Alzheimer's Disease. 2007;11(3):323-335.

# Early Detection and Diagnosis of Demented Disorders Using the MCI Screen and Neuroimaging

Ai Cho, Mika Sugimura, Seigo Nakano, Tatsuo Yamada

Department of Neurology, Fukuoka University

The Dementia Care Program (DCP), developed by Medical Care Corporation, is used in the USA for early detection and management of dementing disorders due to Alzheimer's disease and related disorders (ADRD). The MCI Screen (MCIS)—the DCP's objective memory tool—is 97% accurate in discriminating mild cognitive impairment (MCI) from normal aging. The present study evaluated 63 patients at the Fukuoka University Memory clinic using the Clinical Dementia Rating (CDR) Scale to identify a sample of 52 MCI (CDR=0.5) and 11 normal aging (CDR=0) patients. These patients were administered the MCIS, the Depression Screen, and scanned with brain SPECT and/or quantitative MRI. After excluding 7 patients diagnosed with depression, the neuroimaging and MCIS results of the remaining 56 patients were compared. Among the 48 MCI patients, 46 were correctly classified by the MCIS (96% sensitivity), and 37 (80%) had a specific ADRD etiology diagnosed by neuroimaging. All 8 normal aging patients were correctly identified by both the MCIS neuroimaging studies. These findings support the value of the Japanese version of the MCIS followed by SPECT or quantitative MRI in early detection and diagnosis of MCI.

Reference:
Cho A, Sugimura M, Nakano S, Yamada T. Early Detection and Diagnosis of Demented Disorders Using the MCI Screen and Neuroimaging. The Japanese Journal of Clinical and Experimental Medicine. 2007;84(8):1152-1160.

# The Japanese MCI Screen for Early Detection of Alzheimer's Disease and Related Disorders

Ai Cho; Mika Sugimura; Seigo Nakano, MD, PhD; Tatsuo Yamada, MD, PhD

Department of Neurology, Fukuoka University

Early detection of Alzheimer's disease and related disorders in Japan is increasingly important. The MCI Screen (**MCIS**) - derived from the National Institute of Aging CERAD neuropsychologic battery—differentiates normal aging from mild cognitive impairment (**MCI**) and mild dementia with 97.3% and 99% accuracy, respectively. The Japanese MCIS (**JMCIS**), MMSE, quantitative SPECT (**qSP**) and MRI (**qMR**) were used to classify 63 outpatients at Fukuoka University Hospital who were either normal or had MCI based on Clinical Dementia Rating scores of 0 and 0.5 respectively. Performance statistics for the JMCIS, MMSE, qSP, and qMR were respectively: 1) Accuracy = .964, .768, .722, .733; 2) Sensitivity = .958, .792, .688, .700; 3) Specificity = 1.000, .625, 1.000, 1.000; and 4) Kappa validity = 0.813, 0.420, 0.296, 0.308. This initial study shows negligible differences between the English and Japanese MCIS, supporting its potential use for early detection in Japan.

Reference:
Cho A, Sugimura M, Nakano S, Yamada T. The Japanese MCI Screen for Early Detection of Alzheimer's Disease and Related Disorders. The American Journal of Alzheimer's Disease and Other Dementias. 2008;23(2):162-166.

# Methods to Improve the Detection of Mild Cognitive Impairment

William R. Shankle[*†‡§], A. Kimball Romney[†§¶], Junko Hara[*†§], Dennis Fortier[†§], Malcolm B. Dick–, James M. Chen[†§], Timothy Chan[†§], and Xijiang Sun[†§]

Departments of *Cognitive Science and ¶Anthropology and _Brain Aging Research Unit, University of California, Irvine, CA 92612; and †Medical Care Corporation, Irvine, CA 92612

Contributed by A. Kimball Romney, February 12, 2005

We examined whether the performance of the National Institute of Aging's Consortium to Establish a Registry for Alzheimer's Disease's 10-word list (CWL), part of the consortium's neuropsychological battery, can be improved for detecting Alzheimer's disease and related disorders early. We focused on mild cognitive impairment (MCI) and mild dementia because these stages often go undetected, and their detection is important for treatment. Using standardized diagnostic criteria combined with history, physical examination, and cognitive, laboratory, and neuroimaging studies, we staged 471 community-dwelling subjects for dementia severity by using the Clinical Dementia Rating Scale. We then used correspondence analysis (CA) to derive a weighted score for each subject from their item responses over the three immediate- and one delayed-recall trials of the CWL. These CA-weighted scores were used with logistic regression to predict each subject's probability of impairment, and receiver operating characteristic analysis was used to measure accuracy. For MCI vs. normal, accuracy was 97% [confidence interval (C.I.) 97–98%], sensitivity was 94% (C.I. 93–95%), and specificity was 89% (C.I. 88–91%). For MCI mild dementia vs. normal, accuracy was 98% (C.I. 98–99%), sensitivity was 96% (C.I. 95–97%), and specificity was 91% (C.I. 89–93%). MCI sensitivity was 12% higher (without lowering specificity) than that obtained with the delayed-recall total score (the standard method for CWL interpretation). Optimal positive and negative predictive values were 100% and at least 96.6%. These results show that CA-weighted scores can significantly improve early detection of Alzheimer's disease and related disorders.

Reference:
Shankle WR, Romney AK, Hara J, Fortier D, Dick M, Chen J, Chan T, Sun S. Method to improve the detection of mild cognitive impairment. Proceeding of National Academy of Science. 2005;102(13):4919-4924.

# Development and Validation of the Memory Performance Index: Reducing Measurement Error in Recall Tests

William R. Shankle, Tushar Mangrola, Timothy Chan, Junko Hara

Medical Care Corporation

**Background**: The Memory Performance Index (MPI) quantifies the pattern of recalled and nonrecalled words of the Consortium to Establish a Registry for Alzheimer's Disease Wordlist (CWL) onto a 0 to 100 scale and distinguishes normal from mild cognitive impairment with 96% to 97% accuracy.
**Methods**: In group A, 121,481 independently living individuals, 18 to 106 years old, were assessed with the CWL and classified as cognitively impaired (N 5 5,971) or normal (N 5 115,510). The MPI and CWL immediate free recall (IFR), delayed free recall (DFR), and total free recall (TFR) scores (the outcome measures) were each regressed against predictors of age, gender, race, education, test administration method (in-person or telephone), and wordlist used. Predictor effect sizes (Cohen's f2) were computed for each outcome. In addition, CWL plus Functional Assessment Staging Tests (FAST) were administered to 441 normal to moderately severely demented (FAST stages 1 to 6) patients (group B). Median MPI scores were tested for significant differences across FAST stage.
**Results**: For group A, the variance explained by all predictors combined was MPI 5 55.0%, IFR 5 24.9%, DFR523.4%, and TFR526.9%. The age effect size on MPI score was large, but it was small on IFR, DFR, and TFR. The other predictors all had negligible (<0.02) or small effect sizes (0.02 to 0.15). For group B, median MPI scores progressively declined across all FAST stages (P<.0002).
**Conclusions**: MPI score progressively declines with increasing dementia severity. Also, MPI score explains 2 to 3 times more variance than total scores, which improves ability to detect treatment effects.

Reference:
Shankle WR, Mangrola T, Chan T, Hara J. Development and Validation of the Memory Performance Index: Reducing Measurement Error in Recall Tests. Alzheimer's & Dementia. 2009;5(4):295-306.

# Abnormal Nocturnal Blood Pressure Profile is Associated with Mild Cognitive Impairment in the Elderly: the J-SHIPP Study

Haiyan Guo[1], Yasuharu Tabara[2], Michiya Igase[1], Miyuki Yamamoto[1], Namiko Ochi[1], Tomoko Kido[1], Eri Uetani[1], Keiko Taguchi[1], Tetsuro Miki[1] and Katsuhiko Kohara[1]

1Department of Geriatric Medicine, Ehime University Graduate School of Medicine, Toon City, Ehime, Japan and 2Department of Basic Medical Research and Education, Ehime University Graduate School of Medicine, Toon City, Ehime, Japan

Mild cognitive impairment (MCI), a syndrome characteristic of the transition phase between normal cognitive function and dementia, has been shown to carry the risk of progression to dementia. Dysregulation of blood pressure (BP) is thought to be an indicator of cerebrovascular damage, including cognitive impairment. Here, we investigated the possible association of circadian BP variation with MCI in community-dwelling persons exhibiting no definitive dementia. Our study enrolled 144 persons (68±7 years). Nocturnal BP profile was defined as dipper, with a 10-19% drop in nocturnal systolic BP; extreme dipper, >=20% drop; non-dipper, 0-10% drop; and riser, any increase in nocturnal BP. MCI was assessed using the MCI screen, a cross-validated, staff-administered battery of tests. Subjects with MCI (n=38) were significantly older (74±6, 67±6 years, P<0.001) and had higher frequency of apolipoprotein E e4 allele (36.8, 18.9%, P=0.018). Although the ambulatory measured BP and the percent changes in nocturnal systolic BP (-10±12% and -12±8%, respectively; P=0.291) did not differ between MCI subjects and normal controls, frequency of MCI was significantly higher in the extreme dippers (32.0%), non-dippers (30.0%) and risers (50.0%) than in dippers (13.2%, P=0.018). Multiple logistic regression analysis identified a blunted nocturnal BP decline, non-dipping or increase in nocturnal BP and extreme drop in BP as potent determinants of MCI (odds ratio 3.062, P=0.039), after adjustment for possible confounding factors, including apolipoprotein E e4 genotype. Abnormal nocturnal BP profile was found to be a strong indicator of MCI in otherwise apparently healthy community-dwelling elderly persons.

Reference:
Guo H, Tabara Y, Igase M, Yamamoto M, Ochi N, Kido T, Uetani E, Taguchi K, Miki T, Kohara K. Abnormal nocturnal blood pressure profile is associated with mild cognitive impairment in the elderly: the J-SHIPP study. Hypertension Research. 2010;33(1):32-36. Epub 2009 Oct 23.

# Comparison of the Memory Performance Index with Standard Neuropsychological Measures of Cognition

Michael Rafii, MD, PhD, Curtis Taylor, PhD, Alice Coutinho, BS, Ken Kim, EdD, and Douglas Galasko, MD

Shiley-Marcos Alzheimer's Disease Research Center and the Department of Neurosciences, University of California, San Diego

The Mild Cognitive Impairment Screen (MCIS) is a computer-based cognitive assessment designed for clinical and research use in detecting amnestic mild cognitive impairment (aMCI). Performance on the MCIS is reported as the Memory Performance Index (MPI). However, the comparability between the MPI and traditional neuropsychological tests in detecting aMCI, and in differentiating it from Alzheimer's disease (AD) and normal aging has not been examined. A cross-sectional study was conducted to assess the validity of the MPI relative to standard neuropsychological measures. Participants included 12 individuals diagnosed with aMCI, 49 with mild AD, and 25 healthy elderly. The MCIS significantly discriminated among aMCI, AD, and healthy elderly controls. The MCIS is effective in detecting aMCI, and in discriminating it from cognitive changes observed in AD and normal aging. The MCIS may be a valuable tool in the identification of elderly at high risk for dementia due to its ease-of-use and brief administration time.

Reference:
Rafii M, Taylor C, Coutinho A, Kim K, Galasko D. Comparison of the memory performance index with standard neuropsychological measures of cognition. American Journal of Alzheimer's Disease and Other Dementias. 2011 May;26(3):235-9. Epub 2011 Mar 15.

Review Article

# Assessment of Cognition in Mild Cognitive Impairment: A Comparative Study

Peter J. Snyder[a,b], Colleen E. Jackson[c], Ronald C. Petersen[d], Ara S. Khachaturian[e], Jeffrey Kaye[f], Marilyn S. Albert[g], Sandra Weintraub[h]

[a]Office of the Vice President for Research, Lifespan Hospital System, Providence, RI, USA; [b]Department of Neurology, Alpert Medical School of Brown University, Providence, RI, USA; [c]Department of Psychology, University of Connecticut, Storrs, CT, USA; [d]Alzheimer's Disease Research Center, Mayo Clinic, Rochester, MN, USA; [e]Campaign to Prevent Alzheimer's Disease by 2020 (PAD2020), Rockville, MD, USA; [f]Layton Aging and Alzheimer Center, Oregon Health Sciences University, Portland, OR, USA; [g]Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA; [h]Cognitive Neurology and Alzheimer's Disease Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

The demand for rapidly administered, sensitive, and reliable cognitive assessments that are specifically designed for identifying individuals in the earliest stages of cognitive decline (and to measure subtle change over time) has escalated as the emphasis in Alzheimer's disease clinical research has shifted from clinical diagnosis and treatment toward the goal of developing presymptomatic neuroprotective therapies. To meet these changing clinical requirements, cognitive measures or tailored batteries of tests must be validated and determined to be fit-for-use for the discrimination between cognitively healthy individuals and persons who are experiencing very subtle cognitive changes that likely signal the emergence of early mild cognitive impairment. We sought to collect and review data systematically from a wide variety of (mostly computer-administered) cognitive measures, all of which are currently marketed or distributed with the claims that these instruments are sensitive and reliable for the early identification of disease or, if untested for this purpose, are promising tools based on other variables. The survey responses for 16 measures/batteries are presented in brief in this review; full survey responses and summary tables are archived and publicly available on the Campaign to Prevent Alzheimer's Disease by 2020Web site (http://pad2020.org). A decision tree diagram highlighting critical decision points for selecting measures to meet varying clinical trials requirements has also been provided. Ultimately, the survey questionnaire, framework, and decision guidelines provided in this review should remain as useful aids for the evaluation of any new or updated sets of instruments in the years to come.

Reference:
Snyder PJ, Jackson CE, Petersen RC, Khachaturian AS, Kaye J, Albert MS, Weintraub S. Assessment of cognition in mild cognitive impairment: a comparative study. Alzheimer's & Dementia. 2011;7(3):338–355.